

ISSN 1220-8841 (Print)
ISSN 2344-4959 (Online)

ROMANIAN
NEUROSURGERY

Vol. XXXIV | No. 4 December 2020



Official Journal
"The Romanian Society of Neurosurgery"
- since 1982 -

LONDON ACADEMIC PUBLISHING

ROMANIAN NEUROSURGERY

EDITORIAL AND ADVISORY BOARD

EDITOR-IN-CHIEF

Dr St. M. Iencean, MD, PhD
mirceasteffan@yahoo.com

EXECUTIVE EDITOR

Al. Chiriac, PhD

ASSISTANT EDITORS

B. Costachescu
A. Iordache

ADVISORY BOARD - ROMANIA

Professor D. Adam, Romania
Dr. Fl. Exergian, Romania
Professor St.I. Florian, Romania
Professor R.M. Gorgan, Romania

Professor G.B.I. Iacob, Romania
Dr. Al. Lupsa, Romania
Professor I. Poeata, Romania
Dr. Al. Tascu, Romania
Dr. Marius Dabija (Assist. Prof.), Romania

ADVISORY BOARD - INTERNATIONAL

Professor M.A. Arraez, Spain
Professor V. Astarastoe, Romania
Professor H. Bertalanffy, Germany
Professor J. Brotchi, Belgium
Professor P. Courtheoux, France
Professor J.P. Houtteville, France
Professor Y. Kato, Japan
Professor U. Kehler, Germany
Professor Christopher M. Loftus, USA
Dr. M.R. Mahmud, Nigeria
Professor J.Cl. Marchal, France

Professor P. Mertens, France
Professor B.K. Misra, India
Professor D.F. Muresanu, Romania
Professor L. Pendefunda, Romania
Professor S.C. Robertson, USA
Professor M. Samii, Germany
Professor J. Schramm, Germany
Professor M. Sindou, France
Professor B. Sutter, Austria
Professor F. Umansky, Israel
Professor T.T. Wong, Taiwan

EMERITUS EDITORIAL BOARD

Professor A.V. Ciurea, Romania
Assoc. Prof. Habil. H. Ples, Romania, Former Editor
Professor Al. Constantinovici, Former Editor

FOUNDING EDITOR

Professor Constantin Arseni

ROMANIAN

NEUROSURGERY

Vol. XXXIV | No. 4

December 2020



London
Academic Publishing

Copyright © 2020 Romanian Society of Neurosurgery &
London Academic Publishing

All rights reserved. This book or any portion thereof may not be reproduced or used in any manner whatsoever without the express written permission of the Romanian Society of Neurosurgery or the publisher except for the use of brief quotations in a book review or scholarly journal.

ISSN 1220-8841 (Print)
ISSN 2344-4959 (Online)

First Printing: December 2020
London Academic Publishing Ltd.
27, Old Gloucester Street
WC1N 3AX
London, United Kingdom
Email: contact@lapub.co.uk

london-ap.uk
lapub.co.uk
journals.lapub.co.uk
journals.lapub.co.uk/index.php/roneurosurgery

Company Reg. No. 10941794
Registered in England and Wales

The opinions expressed in the published articles are the sole responsibility of the authors and do not reflect the opinion of the editors or members of the editorial board.

CONTENTS

- 475 Physiological alteration and anaesthetic drugs effects on
intraoperative neurophysiological monitoring procedures
Mihaela Coşman, Andreea Atomei, Nina Straticiu, Alexandru Caragea, Mihai
Soare, Alina Mihaela Neacşu
- 482 Complications after sciatic nerve defect repair in rats
Andrei Marin, Georgiana Gabriela Marin, Carmen Giuglea
- 488 Surgical management of Rolandic area meningioma in the era
of intraoperative neurophysiological monitoring
Mihaela Coşman, Ionuţ Mihail Panţiru, Andrei Ionuţ Cucu, Andreea Lenuţa Atomei,
Gabriela Florenţa Dumitrecu, Ion Poeată
- 495 Endodermal cyst of the cranio-cervical junction. A case report
Bogdanović Ivan, Ilić Rosanda, Miličević Mihajlo, Aleksić Vuk, Milosavljević Filip,
Miljković Aleksandar, Šćepanović Vuk, Stanimirović Aleksandar, Nedeljković
Žarko, Todorović Marko, Joković Miloš, Grujičić Danica
- 498 Dolichoectatic middle cerebral artery masquerading as cerebral
cavernous malformation. A case report and review of literature
Zahraa F. Al-Sharshahi, Saja A. Albanaa, Ahmed M. Jawad, Noor K. Al-Waely, Noor
A. Hummadi, Samer S. Hoz
- 504 The two stages surgery in the management of central
neurocytoma. Case series of 10 patients
W. Bennabi, A. Khelifa, Y. Felissi, L. Houari, A. Morsli
- 509 Multilocular hydrocephalus
Harold Vasquez, Ezequiel Garcia-Ballestas, Luis Rafael Moscote-Salazar, Sergio A
Serrato, William A Florez, Amit Agrawal

- 512 Safety of metoclopramide in traumatic brain injury patients. A systematic review of literature
Said Al Jaadi, Yahya Al Kindi, Tariq Al-Saadi
- 518 Pre-hospital care: demography, current profile and future trends. Improving the health of traumatic brain injury patients
Sateesh Chandra Verma, Abhijeet Singh Sachan, Surjeet Singh, Prakrati Sachan
- 524 Encephalitic syndrome revealing cerebral gliomatosis in an adolescent
Si Ahmed Hakim, Daoudi Smail
- 528 Brain radionecrosis after radiation therapy for atypical meningioma. An unexpected treatment outcome. Case report
Ebtesam Abdulla, Harleen Luther, Tejal Shah, Nisha Chandran
- 533 Traumatic isolated intracerebellar haematoma without any supratentorial lesion. A rare entity. Management strategy
Jain Sachin Kumar, Gupta Tarun Kumar, Jaiswal Gaurav, Lohar Vishnu Kumar, Prateek Patel
- 540 Dorsolumbar angioliipoma. A rare case report and review of literature
Surendra Kumar Gupta, Anuj Chhabra, Hanuman Kumar Prajapati, Faran Ahmad
- 544 Comparative analysis of anterior third ventricle approaches
Deepak Kumar Singh, Kuldeep Yadav, Rakesh Kumar, Arun Kumar Singh, Vipin Kumar Chand
- 550 Spontaneous spinal hematoma. Experiences from a tertiary care centre in South India
Rajeev Mandaka Parambil, Premkumar Sasi, V.M. Pavithran, V.J. Byjo, Akhil Mohan
- 557 Cervical extradural metastasis from follicular carcinoma thyroid after 14 years post-thyroidectomy with Elsberg phenomenon
Vijayan Peettakkandy, Shanavas Cholakkal, Subrat Kumar Soren, Harikrishnan S.

- 561 Surgical options for traumatic fractures of the thoracic and lumbar spine. A series of 20 patients
Elhawary E. Mohamed, Aljboor Ghaith S., Buzantian P. Armand
- 570 Intradural migration of bullet in vertebra corpus after meningitis
Halil İbrahim Gündüz, Turan Kandemir
- 574 Global neurosurgery, Bangladesh and COVID-19 era. A perspective from a low-income country
Robert Ahmed Khan, Moshiur Rahman, Amit Agrawal, Ezequiel Garcia-Ballestas, Luis Rafael Moscote-Salazar
- 577 Giant dorsal sacral meningocele in a child
Amit Agrawal
- 580 Guidelines for authors



Physiological alteration and anaesthetic drugs effects on intraoperative neurophysiological monitoring procedures

Mihaela Coşman¹, Andreea Atomei², Nina Straticiuc³,
Alexandru Caragea¹, Mihai Soare¹,
Alina Mihaela Neacşu^{1,4}

¹ Emergency County Hospital, Braila, ROMANIA

² Student. "Grigore T. Popa" University of Medicine and Pharmacy, Iasi, ROMANIA

³ Department of Anaesthesia and Intensive Care. "N. Oblu" Emergency Clinical Hospital, Iaşi, ROMANIA

⁴ "Carol Davila" University of Medicine and Pharmacy, Bucharest, ROMANIA

ABSTRACT

Intraoperative neurophysiological monitoring (IOM) and especially motor evoked potentials represents an important tool in the evaluation of the nervous system integrity and particularly of the motor tracts. A real and correct registration of the potentials with a proper interpretation of the modification is mandatory for an optimal outcome in eloquent areas, tumours, brainstem and medullary lesions. For all this to happen a suitable anaesthetic protocol must be used. Even though there is a large spectrum of anaesthetic agents at our disposal it is imperative to know their effect on the IOM signals recordings and the fact that some of them are dose-dependent. Drugs effects and physiological changes produced intraoperatively must be corrected before a shift in the direction of the surgical lesion resection it is taken. We present an overview of the action of the anaesthetic agents, most used protocols and the physiological alteration encountered in the operative theatre.

INTRODUCTION

Nowadays tumors located in functional areas of the brain, brainstem and medullary lesions still represents a challenge for many neurosurgeons because of the high risk of postoperatively permanent neurological deficits, but the technological development comes in our aid and the golden standard of maximal resection with minimal neurological disfunction can be reached more often using functional technique perioperatively [12,34,35,41,46].

Considering those date, intraoperative neurophysiological monitoring (IOM) represents a suitable modality for the assessment of the integrity of the nervous system with a real time feedback [32,45,52].

Keywords

intraoperative neurophysiological monitoring, motor evoke potentials, eloquent areas, propofol, volatile agents, intravenous anaesthesia



Corresponding author:
Andreea Atomei

"Grigore T. Popa" University of
Medicine and Pharmacy, Iasi,
Romania

atomei_andreeag6@yahoo.com

Scan to access the online version

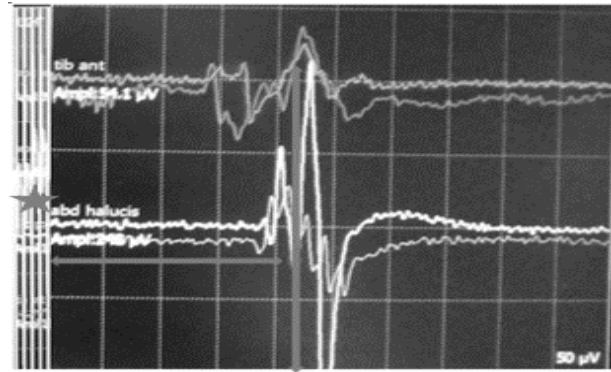
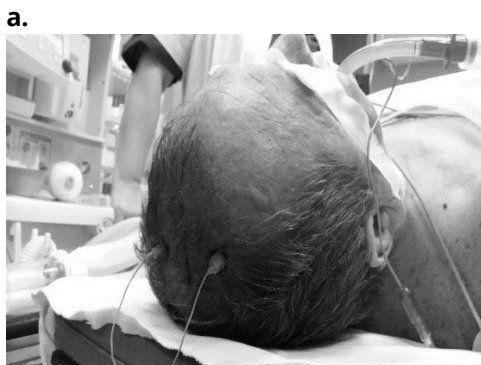


This technique includes various evaluation possibilities e.g., direct cortical / subcortical stimulation and monitoring modalities like motor evoked potentials (MEPs), somatosensory evoked potentials (SSEPs), brainstem auditory evoked potentials (BAEPs), electromyography / free running EMG. For proper recording of the motor / sensitive response special anesthetic drugs are used with differences between the induction step and the stage of maintaining of the sedation [4,9,24]. In order to record the motor response, the drugs used during surgery have a major role in data accuracy [11].

The vast majority of anesthetic drugs decrease the synaptic activity, this effect being dose dependent. They have a direct action on synaptic pathways or indirect effect by altering the influence of inhibitory or excitatory mediators: some anesthetic agents may bind to gamma-aminobutyric acid-a receptors, others may block the excitatory effect of glutamic acid and another group act at the neuromuscular junction level at the " n-type" acetylcholine receptors [43].

Anesthetic agents' effects on intraoperative evoked potentials.

Volatile anesthetic agents (Sevoflurane, Desflurane, Halothane, Nitrous Oxide), dose dependently suppress the MEPs by inhibiting the pyramidal activation of spinal motor neurons, they increase the latency and decrease the amplitude (Figure 1). MEPs are more sensitive to their action in comparison with SEPs [43]. Some studies say that a concentration under 0,5-1 at the alveolar level (MAC) it is safe for IOM recording. Nevertheless, for patients with preoperative neurologic disfunction, motor/sensitive alteration or neuropathy, lower doses may impede or even abolish the potentials [55].



b.

Figure 1. a) cork-screw electrodes placement for transcranial MEPs recordings; **b)** morphology of MEPs from tibialis anterior muscle and abductor hallucis muscle: red star – time of the stimulus application, yellow arrow – latency (unit: seconds), red arrow – amplitude (unit: volts) (images form dr. Coşman M. personal collection).

Between sevoflurane and desflurane the former has a bigger impact on decreasing the amplitude of MEPs. The recordings from the lower limbs seem to be more sensitive to anesthetics than the upper limbs [8]. The action mechanisms of desflurane are on different levels: on pre-postsynaptic receptors, on cellular ionic channels and on serotonin type 3 receptors [33,47] hence its capacity of maintaining proper anesthesia and amnesia at 0,5 MAC [16].

Sevoflurane, halothane, isoflurane are considerate "potent" agents and nitrous oxide is less "potent" being used at higher concentration. The latter is used for IOM in combination with other drugs e.g. nitrous-narcotic technique and the effect depends on the agent already present [43]. His action determines a decrease in amplitude and no effect on cortical potentials latency, without changing the wave morphology [5,42].

Intravenous agents such as Propofol interact with SEPs and MEPs recordings, dose dependent, but in a smaller extent compared with volatile agents [44]. By comparison with the baseline the latency of the evoked potentials is prolonged and the amplitude is decreased after both isoflurane or propofol is administrated, but the former has a bigger inhibitory effect on IOM than the latter [7].

Propofol is been used commonly in TIVA technique (Calanci et al. 2001, Deletis 2002, Langeloo et al. 2003, Chen et al. 2004, MacDonald et al. 2006, Sala et al. 2006, Szeleny et al. 2007, Lieberman et al

2017, Marafona et al.2018, Toossi et al. 2019) [6,7,10,18, 20,24,27,39,49,51] or with inhalant anesthetic agents to decrease their dosage [14,17,25,44]. Although is the preferred drug in IOM procedures, in a study from 2017 it was concluded that hemorrhage may alter the pharmacokinetic properties, the reduction of the cardiac output was associated with increase of the serum concentration which had the capacity to generate false positive results [20].

Etomidate influence only the cortical SEPs (increases the amplitude) and ketamine enhance the response of both potentials, making those agents a good choice for patients with preoperatively functional deficit. Nowadays the former is not used so frequently because of the risk of increasing the intracerebral pressure. Etomidate produces the less depression over potentials amplitude but utilized in continuous infusion may induces adrenocortical suppression [30,42].

Barbiturates (Thiopental) influence significantly the MEPs, but they do not affect the SEPs registration so strongly. Benzodiazepines – Midazolam decreases the potential recordings, especially of MEPs but has an advantage by inducing amnesia [30].

Dexmedetomidine ensure analgesia and sedation acting on α_2 agonist receptors with minimal respiratory depression. In a study from 2015 published by Rozet it is shown that this agent does not have a significant effect on the potential's latency and amplitude [36].

As an adjuvant, when propofol is utilized for IOM anesthesia, dexmedetomidine determine smaller changes on MEPs recordings in comparison with midazolam but alters in a bigger way the hemodynamical parameters [1]. Also in a randomized double blinded study the use of dexmedetomidine before induction (1 $\mu\text{g}/\text{kg}$ over 10 minutes) and at the maintenance stage (0,2 $\mu\text{g}/\text{kg}/\text{hr}$) was associated with a need of lower doses of propofol and stable hemodynamical parameters [48].

From opioids, fentanyl may even improve the myogenic reaction when utilized for IOM by reducing the spontaneous muscular contraction from the background [43]. Another intravenous agent, remifentanil can be used in infusion, being an ultra-short action narcotic, but he has the disadvantage of opioid-induced hyperalgesia [14].

Muscular relaxants have little effect on SEPs recordings but interact with MEPs registration. Partial muscular blockade has the advantage of reducing the patient movements and facilitate the tissue retraction. To determine the degree of blockage we can use two methods: we measure the amplitude produced by supramaximal stimulation of the peripheral motor nerve – T1 (M wave) and compare with the baseline value obtained after the drugs where administrated. Another technique requires to evaluate the motor response after 4 stimuli are delivered at 2 Hz rate [43].

Various anesthetic techniques were used and some combination have been tested with the aim of minimum effect on IOM recordings. It was observed that at the same MAC concentration volatile drugs have a greater suppression effect. However, the best protocol is still controversial [9,54]. However, it is important to know that: the most resistant type of potential at anesthetic drugs are BAEPs, visual evoked potentials are the most sensitive, MEPs can be totally blocked by skeletal muscle relaxants and the recordings of SEPs depends on type of the anesthetic drugs [15]. Sometimes to assess the depth of the anesthesia can be a challenge for the anesthesiologist because the placement of the electrodes may coincide with the skin incision and so the type of the anesthesia must be chosen keeping in mind the site of the operation and the general status of the patient [17].

A summary of medications interactions with neurophysiological monitoring, especially with the MEPs recordings is presented in **Table 1**.

Table 1. Aesthetic drugs influence on Motor Evoked Potentials [15,22,30].

Anesthetic drug	MEP - Latency	MEP- amplitude	Observation
Sevoflurane	Increase	Decrease	Use: MAC – 0,5
Nitrous oxide	Increase	Decrease	Strong effect, should be avoided
Fentanyl	Preserved	Slight depression	Dose dependent
Remifentanyl	Preserved	Decrease	Rapid metabolism – rapid titration
Propofol	Increase	Decrease	Dose dependent;

			Rapid metabolism – rapid titration
Thiopentone	High increase	High decrease	Marked suppression
Etomidate	Decrease	Increase	Enhances the potentials
Ketamine	Increase	Increase	Enhances the potentials
Midazolam	High increase	High decrease	Marked suppression; indicated only in premedication administration
Dexmedetomidine	Increase	Decrease	Use to lower other TIVA agents dose

A combination of those drugs may be used as well with proper sedation and without impairing the IOM measuring's. Gunter presented in 2016 a protocol which includes inhalant agent at a MAC= 0,5 associated with remifentanil and dexmedetomidine. This technique has the advantage of a quick emergency from the general anesthesia due to the latter drug, which produces the sedation effect by acting in locus ceruleus [14].

Another study presented by Isik *et al.* in 2017, where optimal potentials recordings were obtained by using desflurane (0,5 MAC) with remifentanil (0,05-0,3µg/kg/min at 50% O₂) considers this association safe and an alternative for more used TIVA technique [16].

In a randomized survey published by Martin *et al.* in 2014 a comparison has been made between the two classes of drugs: the total intravenous technique (Propofol – Remifentanil) with volatile agents (Desflurane – Remifentanil). The results showed the necessity of a higher voltage to elicit response in volatile agent anesthesia [14,28]. Similar results have been found by Velayutham *et al.* in a study on spinal cord tumors from 2019 where the stimulation applied was 205 ± 55 Volts for propofol anesthesia (6-8mg/kg/hr) and 274 ± 60 Volts for isoflurane [53].

Sloan *et al.* presents in 2015 a combination of inhalant and intravenous anesthesia (0,5 MAC Desflurane with Propofol) with good results regarding electrophysiological monitoring and this technique may be an advantage for patients with opioid tolerance [3,44].

In a retrospective cohort study published in 2020 by Oh *et al.* it was evaluated the postoperatively liver function in patients with preoperative transaminase alteration comparing the group cases operated using total intravenous anesthesia (Propofol) with those operated using inhalator agents (Sevoflurane). The halogenated inhalational drugs are frequently used but they are associated with hepatotoxicity which is less encountered in latest anesthetic agents like sevoflurane or desflurane. The study concluded that the changes in liver enzyme levels were obviously lower for patients from the TIVA group and this type of anesthesia is indicated in neurosurgical intervention especially because of the longer time of the operation [2,31,37].

Other study from 2020 presented by Grau *et al.* discusses de impact of the anesthesia type on tumors recurrence and how the surgical stress can affect the mechanisms of the immune response inducing a vulnerable perioperative period. The idea started from the results obtain in vitro, where anesthetic drugs acted over tumor cells culture. Propofol induced apoptosis in contrast with isoflurane which increased proliferation of glioblastoma stem cells, however the results have not been consistent because of the differences induced by the cell line [29,38]. The conclusion that Grau *et al.* have reached shows no difference between volatile agents and TIVA regarding glioblastoma recurrence (volatiles 8 vs. propofol 8,4 months) or overall survival (volatiles 16,9 vs. propofol 17,4 months) [13].

Another thing to keep in mind when there is a oscillation between TIVA and inhalational anesthesia is the fact that in a study from 2014 published by Tamkus *et al.* volatile drugs were associated with obviously higher false positive responses (15% vs. 3,2%) compared with intravenous agents, when recording transcranial MEPs [50].

Modification in potentials amplitude and the need of a higher voltage to elicit the same result was observed as independent of anesthetic drugs concentration during the intervention, phenomenon named "anesthetic fade". This situation is produced by a long exposure of the nervous system to the drugs action [23]. In contrast with this decrease effect, it was observed and an increase impact called "anesthetic fade-in". This may happen if the baseline measurements of the MEPs were recorded before the surgical procedure started and before the effect

of the myorelaxants drugs used at induction disappeared [19].

Therefore, the mainstay in anesthesia protocols are synthetic opioid (fentanyl, sufentanyl) and propofol which under continuous administration have the capacity to maintain a constant serum concentration. Due to their pharmacokinetic properties the influence on amplitude, latency of MEPs and direct cortical stimulation is negligible [30]. This makes TIVA (Lo et al.2006, Martin et al. 2014, Tamkus et al. 2014, Sloan et al.2015, Malcharek et al. 2015, Velayutham et al. 2019, Oh et al.2020) more suitable for MEPs recording than inhalant anesthesia [21,26,28, 31,44,50,53].

Physiological changes on intraoperative evoked potentials.

Temperature. Cortical SEPs are the most vulnerable to temperature changes. Brain irrigation with cold serum affects the potential recordings [15]. Hyperthermia decrease the latency of MEPs where the hypothermia increases the latency. The effect of temperature on the conduction velocity of both MEPs and SEPs is raised in case of hyperthermy and reduced in case of hypothermia [27,40].

Ventilation. On the one hand the most visible alteration induced by hypoxemia is on SEPs, on the other hand hypocapnia has a smaller effect on SEPs and MEPs [15]. Hypercapnia has inhibitory effect on anterior horn cell and on cortical level, but the registration of the potential is altered only when extreme level of CO₂ is reached [22].

Blood rheology. The blood viscosity and oxygenation depend on hematocrit values. Studies have shown that mild anemia is associated with increase in SEPs amplitude, but no results are cited about MEPs [22,43].

Intracranial pressure. Intracranial hypertension decreases the amplitude of SEPs and prologs the latency. When the uncal herniation occurs the brainstem response is lost and MEP signal can no longer be recorded [22,43].

Blood pressure. Of all the above, hypotension may induce severe potential alteration. At first when the perfusion pressure is raised again the changes

restore to baseline. If the perfusion pressure is decreased under 15 ml/ min/100g tissue there are important changes, severe alteration and even the evoked potentials may be abolished [40]. Usually mild to moderate changes do not affect MEPs values [22]. Sometimes systemic blood pressure values may not predict regional ischemia induced by local factors like: prolong tissue retraction, vasospasm, positioning, head extension which can be discovered by potentials alterations [15,40,43].

CONCLUSION

A good neurological outcome for lesion located in eloquent area or for those with medullary development depends on the correct interpretation of the IOM signals and surgical maneuvers. But all of those are interconnected with proper anesthesia management and a teamwork. So far, a standard anesthetic protocol is missing, but general recommendations have been made. Even though the intravenous agents are more appropriate, the use of volatile anesthetic agents or a combination of them it is up to the anesthesiologist and the particularity of the case.

REFERENCES

1. Aggarwal D, Mahajan HK, Chauhan PR. A comparative evaluation of dexmedetomidine with midazolam as an adjuvant to propofol anesthesia for spinal surgical procedures under motor evoked potential monitoring. *Anaesth Pain & Intensive Care*, 20(2):154-158, 2016.
2. Ahmed Z, Ahmed U, Walayat S, et al. Liver function tests in identifying patients with liver disease. *Clin Exp Gastroenterol*, 11:301-307, 2018.
3. Alkire MT, Hudetz AG, Tononi G. Consciousness and anesthesia. *Science*, 322(5903):876-80, 2008.
4. Biscevic M, Sehic A, Krupic F. Intraoperative neuromonitoring in spine deformity surgery: modalities, advantages, limitations, medicolegal issues – surgeons' views. *EFORT Open Rev*, 5:9-16, 2020.
5. Bithal PK. Anaesthetic considerations for evoked potentials monitoring. *J Neuroanaesthesiol Crit Care*, 1:2-12, 2014.
6. Calancie B, Harris W, Brindle GF, Green BA, Landy HJ. Threshold-level repetitive transcranial electrical stimulation for intraoperative monitoring of central motor conduction. *J Neurosurg*, 95(2 Suppl.):161-8, 2001.
7. Chen Z. The effects of isoflurane and propofol on intraoperative neurophysiological monitoring during spinal surgery. *J Clin Monit Comput*, 18(4):303-8, 2004.

8. Chong CT, Manninen P, Sivanaser V et al. Direct comparison of the effect of desflurane and sevoflurane on intraoperative motor-evoked potentials monitoring. *J Neurosurg Anesthesiol*, 26(4):306-12, 2014.
9. Deiner S. Highlights of anesthetic considerations for intraoperative neuromonitoring. *Semin Cardiothorac Vasc Anesth*, 14(1):51-53, 2010.
10. Deletis V. Intraoperative neurophysiology and methodologies used to monitor the functional integrity of the motor system. In: Deletis V, Shils JL, editors. *Neurophysiology in neurosurgery*. San Diego: Academic Press; 2002. p. 25–51.
11. Gheorghita E, Ciurea J, Balanescu E. Considerations on anesthesia for posterior fossa-surgery. *Romanian Neurosurg XIX* 3:183-192, 2012.
12. Giamouriadis A, Lavrador JP, Bhangoo R et al. How many patients require brain mapping in an adult neuro-oncology service? *Neurosurg Rev*, 43(2):729-738, 2020.
13. Grau SJ, Lohr M, Taurisano V et al. The choice of anaesthesia for glioblastoma surgery does not impact the time to recurrence. *Sci Rep* 10: 5556, 2020.
14. Gunter A, Ruskin KJ. Intraoperative neurophysiologic monitoring: utility and anesthetic implications. *Curr Opin Anesthesiol*, 29:539–543, 2016.
15. Helal SA, Abd Elaziz AA, Dawoud AGE. Anesthetic considerations during intraoperative neurophysiological monitoring in spine surgery. *Menoufia Med J*. 31: 1187-92, 2018.
16. Isik B, Turan G, Abitagaoglu S et al. A comparison of the effects of desflurane and total intravenous anaesthesia on the motor evoked responses in scoliosis surgery. *Int J Res Med Sci*,5(3):1015-1020, 2017.
17. Kawaguchi M, Iida H, Tanaka S et al. A practical guide for anesthetic management during intraoperative motor evoked potential monitoring. *J Anesth*, 34(1):5-28, 2020.
18. Langeloo DD, Lelivelt A, Journée HL, Slappendel R, de Kleuver M. Transcranial electrical motor-evoked potential monitoring during surgery for spinal deformity: a study of 145 patients. *Spine*, 28:1043–50, 2003.
19. Lee JY, Lim BG, Lee IO. Progressive enhancement of motor-evoked potentials during general anesthesia: the phenomenon of "anesthetic fade-in". *J Neurosurg Anesthesiol*, 25(1):87-9, 2013.
20. Lieberman JA, Feiner J, Rollins M, Lyon R. Changes in transcranial motor evoked potentials during hemorrhage are associated with increased serum propofol concentrations. *J Clin Monit Comput*, 32(3):541-548, 2018.
21. Lo YL, Dan YF, Tan YE et al. Intraoperative Motor-evoked Potential Monitoring in scoliosis surgery: comparison of Desflurane/Nitrous Oxide with Propofol Total Intravenous Anesthetic regimens. *J Neurosurg Anesthesiol*, 18:211–214, 2006.
22. Lotto ML, Banoub M, Schubert A. Effects of anesthetic agents and physiologic changes on intraoperative motor evoked potentials. *J Neurosurg Anesthesiol*, 16:32–42, 2004.
23. Lyon R, Feiner J, Lieberman JA. Progressive suppression of motor evoked potentials during general anesthesia: the phenomenon of "anesthetic fade". *J Neurosurg Anesthesiol*, 17(1):13-9, 2005.
24. MacDonald DB. Intraoperative motor evoked potential monitoring: overview and update. *J Clin Monit Comput*, 20:347–77, 2006.
25. MacDonald DB, Skinner S, Shils J, Yingling C. Intraoperative motor evoked potential monitoring – A position statement by the American Society of Neurophysiological Monitoring. *Clin Neurophysiol*, 124(12):2291-316, 2013.
26. Malcharek MJ, Loeffler S, Schiefer D et al. Transcranial motor evoked potentials during anesthesia with desflurane versus propofol – A prospective randomized trial. *Clin Neurophysiol*, 126(9):1825-32, 2015.
27. Marafona AS, Machado HS. Intraoperative evoked potentials: A review of clinical impact and limitations. *J Anesth Clin Res*, 9:2-11, 2018.
28. Martin DP, Bhalla T, Thung A et al. A preliminary study of volatile agents or total intravenous anesthesia for neurophysiological monitoring during posterior spinal fusion in adolescents with idiopathic scoliosis. *Spine*, 39(22):1318-1324, 2014.
29. Meier, A. et al. Isoflurane Impacts Murine Melanoma Growth in a Sex-Specific, Immune-Dependent Manner. *Anesth Analg*. 126(6), 1910–1913, 2018.
30. Nunes RR, Bersot CDA, Garritano JG. Intraoperative neurophysiological monitoring in neuroanesthesia. *Curr Opin Anesthesiol*, 31:532–538, 2018.
31. Oh SK, Lim BG, Kim YS, Kim SS. Comparison of the postoperative liver function between total intravenous anesthesia and inhalation anesthesia in patients with preoperatively elevated liver transaminase levels: A retrospective cohort study. *Ther Clin Risk Manag*, 16:223-232, 2020.
32. Olesnicki BL, D'Souza RJ, Jayram D et al. The establishment of an anaesthetist-managed intraoperative neurophysiological monitoring service and initial outcome data. *Anaesth Intensive Care*, 46(1):74-78, 2018.
33. Pavel MA, Peterson EN, Wang H, Lerner RA, Hansen SB. Studies on the mechanism of general anesthesia. *PNAS*, 24: 13757-13766, 2020.
34. Petrescu G, Gorgan C, Giovani A et al. Preoperative mapping of the eloquent cortical areas using navigated transcranial magnetic stimulation combined with intraoperative neuronavigation for intracerebral lesions. *Romanian Neurosurg XXXIII* 1: 16-14, 2018.
35. Rossi M, Nibali MC, Vigano L et al. Resection of tumors within the primary motor cortex using high-frequency stimulation: oncological and functional efficiency of this versatile approach based on clinical conditions. *J Neurosurg*, 9;1-13, 2019.
36. Rozet I, Metzner J, Brown M, et al. Dexmedetomidine

- does not affect evoked potentials during spine surgery. *Anesth Analg*, 121:492-501, 2015.
37. Safari S, Motavaf M, Seyed Siamdoust SA, Alavian SM. Hepatotoxicity of halogenated inhalational anesthetics. *Iran Red Crescent Med J*, 16(9):20153-20153, 2014.
 38. Saito J, Masters J, Hirota K, Ma D. Anesthesia and brain tumor surgery: Technical considerations based on current research evidence. *Curr Opin Anaesthesiol*, 32(5), 553-562, 2018.
 39. Sala F, Palandri G, Basso E et al. Motor evoked potential monitoring improves outcome after surgery for intramedullary spinal cord tumors: a historical control study. *Neurosurgery*, 58:1129-43, 2006.
 40. Sanders B, Catania S, Luoma AM. Principles of intraoperative neurophysiological monitoring and anaesthetic considerations. *Anesth & intensive care med*, 21(1): 39-44, 2020.
 41. Sandu AM, Furtos MA, Petrescu G et al. Primary intramedullary spinal cord non-Hodgkin lymphoma - case report and review of the literature. *Romanian Neurosurg XXXII* 4: 538-546, 2018.
 42. Sloan TB. Anesthesia management and intraoperative electrophysiological monitoring. In: Kohta A, Sloan TB, Toleikis JR, editors. *Monitoring the nervous system for anesthesiologists and other healthcare professionals*, 2nd ed. Cham: Springer; 2017. pp. 317-341.
 43. Sloan TB, Heyer EJ. Anesthesia for Intraoperative Neurophysiologic Monitoring of the Spinal Cord. *J Clin Neurophysiol*, 19(5):430-43, 2002.
 44. Sloan TB, Toleikis JR, Toleikis SC, Koht A. Intraoperative neurophysiological monitoring during spine surgery with total intravenous anesthesia or balanced anesthesia with 3 % desflurane. *J Clin Monit Comput*, 29(1):77-85, 2015.
 45. Skinner S. The patient-centered care model in IONM: a review and commentary. *J Clin Neurophysiol*, 30:204-209, 2013.
 46. So EL, Alwaki A. A Guide for Cortical Electrical Stimulation Mapping. *J Clin Neurophysiol*, 35(2):98-105, 2018.
 47. Son Y. Molecular mechanisms of general anesthesia. *Korean J Anesthesiol*, 59(1): 3-8, 2010.
 48. Suvadeep S, Chakraborty J, Santra S, Mukherjee P, Das B. The effect of dexmedetomidine infusion on propofol requirement for maintenance of optimum depth of anaesthesia during elective spine surgery. *Indian J Anaesth*, 57:358-63, 2013.
 49. Szelényi A, Kothbauer KF, Deletis V. Transcranial electric stimulation for intraoperative motor evoked potential monitoring: stimulation parameters and electrode montages. *Clin Neurophysiol*, 118:1586-95, 2007.
 50. Tamkus AA, Rice KS, Kim HL. Differential rates of false-positive findings in transcranial electric motor evoked potential monitoring when using inhalational anesthesia versus total intravenous anesthesia during spine surgeries. *Spine J*, 14(8):1440-6, 2014.
 51. Toossi A, Everaert DG, Uwiera RRE et al. Effect of anesthesia on motor responses evoked by spinal neural prostheses during intraoperative procedures. *J Neural Eng*, 16(3):036003, 2009.
 52. Van Der Walt JJN, Thomas JM, Figaji AA. Intraoperative neurophysiological monitoring for the anaesthetist. *South Afr J Anaesth Analg*, 19(3):139-144, 2013.
 53. Velayutham P, Cherian VT, Rajshekhar V, Babu KS. The effects of propofol and isoflurane on intraoperative motor evoked potentials during spinal cord tumour removal surgery - A prospective randomised trial. *Indian J Anaesth*, 63(2): 92-99, 2019.
 54. Wang AC, Than KD, Etame AB, La Marca F, Park P. Impact of anesthesia on transcranial electric motor evoked potential monitoring during spine surgery: a review of the literature. *Neurosurg Focus*, 27(4): E7, 2009.
 55. Wing-hay HY, Chun-kwong EC. Introduction to Intraoperative Neurophysiological Monitoring for Anaesthetists. *ATOTW*, 397, 2019.



Complications after sciatic nerve defect repair in rats

Andrei Marin¹, Georgiana Gabriela Marin², Carmen Giuglea^{1,3}

¹ Plastic Surgery Department, "St. John" Emergency Hospital, Bucharest, ROMANIA

² Cardiology Department, "C.C. Iliescu" Hospital, Bucharest, ROMANIA

³ Carol Davila University of Medicine and Pharmacy, Bucharest, ROMANIA

ABSTRACT

Experimental microsurgery is a provocative field with great rewards. Nerve microsurgery is particularly challenging because the results of the operation can only be tardily observed. During this time frame, multiple complications can appear to the laboratory rats, which can influence the final results.

For this reason, when experimenting with Wistar rats, one must be familiarized with the possible complications in order to know the suitable solutions for all the issues. Lack of information and henceforth lack of action might result in compromising the final data.

INTRODUCTION

On a simple internet search with the phrase "sciatic rat nerve", there are a total of over 3,2 million results. [1] This goes to prove that there is a great interest in experimental surgery on the sciatic nerve conducted on laboratory rats.

The rat, particularly the Wistar rat, represents the most suitable candidate for experimental nerve surgery, as it is affordable, easy to manipulate and has a suitable anatomy for different types of experiments. Furthermore, the faster nerve regeneration period (compared to that of humans) represents a major advantage in working with these laboratory animals.

The anatomy of the sciatic nerve in rats is similar to that in humans: the main nerve divides into 3 branches - common peroneal nerve, tibial nerve and sural nerve. [2] The anesthesia is another positive aspect for choosing Wistar rats - it can be performed by the operator by direct intraperitoneal injection. There are more solutions which can be used, depending on the type and length of the operation. [3]

In all experimental surgery performed on animals, a good collaboration with a veterinary is crucial, as he/she provides important expertise regarding anesthesia, post-operative evolution, solutions to problems; it is also stated in the law that in all animal projects, the

Keywords

sciatic nerve,
rats,
microsurgery



Corresponding author:
Andrei Marin

Plastic Surgery Department, "St. John" Emergency Hospital,
Bucharest, Romania

marin_dpt@yahoo.com

Scan to access the online version



presence of a veterinary in the team is compulsory. Furthermore, all types of animal experimentation require approvals from the Ethics Committee and the Sanitary Veterinary Department. [4]

MATERIAL AND METHOD.

The complications presented in the article were mostly observed and handled during an experimental project for a PhD thesis, where 4 methods of defect nerve reconstruction were compared:

- nerve graft,
- nerve conduit made from a rat aorta (simple aortic conduit),
- platelet-rich plasma (PRP) inside an aortic conduit,
- stem cells inside the aortic conduit.

Each batch consisted of 10 lab rats and 2 extra lab rats were sacrificed to obtain PRP and aortic conduits.

The anesthesia used was a mixture of xylazine 10mg/kg and ketamine 75mg/kg. After injecting the anesthesia and preparing the operation site (shaving the dorsal gluteal-thigh region), the Wistar rat was placed in prone position and the incision was performed along the femur, 0,5cm inferior to it. A breach was created through the biceps femuri muscle and the sciatic nerve was exposed for a length of 4 cm to be able to observe the emerging branches. 2 separate incisions at a distance of 0,5cm were performed on the sciatic nerve, proximal to the emergence of its branches and the resulting defect was repaired using one of the above-mentioned methods. After nerve reconstruction, the muscle was close using absorbable suture and the skin was close using non-absorbable sutures.

Postoperatory, the rats were placed 2 in a cage, between the 2 existing a separating transparent plastic support. This was to prevent cannibalism between the rats.

The post-operative treatment consisted of enroxil 0,003mg/kg and meloxicam 1mg/kg both injected subcutaneously for 3 days. The wounds were treated locally with betadine solution alternating with baneocin powder.

The rats were monitored for 3 months and afterwards they were euthanized using an overdose of the anesthetic mixture and KCl injected intracardiac.[5] During this period, some rats experienced several complications which were treated accordingly.

RESULTS

Out of the 40 rats included initially in the study, 2 rats were excluded due to major complications which could influence the final results – one due to postoperative death, the other one due to sciatic nerve rupture.

The one death recorded was due to an anesthetic overdose – because the rat would not sleep under anesthesia, multiple doses were administered. This resulted in a profound anesthesia once the drugs took effect, and a prolonged anesthesia time (even after the surgery was over). The rat died the day after the operation.

The first postoperative complication observed was wound dehiscence. This occurred in all batches 1-5 days after surgery due to chewing on the surgical knots. Some dehiscence were partial, others were total. 2 different measures were taken, unfortunately without the desired effect.

The first solution was to redo the suture under local anesthesia with the help of an assistant who would firmly restrain the rat not to bite during the procedure. This proved ineffective and dangerous as the rat would bite through the second knots as well.

The second solution was to try to perform a dressing so that the operated rat could no longer reach the wound. This also proved ineffective, as the rat could easily slip out of the dressing and attempt to nibble on the knots.



Special designed plastic cages with a plastic support to create 2 separate compartments





Sutured wound with different types of dressings

The wounds were treated with different antiseptic solutions and they closed per secundam in maximum one week.

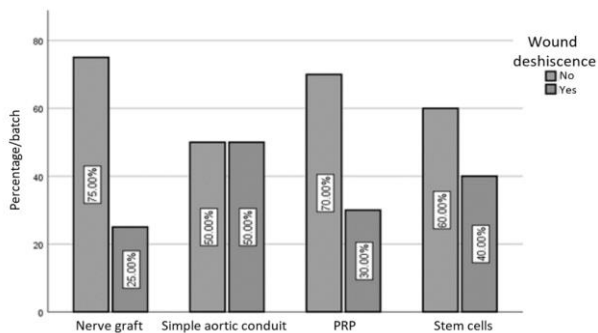
A statistical analysis performed to see which batch presented more wound dehiscence

revealed that there was a higher prevalence in the second batch (simple aortic conduit), followed by the stem cells batch. However, this analysis didn't have statistical power ($X^2 = 1.479$ (3); $p=0.687$).

Presence/absence of dehiscence wound in the 4 batches

Batch		Dehiscence		Total rats / batch
		No	Yes	
Nerve graft	No.	6	2	8
	Pct.	75%	25%	100%
Simple aortic conduit	No.	5	5	10
	Pct.	50%	50%	100%
PRP	No.	7	3	10
	Pct.	70%	30%	100%
Stem cells	No.	6	4	10
	Pct.	60%	40%	100%
Total per wound	No.	24	14	38
	Pct.	63.2%	36.8%	100%

Graphic of the wound dehiscence distribution in the 4 batches



Another complication encountered was that of self-mutilation of the affected limb. Luckily, the mutilation was limited at the fingernails and like the wound dehiscence it was self-limiting.



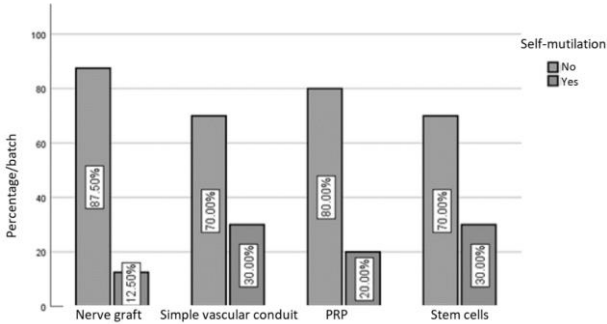
Limb autophagy after sciatic nerve transection – erythema and swelling of the foot and mutilated fingernails (footprint covered with ink due to footprint test).

Presence/absence of self-mutilation in the 4 batches

Batch		Self-mutilation		Total rats/batch
		No	Yes	
Nerve graft	No.	7	1	8
	Pct.	87.5%	12.5%	100%
Simple aortic conduit	No.	7	3	10
	Pct.	70%	30%	100%
PRP	No.	8	2	10
	Pct.	80%	20%	100%
Stem cells	No.	7	3	10
	Pct.	70%	30%	100%
Total self-mutilations	No.	29	9	38
	Pct.	76.3%	23.7%	100%

Similar to the wound dehiscence percentage, the self-mutilation of the denervated limb was predominant in the prevalence in the second batch (simple aortic conduit) and the stem cells batch, without statistical difference.

Graphic of self-mutilation distribution in the 4 batches



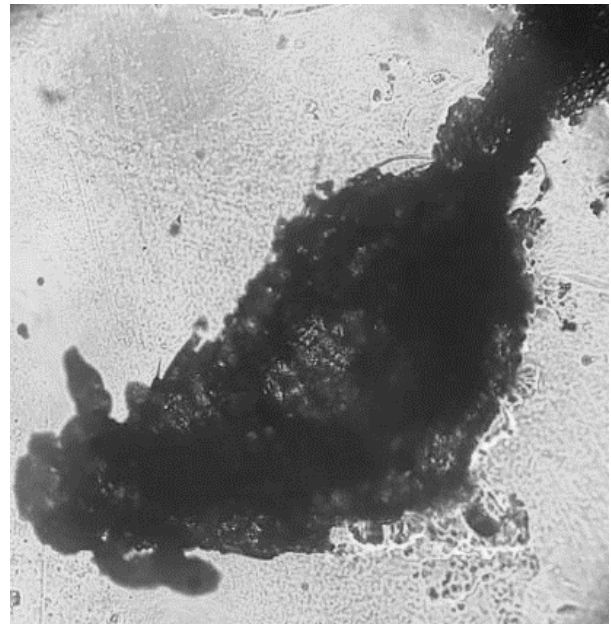
One month after the beginning of the project, all rats presented severe pruritus. As differential diagnoses, allergic dermatitis and parasitologic contamination were taken into consideration. Due to scratching, some rats presented crusts and erosions, especially around the neck and back.

Weight loss occurred to all rats experiencing these symptoms. Due to severe scratching, there was an important hair loss in the area with the pruritus. Until the diagnosis was established, the wounds were treated locally with methylene blue, to prevent infection.



Scratching lesions with hair loss and methylene blue application.

After a dermatologic consult, tape was applied on the skin and the sample was then examined under the microscope. The diagnosis of pediculosis with *Polyplax* spp. was put and all rats underwent treatment with Stronghold 15mg (Selamectin). This treatment was repeated after 2 weeks. Thorough mechanic sanitation of all cages was performed, as well as of the rooms where the cages laid. Furthermore, the rooms were sterilized for 24 hours using a UV lamp.



Microscopic aspect of the parasite *Polyplax* spp.

After the first application of Selamectin, there was a complete relief of the pruritus and a significant improvement of the scratching lesions. All rats recovered both locally (regaining the lost hair) as well as in terms of general state (in the following weeks there was a progressive weight gain).



3rd week after Selamectin treatment

DISCUSSIONS

Proper anesthesia is the key to a successful surgery with optimal results. While it would help to sedate the animals using inhaling substances such as isoflurane before injecting them, direct intraperitoneal injection with ketamine, xylazine or acepromazine (or a mixture of these solutions) can be performed even without sedation but with proper contention. [6,7,8]

Correct calculation of the proper dose is crucial for the outcome. If a rat doesn't fall asleep in 5 minutes after the normal dose is administered, this doesn't mean it has drug resistance, but rather that it takes the anesthetic a longer time to come into effect. Therefore, if a rat doesn't respond in the 5-minute time frame, it should be left aside and another rat should be prepared for surgery. Otherwise, administering a new dose of anesthetic might result in a prolonged anesthesia or even death.

After the rat is under anesthesia, another important aspect is the handling or moving of the rat. Taking into consideration the muscle relation induced by the anesthesia, the rat is susceptible to aspiration if it is grabbed by the tail, with the head down. If this occurs, one should try freeing the airways using a small cannula attached to a vacuum. The typical symptoms a rat experiences in such cases are hiccup-like movement, with desaturation; if no prompt intervention is performed, this will also lead to its death. The best way to prevent this is to manipulate the rat by grabbing it by the back of its neck, heads up. Although Britto et al believe that total fasting or only-solids deprivation does not induce gastric emptying in mice, a preoperative total fasting for 6-8 hours could reduce this risk. [9]

Cannibalism immediately after surgery is another issue to be considered. The rats need to be separated a few days after the operation until the wound is closed. Afterwards, they can be placed together and it would also be recommend not keeping them separated as they have a tendency to self-mutilate by chewing on the operated, senseless leg when left alone.

One difficult complication to treat is self-mutilation – either limb mutilation (in case of peripheral nerve injuries) or wound dehiscence caused by biting the threads which hold the wound tight. Hindlimb autotomy/autophagy represents the mutilation of the anesthetic foot by the animal which

doesn't feel the limb and therefore doesn't recognize it as part of its body. Wall et al described degrees of hindlimb autotomy differentiating on the type of nerve injury (cut nerve and encapsulated in polythene tube, sectioning with immediate repair, nerve ligation and nerve crush). [10]

Prevention of self-mutilation until nerve regeneration occurs is therefore a necessity. Plastic head collars could be useful for dogs or other large animals but are not appropriate for the rat, as it can easily get out of this restraint due to its neck anatomy. Repelling solutions (such as quinine) applied on the limb or on the wound could prove effective because of its bitter taste. Al-Adawi et al also proved the efficiency of 6-hydroxydopamine injected in the ascending noradrenergic bundle 1 week prior to transection or N-(2-) Chloroethyl-N-ethyl-2-bromobenzylamine (DSP4) injection 24 h prior to transection. [11] Picric acid is another solution that showed better results in reducing limb autophagy compared to the commercial bite-deterrent chemical (denatonium benzoate). [12]

Another possible complication which fortunately did not occur in this project is infection. Although rodents are quite resistant to infection, it would be recommended that postoperative antibiotic be given and sterile conditions during the operation be used.

Graft versus host disease is another possible complication when using foreign allogeneic tissue. Although no such reaction was noted during the project, even without the use of immunosuppressant medication, this could become a serious problem when transplanting tissues which determine a strong antigenic reaction.

Even though the project was conducted in a restricted environment in a building located in the veterinary university campus especially dedicated to this experiment, rat contamination occurred. There were 2 possible explanations. One would be the human factor – the people who come in contact with these animals to feed and clean after the rats. The second explanation, although unlikely, could be the 2 windows located at 2,5m altitude in the rooms where the experiments took place. A fast diagnosis and rapid intervention were the key in saving the animals and the project in this case.

CONCLUSIONS

Animal experimentation requires not only feeding and cleaning, but also attending to the possible

complications generated by human intervention. When it comes to nerve surgery, the most frequent complications are self-mutilation (either wound dehiscence or autotomy of a limb that is no longer sensitive innervated).

This study shows that the rats that presented wound dehiscence were predominantly in the simple aortic conduct batch; the same batch manifested self-mutilation of the denervated inferior limb.

The laboratory animals present all possible complications of the surgical intervention, as well as health complications specific to the animals. However, some solutions which may apply to human patients may not be a proper solution for animals.

REFERENCES

1. https://www.google.com/search?q=sciatic+nerve+rat&rlz=1C1GCEA_enRO877RO877&oq=sciatic+nerve+&aqs=chrome.69l57j35i39j0l6.4694j0j7&sourceid=chrome&ie=UTF-8.
2. Marin Andrei, Mihai Ruxandra Ioana, Marin Georgiana Gabriela. Pitfalls and problems encountered in rat model sciatic nerve surgery. *Romanian Neurosurgery* (2019) XXXIII (4): pp. 396399DOI: 10.33962/roneuro-2019-064.
3. Costea Ruxandra, Daniel Lastofka, and Mihai Mehedințu. "Comparison of Ketamine–Medetomidine–butorphanol and Ketamine – dexmedetomidine - butorphanol Anesthesia in Rats." *Agriculture and Agricultural Science Procedia* 6 (2015): 305-308.
4. Marin A., Marin G., Patea A. and Enescu D. (2019). Timing, logistics and bureaucratic process in planning an experimental in vivo nerve project from A to Z. *Modern Medicine* | 2019, Vol. 26, No. 2.
5. Montford JR, Linas S. How Dangerous Is Hyperkalemia? *Am Soc Nephrol.* 2017;28(11):3155–3165. doi:10.1681/ASN.2016121344.
6. Greenfield EA. Administering Anesthesia to Mice, Rats, and Hamsters. *Cold Spring Harb Protoc.* 2019;2019(6):10.1101/pdb.prot100198. Published 2019 Jun 3. doi:10.1101/pdb.prot100198.
7. He S, Atkinson C, Qiao F, Chen X, Tomlinson S. Ketamine-xylazine-acepromazine compared with isoflurane for anesthesia during liver transplantation in rodents. *J Am Assoc Lab Anim Sci.* 2010;49(1):45-51.
8. Lascar I., Zamfirescu D. *Microchirurgie experimentală*, 2000, 34-37.
9. Brito MV, Yasojima EY, Teixeira RK, Houat Ade P, Yamaki VN, Costa FL. Fasting does not induce gastric emptying in rats. *Acta Cir Bras.* 2015;30(3):165-169. doi:10.1590/S0102-865020150030000001.
10. Wall PD, Devor M, Inbal R, et al. Autotomy following peripheral nerve lesions: experimental anaesthesia dolorosa. *Pain.* 1979;7(2):103-111. doi:10.1016/0304-3959(79)90002-2.
11. Al-Adawi S, Dawe GS, Bonner A, Stephenson JD, Zarei M. Central noradrenergic blockade prevents autotomy in rat: implication for pharmacological prevention of postdenervation pain syndrome. *Brain Res Bull.* 2002; 57(5):581-586. doi:10.1016/s0361-9230(01)00747-x.
12. Firouzi MS, Firouzi M, Nabian MH, et al. The effects of picric acid (2,4,6-trinitrophenol) and a bite-deterrent chemical (denatonium benzoate) on autotomy in rats after peripheral nerve lesion. *Lab Anim (NY).* 2015;44(4):141-145. doi:10.1038/labam.711.



Surgical management of Rolandic area meningioma in the era of intraoperative neurophysiological monitoring

Mihaela Coşman¹, Ionuț Mihail Panțiru²,
Andrei Ionuț Cucu², Andreea Lenuța Atomei³,
Gabriela Florența Dumitrecu⁴, Ion Poeată⁵

¹ Department of Neurosurgery. Emergency County Hospital, Braila, ROMANIA

² Department of Neurosurgery. "N. Oblu" Emergency Clinical Hospital, Iași, ROMANIA

³ 6th-year student. Gr. T. Popa University of Medicine and Pharmacy, Iași, ROMANIA

⁴ Department of Anatomopathology. "N. Oblu" Emergency Clinical Hospital, Iași, ROMANIA

⁵ Department of Neurosurgery. Gr. T. Popa University of Medicine and Pharmacy, Iași, ROMANIA

ABSTRACT

Introduction. The advantages and the necessity of intraoperative neurophysiological monitoring (IOM) in the surgery of motor area infiltrative tumours is well known. The use of this technique for Rolandic meningioma is still debatable. The absence or the loss of the cleavage plan and an infiltrative border make the dissection exceedingly difficult and increase the risk of new postoperative motor dysfunction.

Materials and methods. We evaluated the impact of IOM, especially direct cortical stimulation on the degree of resection, new postoperative deficits, symptom remission and clinical-imagistic aspects at one-year follow up of 19 cases of Rolandic meningioma admitted in Third Department of Neurosurgery, "Prof. Dr N. Oblu" Emergency Clinical Hospital, Yassi, Romania, between January 2014 and July 2018.

Results. More than half of the cases (57,88%) had epileptic manifestations as the main clinical symptom with the Jacksonian seizures being on the first place (31,57%), followed by progressive paresis (26,31%) and other nonspecific symptoms. Intraparenchymal preoperative oedema was observed in 36,84% of patients. The intensity of direct cortical stimulation was between 6-13 mA (median = 9mA; mode = 12mA). Simpson degree of resection was dominated by S3- 47,36% and S4 was obtained in 15,78% of cases. Postoperative the outcome was favourable for 73,68% patients with 5,26% motor aggravation and 10,52% new deficits. At one-year follow up no imagistic recurrence was observed and the permanent motor deficit was maintained in one of the three cases (5,26%).

Conclusion. Even though meningiomas are extranevaxial lesions and those located on the convexity have a low risk of complication, the absence of a clear dissection plan between the tumour and the adjacent motor cortex is associated with a high risk for new postoperative neurological deficits. Therefore, it is important to perform

Keywords

Rolandic area,
intraoperative
neurophysiological
monitoring,
meningioma,
tumour resection,
motor cortex,
cortical mapping



Corresponding author:
Ionuț Mihail Panțiru

"N. Oblu" Emergency Clinical
Hospital, Iași, Romania

ionut.mihail26@yahoo.com

Scan to access the online version



cortical mapping for Rolandic meningioma, to determine the location of the primary motor area and to protect it from mechanical and vascular trauma, during tumour resection.

INTRODUCTION

Resection of lesion located in eloquent areas e.g., primary motor area is associated with an increased risk of postoperatively neurologic deficits. For a good outcome it is mandatory, for us, to know the location of this area and to protect it from mechanical and vascular intraoperative injuries. The landmarks offered by the preoperative radiological images are of great help, but not sufficient [10,35]. The continuous development of medical technology comes in our aid to perform maximal resection with minimal motor dysfunction, knowing the impact on overall survival and on the progression free survival [8,29,32].

On this line, intraoperative neurophysiological monitoring (IOM) which includes mapping procedures (direct / subcortical stimulation) and monitoring technique (evoked potentials) offers a real time feedback and helps to establish the location of the functional area from the operative field. If the use of IOM is clear for infiltrative lesions like gliomas, the necessity of it in cases of meningiomas remains questionable [2,21,31].

One functional area in which this lesion may appear is the central gyrus region. The definition of Rolandic meningioma is represented by the direct anatomical contact, observed on T2 Weighted magnetic resonance imaging (T2W-MRI) of the tumour with the precentral and postcentral gyrus [25]. The presence of the cleavage plan around the eloquent brain help protect it during resection. When this landmark is lost or its not present mechanical trauma and vascular alterations over the cortex may generate new motor deficits. An intraoperative evaluation of the surrounding brain with the enhancement of the primary motor area is important, with the purpose of maximal resection with minimal neurological dysfunction. This goal is desirable especially when the most common symptoms of presentation are the epileptic seizures and the nature of the lesion is with good prognosis [6,21,31].

We proposed in this article to present the impact of using IOM in meningioma surgery located in central gyrus region regarding the clinical and radiological postoperative evolution first day after

surgery and at one year follow up period along with a review of the literature.

MATERIALS AND METHODS

The study group included patients with meningioma located in central region, diagnosed using contrast enhancement head MRI imaging, admitted in the 3rd neurosurgery department of 'Prof. Dr N. Oblu' Clinical Emergency Hospital Iasi, between 1 January 2015 and 1 July 2018, who underwent surgical resection. *Inclusion criteria in the study group:* meningioma located in central gyrus region, imagistic diagnosed and histologically confirmed; age over 18 years; intraoperative use of IOM; consent to be included in the study. *Exclusion criteria from the study group:* other histological tumour subtypes localized in central region; cases to which conservative management was performed; patients with pacemaker; patients who failed to come for their one-year follow-up examination and incomplete cases data.

This technique was performed using the Nim Eclipse device from Medtronic. Direct cortical / subcortical stimulation was achieved by means of the short-train technique or train of five. The parameters used were: 3Hz, interstimulus interval = 4mseconds, length = 500µseconds. The intensity was included in the interval 6 – 13mA. The recording electrodes were placed in abductor pollicis brevis muscle (m.), biceps brachii m., orbicularis orris and oculi m., tibialis anterior m. and abductor hallucis m, depending on tumour precise location.

RESULTS

76 patients with various histological tumour types were initially enrolled in the study group, but 6 of them were excluded because they did not come to the one-year follow-up examination after surgery and 4 were excluded because they had a pacemaker and we could not perform IOM. In the end, the group included 19 cases of meningioma with Rolandic location. The age distribution interval was between 25 – 73 years with a female dominance – 52,63% of all the cases. Most frequent symptom was Jacksonian seizure (31,57%), followed by motor deficit – progressive brachial/ crural paresis (26,31%), partial seizures (15,73%) and nonspecific manifestation like headache, intracranial hypertension and grand mall seizure (each 10,52%).

From the anatomical point of view 47,36% (9 cases) were located on the convexity, 47,36% were parasagittal and 5,26% (one case) had the insertion of the falx cerebri. 5,26% of the patients underwent preoperative embolization. Intraparenchymal oedema was observed in T2 / FLAIR MRI sequences in a proportion of 36,84% (7 cases). An illustrative is presented in Figure 1.

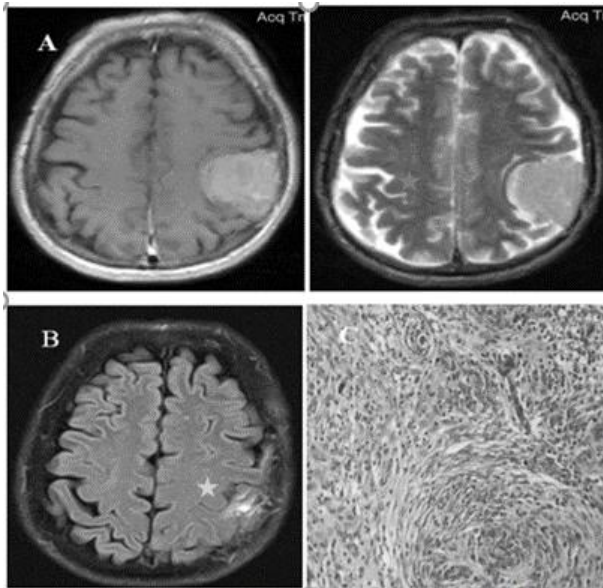


Figure 1. Clinical case: female, 48 years, Jacksonian seizures, no motor deficit, Rolandic lesion. **(A)** preoperative MRI (T1WI with enhancement and T2WI), yellow star = contralateral primary motor area (omega sign), no clear demarcation of the ipsilateral motor area, no perilesional oedema. **(B)** one-year postoperative follow-up MRI (T2 dark-fluid), pink star=reshaping of the motor area with normal morphology. **(C)** Meningioma grade II (WHO classification): densely cellularized lesion with meningothelial cells arranged in wide cords. (Hemalaun-Eozina staining, X20).

According to World Health Organisation (WHO) the histological result was classified as WHO grade I: 84,21% and WHO grade II: 15,78%. Simpson degree of resection was: S1 – 2 patients (10,52%), S2 – 5 patients (26,31%), S3– 9 cases (47,36%) and S4 – 3 cases (15,78%). The intensity of direct cortical stimulation was between 6-13 mA, with the following statistical parameters: median = 9mA and the mode = 12mA. Postoperative the outcome was favourable with symptoms resolution for 73,68% cases, stationary for 10,52% cases and with functional alteration for 15,78% cases (2 patients presented new neurologic deficit and one aggravated the initial motor dysfunction).

One-year evaluation reveal favourable outcome in 89,47% and stationary in 10,52%. From the three cases with postoperative motor dysfunction, in 5,26% of them persisted the deficit. No recurrence was observed on the control MRI and no tumour growth on the 15,78% of Simpson IV cases.

DISCUSSIONS

Meningioma represent the most common benign primary brain tumour with an increasing incidence, being more frequent in elderly and in women [1,11,16]. Usually between the brain and the lesion there is a cleavage plan which allows a safe resection. When this plan is lost or it does not exist, vascular impairment and mechanical trauma of the brain tissue may be a consequence of tumour ablation. This is very important when the perilesional tissue is represented by functional areas, e.g., central gyrus region, hence the higher postoperatively motor deficit and an increased rate of complication for Rolandic meningioma compared with other convexity meningioma [3,9,18,23].

Perioperatively imaging techniques characterizes the relationship between the tumour and the eloquent cortex. Standard MRI, functional MRI, 3D tractography and neuronavigation system are important tools regarding the resection of lesions located in eloquent cortex, planning the approach and guiding further tumour ablation [20,22,27,30].

In some meningioma cases, the landmarks may not correspond intraoperatively because of the displacement of the normal anatomy induced by the tumour growth. In others the cleavage plan may be lost near the central gyrus region and the arachnoid may be invaded [5]. To avoid such situation where the dissection is difficult to realise without harming the surrounding cortex intraoperative neurophysiological monitoring is being used for a real time functional feedback. In a study from 2019 published by Raffa et al., it is evaluated even the advantage of combining the navigated transcranial magnetic stimulation with IOM for detection of the presence or the absence of the arachnoid cleavage plan and the functional tissue. The correspondence with the IOM results was in a percentage of 94,2% [28]. With all those tools available, in the literature there is still a controversy about the techniques association and intraoperative necessity of neurophysiological monitoring for all meningioma [25,26,31].

From the anatomical point of view Rolandic meningioma compresses convexity meningioma, falx, falx-sinus lesions of middle one third of the sagittal sinus in contact with precentral and postcentral gyrus and sinus. Beside the surrounding functional areas, the vascular representation is of the same importance e.g., Rolandic draining vein [6]. Because these lesions have a tendency of being smaller, the difficulty of the intervention can be underestimated and so may be associated with higher complication [25].

Motor area meningioma need special anaesthesia protocols when IOM is used, the aim being to avoid the medication that interacts with muscle relaxation. Synthetic opioids such as Fentanyl and sedative-hypnotic agents (Propofol) are preferred when cortical stimulation or evoked potentials are recorded, since those drugs can maintain a constant serum concentration with insignificant effect over motor response registration [14,15,24].

Usually, one of the most common presentation symptoms is represented by epileptic seizure (47,6% - Ostry et al.,2012; 38,46% - Bi et al., 2013; 42% - Deng et al.,2014) [4,6,25]. In our study this manifestation occurred in 57,88% of patients, with a dominance of Jacksonian seizures (31,57%). Especially for these patients with no motor deficit preoperatively it is important to determine the relation between the meningioma and the surrounding brain tissue.

The dominance of this clinical presentation is explained by the tumour mechanism of action. Being an extranevaxial lesion, it compresses the brain tissue inducing hemodynamical changes at the level of myelin, oxygenation and intracellular water. This is important because there is not a real loss of neurons and explains the remission of the symptoms after resection. Even the patients with preoperative motor deficits may improve the muscle strength postoperatively [17]. Though the meningioma is completely resected in some patients the outcome after the operation is stationary. The persistence of the seizures after the surgery is explained, in some cases by the cerebral changes induced by a slow-growing tumour with the appearance of epileptogenic foci e.g., hippocampal scleroses and cortical dysgenesis, beside local microenvironment abnormal discharges. In these cases, it seems that only the removal of the central gyrus region tumour is not enough [7,33]. In a study

published by Deng et al., in 2014 from all 26 patients presented with epilepsy, after tumour resection 88, 46% were seizures free at mean follow up of 16 months under antiepileptic drug medication and one patient had seizures recurrence in less than 6 months postoperatively [6]. In our study, after symptoms remission the patient did not report any new seizure at the one-year follow up or recurrence.

When there is pial adhesions, brain invasion or irregular borders intracapsular resection is recommended to preserve the functional cortex which is usually identified by direct cortical stimulation (e.g., monopolar anodic stimulation – Ostry et al.,2012) [25]. In our study we performed brain mapping before starting to remove the meningioma to identify the primary motor area. Usually, this area was modified being pushed by the tumour growth and surrounded the lesion. The intensity interval was between 6 – 13 mA, the most frequent threshold value which generated motor response was 13 mA. The cortical stimulation was repeated every time when the junction brain-tumour was reached, to assure that further dissection does not affect the eloquent cortex. Intermittent minimal traction was applied.

The surgical aim is symptom remission and if it is the case to leave the smallest cortical layer of tumour to prevent neurological alteration, even though this means subtotal resection – Simpson IV [12,19]. On the one hand this approach is preferable because of the slow growth pattern of the lesion and because gross resection is associated with increased morbidity for the infiltrative borders type, on the other hand some studies found that Simpson resection grade is a predictor factor for recurrence. In this condition the intraoperative decision is tailored depending on the particularities of the case [13,36].

In our study Simpson IV was obtained at 15,74% of patients, all of them were located parasagittal with no cleavage plan and with positive stimulation response surrounding the tumour. Other characteristic of those three cases was the fact that it was observed an important venous component involvement, with the Rolandic vein being encased in tumour capsule and the superior sagittal sinus being partially obstructed. In other publication various results of subtotal resection were presented from 26,2% (Ostry et al., 2012) to 1,1% (Ottenhouse et al., 2018) [25,26]. Ostry et al., mentioned that in some

patients the remanent tumour was not even detected on the postoperative MRI, the estimated volume being of 0,1cm³ and the Simpson IV grade of the case was based on surgeons' report. Usually, the residual layer was less than 0,5cm³ [25]. Even though Simpson grad IV was present in our result one the first place from the point of view of resection was Simpson grade II (47,36%) matching with the literature results.

It is important to keep in mind that clinical presentation with preoperative muscular strength dysfunction may alter the stimulation response, decreasing the technique accuracy. From our patients 26,31% presented progressive paresis and the intensity used to generate motor response was the highest from the study group. An aggressive traction and dissection, when the cleavage plan is lost, is associated postoperatively with a higher risk for motor deficit [17,34]. Ostry *et al.*, in a study from 2012 observed that the difference of the threshold value between the direct cortical stimulation and the value obtained after stimulating through the mass lesion was ≤ 2 mA has an impact over outcome. In this situation he stopped the resection even though it was intracapsular, to prevent new motor deficits. When the motor evoked potentials are used, the need for an increased threshold to generate response is a warning signal [25].

How is to be expected, the motor preservation is the main goal in surgical resection of Rolandic meningioma. Starting from this idea some authors studied the prognostic factors for the risk of motor impairment (aggravation of the symptoms or new ones). Ottenhausen *et al.*, found that a high rate of neurological deficit was associated with parafalcine insertion, large tumoral mass and perilesional oedema. Another negative prognostic factor was found to be the necessity for preoperative embolization and the involvement of the Rolandic drainage vein [26]. From our group of patients in one case it was necessary to perform an endovascular procedure, tumour's location being on the falx cerebri to facilitate the resection.

Progressive paresis as an admitting symptom beside disturbing the IOM is considered to be a negative prognostic factor for the motor outcome (47,2 % vs 22,2%, $p = 0,017$, Ottenhausen *et al.*, 2018) [26]. In our group of patients in one case we had aggravation of the pre-existent deficit and new deficit was observed in 10,52% of the cases. The image

control showed central gyrus region oedema and no haemorrhage.

Other values from the literature regarding the new motor deficit range from 7,69% (Lee *et al.*, 2016) to 34,61% (Bi *et al.*, 2013) [4,17]. The latter reference presents the results from 26 parasagittal central region meningioma microsurgical resected. No Simpson grade IV was found, only grade I (30,8%), grade II (46,2%) and grade III (23,1%) but as mentioned the aggravation was observed in one third of the cases. Therefor complete tumor removal was associate with a higher negative outcome. Another important fact is that the authors do not report the use of cortical stimulation or evoked potential generation [4].

The main postoperative outcome of our patients was favourable with symptom remission in 73,68%. Almost the same percentage was obtained and by Lee *et al.*, in 2016 – 76,92%. The first place for clinical evolution is maintained and with 60,3% (Ottenhausen *et al.*, 2018), 65,39% (Bi *et al.*, 2013) and the high clinical amelioration was 81% (Ostry *et al.*, 2012) [4,17,25,26].

An important remark it that at one year follow up period just one patient of the three with postoperatively aggravated or new deficit maintained the motor disfunction. Practically the permanent neurologic deficit for our group was 5,26%. Overall, the neurological outcome was favourable in 89,47% of the cases, no imagistic recurrence was observed on the control MRI but further follow up must be done.

CONCLUSIONS

Rolandic meningiomas, even though are extranevraxial lesions represents a challenge from the surgical point of view. A careful dissection is mandatory, the venous drainage must be preserved and the surrounding functional tissue must be protected from mechanical trauma. When the cleavage plan is lost precentral and postcentral cortex may be affected and secondary after the resection new motor deficits may appear. To prevent unwanted cortical damage intraoperative neurophysiological monitoring is used and if necessary, a thin layer of meningioma is left over the cortex.

DISCLOSURES

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

REFERENCES

- Achey RL, Gittleman H, Schroer J et al. Non-malignant and malignant meningioma incidence and survival in the elderly from 2005-2015 using the Central Brain Tumor Registry of the United States. *Neuro Oncol*, 21(3):380-391, 2019.
- Bander DE, Shelkov E, Modik O et al. Use of the train-of-five bipolar technique to provide reliable, spatially accurate motor cortex identification in asleep patients. *Neurosurg Focus*, 48: 1-6, 2020.
- Berg-Johnes J, Hogestol EA. Supplementary motor area syndrome after surgery for parasagittal meningiomas. *Acta Neurochir (Wien)*, 160(3):583-587, 2018.
- Bi N, XU RX, Liu RY et al. Microsurgical treatment for parasagittal meningioma in the central gyrus region. *Oncol Lett* 6: 781-784, 2013.
- Cimino PJ. Malignant progression to anaplastic meningioma: Neuropathology, molecular pathology, and experimental models. *Exp Mol Pathol*, 99(2):354-9, 2015.
- Deng WS, Zhou XY, Li ZJ et al. Microsurgical treatment for central gyrus region meningioma with epilepsy as primary symptom. *J Craniofac surg*, 25: 1773-1775, 2014.
- Dhiman V, Rao S, Sinha S et al. Outcome of lesionectomy in medically refractory epilepsy due to non-mesial temporal sclerosis (non-MTS) lesions. *Clin Neurol Neurosurg*, 115(12):2445-53, 2013.
- Duffau H. Diffuse low-grade glioma, oncological outcome and quality of life: a surgical perspective. *Curr Opin Oncol*, 30:383-389, 2018.
- Elzarief AA, Ibrahim MF. Long-term follow-up of motor function deterioration following microsurgical resection of middle third parasagittal and falx meningioma. *Egypt J Neurol Psychiatr Neurosurg*, 54(1):9, 2018.
- Giamouriadis A, Lavrador JP, Bhango R et al. How many patients require brain mapping in an adult neuro-oncology service? *Neurosurg Rev*, 43:729-738, 2020.
- Holleczeck B, Zampella D, Urschart S et al. Incidence, mortality and outcome of meningiomas: A population-based study from Germany. *Cancer Epidemiol*, 62:101562, 2019.
- Hou W, Ma Y, Xing H, Yin Y. Imaging characteristics and surgical treatment of invasive meningioma. *Oncol Letters*, 13: 2965-2970, 2017.
- Hwang WL, Marciscano AE, Niemierko A et al. Imaging and extent of surgical resection predict risk of meningioma recurrence better than WHO histopathological grade. *Neuro Oncol*, 0:1-10, 2015.
- Isik B, Turan G, Abitagaoglu S et al. A comparison of the effects of desflurane and total intravenous anaesthesia on the motor evoked responses in scoliosis surgery. *Int J Res Med Sci*,5(3):1015-1020, 2017.
- Kawaguchi M, Iida H, Tanaka S et al. A practical guide for anesthetic management during intraoperative motor evoked potential monitoring. *J Anesth*, 34(1):5-28, 2020.
- Ko CC, Chen TY, Lim SW et al. Prediction of Recurrence in Parasagittal and Parafalcine Meningiomas: Added Value of Diffusion-Weighted Magnetic Resonance Imaging. *World Neurosurg*, 124: e470-e479, 2019.
- Lee SJ, Hwang SC, Im SB, Kim BT. Surgical resection of non-glial tumors in the motor cortex. *Brain Tumor Res Treat*, 4 (2):70-76, 2016.
- Lemee JM, Corniola MV, Broi MD et al. Early Postoperative Complications in Meningioma: Predictive Factors and Impact on Outcome. *World Neurosurg*, 128: e851-e858, 2019.
- Lin Q, Ling F, Xu G. Invasive benign meningioma: Clinical characteristics, surgical strategies and outcomes from a single neurosurgical institute. *Exp Ther Med*, 11(6):2537-2540, 2016.
- Low D, Lee CK, Dip LLT et al. Augmented reality neurosurgical planning and navigation for surgical excision of parasagittal, falcine and convexity meningiomas. *Br J Neurosurg*, 24(1):69-74, 2010.
- Magill ST, Han SJ, Li J et al. Resection of primary motor cortex tumors: feasibility and surgical outcomes. *J Neurosurg*, 129:961-972, 2018.
- Morin O, Chen WC, Nassiri F et al. Integrated models incorporating radiologic and radiomic features predict meningioma grade, local failure, and overall survival. *Neurooncol Adv*, 1(1):011, 2019.
- Nanda A, Bir SC, Konar S, Maiti TK, Bollam P, World Health Organization Grade I Convexity Meningiomas: Study on Outcomes, Complications and Recurrence Rates, *World Neurosurg*, 89:620-627.e2, 2016.
- Nunes RR, Bersot CDA, Garritano JG. Intraoperative neurophysiological monitoring in neuroanesthesia. *Curr Opin Anesthesiol*, 31:532-538, 2018.
- Ostry S, Netuka D, Beneš V. Rolandic area meningioma resection controlled and guided by intraoperative cortical mapping. *Acta Neurochir (Wien)*, 154:843-53, 2013.
- Ottenhausen M, Rumalla K, Younus I et al. Predictors of postoperative motor function in rolandic meningiomas. *J Neurosurg*, 1:1-6, 2018.
- Panesar SS, Abhinav K, Yeh FC et al. Tractography for surgical neuro-oncology planning: towards a gold standard. *Neurotherapeutics*, 16: 36-51, 2019.
- Raffa G, Picht T, Scibilia A et al. Surgical treatment of meningiomas located in the rolandic area: the role of navigated transcranial magnetic stimulation for preoperative planning, surgical strategy, and prediction of arachnoidal cleavage and motor outcome. *J Neurosurg*, 14;1-12, 2019.
- Ritaccio AL, Brunner P, Schalk G. Electrical stimulation mapping of the brain: basic principles and emerging alternatives. *J Clin Neurophysiol*, 35: 86-97, 2018.
- Romero-Garcia R, Erez Y, Oliver G et al. Practical

- application of networks in neurosurgery: combined 3D printing, neuronavigation, and pre-operative surgical planning. *World Neurosurg*, 137:1-22, 2020.
31. Rossi M, Nibali MC, Vigano L et al. Resection of tumors within the primary motor cortex using high-frequency stimulation: oncological and functional efficiency of this versatile approach based on clinical conditions. *J Neurosurg*, 9:1-13, 2019.
 32. Sala F. Penfield's stimulation for direct cortical motor mapping: An outdated technique? *Clin Neurophysiol*, 129:2635-2637, 2018.
 33. Spencer S, Huh L. outcome of epilepsy surgery in adults and children. *Lancet Neurol* 7: 525-37, 2008.
 34. Tang H, Xu F, Lin L et al. Intra-operative motor function preservation for resection of primary motor cortex meningioma. *Transl Cancer Res*, 7(6):1666-1674, 2018.
 35. Thon N, Tonn JC, Kreth FW. The surgical perspective in precision treatment of diffuse gliomas. *Onco Targets Ther*, 12: 1497-1508, 2019.
 36. Winther WL, Torp SH. The significance of the extent of resection in modern neurosurgical practice of WHO grade I meningiomas. *World Neurosurg*, 99:104-110, 2017.



Endodermal cyst of the cranio-cervical junction. A case report

Bogdanović Ivan¹, Ilić Rosanda¹, Milićević Mihajlo¹,
Aleksić Vuk^{1,2}, Milosavljević Filip¹, Miljković Aleksandar¹,
Šćepanović Vuk¹, Stanimirović Aleksandar¹,
Nedeljković Žarko¹, Todorović Marko¹,
Joković Miloš¹, Grujičić Danica¹

¹ Neurosurgery Clinic, Clinical Centre of Serbia, Medical School,
University of Belgrade, SERBIA

² Department of Neurosurgery, Clinical Hospital Centre Zemun,
Belgrade, SERBIA

ABSTRACT

We report an extremely rare case of an endodermal cyst of the cranio-cervical junction located dorsally to the brainstem and upper cervical spine in a 27-year-old female presented with occipital headache, vertigo and pain in both shoulders. Neurological examination showed neck stiffness with bilateral XIth nerve palsy. Magnetic resonance imaging revealed a cystic lesion at the cranio-cervical junction and slight compression of the brain stem. The lesion was totally removed through the posterior approach. The histological diagnosis was endodermal cyst. To our knowledge, the only one such case has been reported in the literature.

INTRODUCTION

Endodermal cysts can be found in literature by a variety of different names including neurenteric, epithelial, bronchogenic, enterogenous, respiratory and foregut cysts. These cysts are a benign congenital condition resulting from the persistence of an abnormal communication between endoderm and neuroectoderm at 3 weeks life of the embryo. This malformation is encircled by a mucosal secreting epithelioma mimicking the normal gastrointestinal epithelioma tractus (1). Exact histopathological diagnosis may be hard to establish, since there are many similarities with other cystic lesions such as Rathke cysts, colloidal cysts, and/or cystic teratomas (9). Intracranial locations are rare, and location of such cysts in the cranio-cervical junction is exceptional. They are located in the midline, in ventral or ventrolateral locations. Endodermal cysts may occur at any age, but there is a slight predominance of male patients in their forties. Since they are slow growing tumours, many patients have only mild symptoms relative to the tumour size. The main symptoms are due to compression and mass

Keywords

endodermal cyst,
cranio-cervical junction



Corresponding author:
Vuk Aleksić

Department of Neurosurgery,
Clinical Hospital Centre Zemun,
Belgrade, Serbia

aleksicvuk@hotmail.com

Scan to access the online version



effect. However, cases of recurrent aseptic meningitis can be found in literature (2).

Neurenteric cysts are treated surgically. With only partial resection, endodermal cysts may recur at the original site on long-term follow-up (3-6). The incomplete resection may be associated with postoperative malignant transformation or widespread cranial-spinal dissemination. Almost all authors advocate the aggressive resection to reduce the possibility of endodermal cyst recurrence (7, 8).

CASE REPORT

We present a case of a 27-year-old woman admitted with a history of recurrent episodes of occipital headache, vertigo and pain in region of both shoulders of six months duration prior to admission. She had no difficulty with swallowing or speech, and the strength of all extremities, gait, and coordination were normal. The neurological examination presented only moderate neck stiffness with bilateral XIth nerve palsy. There was neither sensibility deficit nor extra neurologic signs.

Magnetic resonance imaging (MRI) of the cranio-cervical junction revealed a well-defined, round, intradural cystic lesion located dorsally to the spinal cord and the medulla, extending from the foramen magnum to the upper level of C1 lamina, with neither bony nor soft tissue associated abnormalities. T2-weighted images displayed a hypointense signal, and T1-weighted MRI demonstrated a hyperintense mass without enhancement. The lower medulla and C1 spinal cord were found to be slightly compressed in the posterior aspect in the sagittal image. This intradural extraaxial process was measuring 20,7 x 12,7 x 8,3 mm (Figure 1). Preoperative CT scan showed a high density area at the cranio-vertebral junction, well delimited, dorsal to the medulla and upper cervical spine. In our case the cyst appeared spontaneously hyperdense.

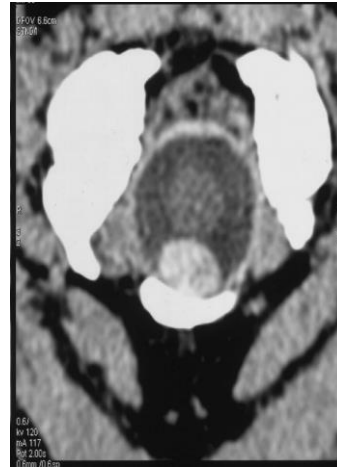


Figure 1. Cranio-cervical junction MRI showing intradural cystic lesion located dorsally to the spinal cord and the medulla.

The patient was operated in a prone position through a posterior approach and midline incision. Surgery consisted in a reduced sub-occipital craniotomy

associated to partial C1 laminectomy. After opening of the dura a thin-walled yellowish cyst was noted below atlanto-occipital membrane, in the region of cerebellomedullaris cistern. It was floating in liquor, attached with bulbo-medullary junction only with thin arachnoidal connection. The lesion had not adhered to any other surrounding structures. Surgical excision was complete in one piece.

On pathohistological examination, the cyst membrane was underlined by unistratified cylindrical enteroid cells with basal nucleus and apical muco-secreting pole, with supra-nuclear accumulation of alcain-blue positive mucine. The diagnosis was endodermal cyst.

Postoperatively, the patient showed no neurological deficits. In the next few months' clinical signs resolved completely. Postoperative CT (Figure 2) and MRI revealed no evidence of a residual cyst.

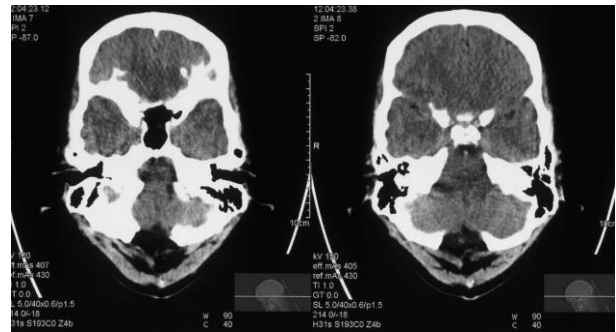


Figure 2. Postoperative CT scan showing complete resection of cyst.

DISCUSSION

Endodermal cysts are congenital abnormalities belonging to notochordodysraphies which are result of an abnormal adherence between ectoderm and

endoderm. A failure during embryogenic development is probably responsible for cyst formation (1,9,10,11). The pathogenesis of this lesion is not clarified. However, the most convincing hypothesis is a dysgenesis of the endoderm from the neuroectoderm in the 3rd week of foetal development (12). Usually, these lesions occur at the lower cervical and upper thoracic region, and their ventral origin is suggested by defects in the vertebral bodies. The lesions may be either intradural or extradural (13). The present case is unusual because cyst is found in the cranio-cervical junction and exceptionally unusual because of dorsal location, representing the only one such case reported in the literature (14, 15, 16). They show slow growing rate, remaining asymptomatic for a long time, but without surgical removal they can produce a brain stem and spinal cord compression syndrome followed-up by a neurological impairment. In this case, according to our opinion, surgery was justified in order to achieve total removal of the cyst and to prevent recurrence, malignant transformation or subarachnoid dissemination.

REFERENCES

- Harris CP, Dias MS, Brockmeyer DL, et al: Neurenteric cysts of the posterior fossa: recognition, management, and embryogenesis. *Neurosurg* 1991, 29(6): 893-897;
- Goel A, Muzumdar D, Chagla A. Endodermal cyst anterior and anterolateral to the brainstem: a report of an experience with seven cases. *Br J Neurosurg* 2005;19(2):163-6.
- Chavda SV, Davies AM, Cassar-Pullicino VN Enterogenous cysts of the central nervous system: a report of eight cases. *Clin Radiol*. 1985; 36(3):245-51.
- Fuse T, Yamada K, Kamiya K, Inagaki H (1998) Neurenteric cyst at the craniovertebral junction: report of two cases. *Surg Neurol*. 1988; 50: 431-436.
- de Oliveira RS, Cinalli G, Roujeau T, Sainte-Rose C, Pierre-Kahn A, Zerah M J Review Neurenteric cysts in children: 16 consecutive cases and review of the literature. *Neurosurg*. 2005;103(6 Suppl):512-23.
- Abe K, Oyama K, Mori K, Ishimaru S, Eguchi M, Maeda M *Neurol Med Chir (Tokyo)*. Review Neurenteric cyst of the craniocervical junction--case report. 1999; 39(12):875-80.
- Gessi M, Legnani FG, Maderna E, Casali C, Solero CL, Pollo B, DiMeco Mucinous low-grade adenocarcinoma arising in an intracranial enterogenous cyst: case report. *F Neurosurgery*. 2008; 62(4):E972-3;
- Perry A, Scheithauer BW, Zaias BW; Aggressive enterogenous cyst with extensive craniospinal spread: case report. *Minassian HV Neurosurgery*. 1999; 44(2):401-4; discussion 404-5.
- Filho FL, Tatagiba M, Carvalho GA, Weichhold W, Klekamp J, Samii M. Neurenteric cyst of the craniocervical junction. Report of three cases. *J Neurosurg*. 2001 Jan;94(1 Suppl):129-32.
- Houssine Ghannane, M Laghmari, K Aniba, M Lmejjati, S Ait Benali . Craniocervical intradural neurenteric cyst: Case report. *Pan Arab journal of neurosurgery*. 2011; 15(1)(p64-67)
- Yunoki M, Hirashita K, Gohda Y, et al: True intraspinal neurenteric cyst in the lumbosacral region - Case report. *Neurol Med Chir (Tokyo)* 2007, 47(5): 237-239.
- Malcolm G, Symon L, Kendall B, Pires M: Intracranial neurenteric cysts. Report of two cases. *J Neurosurg* 1991;75(1): 115-120.
- Pierot L, Dormont D, Oueslati S, et al: Gadolinium-DTPA enhanced MR imaging of intradural neurenteric cyst. *J Comput Assist Tomogr* 1998;12(5):762-764.
- S. Ohba, T. Akiyama, R. Kanai, S. Onozuka, T. Kawase. Endodermal cyst of the cranio-cervical junction. *Acta Neurochirurgica*. 2008;150:257-263
- Zahos PA, Goodman LA, Onesti ST, Michelsen WJ. Dorsal endodermal cyst of the upper cervical spine. *J Spinal Disord*. 1996;9(6):536-9.
- King NK, Joshi SM, Marino S, Yeh JS, Ellamushi H. Dorsally located endodermal cyst: case report and review. *Br J Neurosurg*. 2009;23(3):318-20.



Dolichoectatic middle cerebral artery masquerading as cerebral cavernous malformation. A case report and review of literature

Zahraa F. Al-Sharshahi¹, Saja A. Albanaa², Ahmed M. Jawad³, Noor K. Al-Waely⁴, Noor A. Hummadi⁵, Samer S. Hoz¹

¹ Department of Neurosurgery, Neurosurgery Teaching Hospital, Baghdad, IRAQ

² Medical student, College of Medicine, Baghdad University, Baghdad, IRAQ

³ Medical student, Royal College of Surgeons in Ireland, Dublin, IRELAND

⁴ FIBMS-Diagnostic Radiology. Al-Nahrain University. College of Medicine, Department of Surgery, IRAQ

⁵ C.A.B.H.S-Diagnostic Radiology. Al-Imamain Al-Kadhmain Medical City, IRAQ

ABSTRACT

Background. Intracranial dolichoectasia (IADE) is a rare vascular disease characterized by distension, elongation and tortuosity of an artery. IADE rarely involves paediatric aged groups. It is either asymptomatic or manifests as ischemic or haemorrhagic attacks.

Case description. A healthy, 30-year-old, female teacher presented with recurrent attacks of bi-frontal headaches associated with dizziness and dropping attacks of two-week duration. She was referred by her general physician to our institution of Neurosurgery Teaching Hospital in Baghdad, Iraq with a suspicion of medial temporal lesion on a cranial computed tomography (CT) scan. Magnetic resonance imaging study excluded the diagnosis suggesting a dolichoectatic middle cerebral artery that was confirmed by CT-angiography.

Conclusion. Dolichoectasia of the middle cerebral artery is a rare and benign lesion. However, it can masquerade as cerebral cavernous malformation or intracranial arterial aneurysm. Thus, careful radiological evaluation with the suggested diagnostic criteria are of paramount importance to prevent its misdiagnosis.

BACKGROUND

Intracranial arterial dolichoectasia (IADE) is sporadic angiopathy characterized by dilatation, elongation and tortuosity of an intracranial artery. IADE is approximately 0.1-6.5% prevalent in the general popula-

Keywords

dolichoectasia,
middle cerebral artery,
anterior circulation,
arteriopathy,
tortuous artery



Corresponding author:
Saja A. Albanaa

College of Medicine, Baghdad
University, Baghdad, Iraq

sajaalbanaa@gmail.com

Scan to access the online version



tion and 12 % in stroke patients [1]. IADE preferentially involves the basilar artery and posterior circulation; anterior circulation IADE constitutes only one third of all cases [2]. IADE is usually an incidental finding but symptoms may arise due to ischemia, hemorrhage or cranial nerve compression [3]. Although uncommon, hydrocephalus was also reported as a manifestation of IADE due to the obstruction of cerebrospinal fluid flow through the foramen of Monro or the cerebral aqueduct [4]. IADE may co-exist with several vascular pathologies such as abdominal aortic aneurysms, intracranial aneurysms and coronary artery disease [5]. A diagnostic criterion for dolichoectatic basilar artery was suggested by smoker et al, but no criteria for dolichoectasia in other intracranial arteries have been validated thus far [6].

Herein, we present a case of middle cerebral artery dolichoectasia, initially diagnosed as cerebral cavernous malformation along with proposed diagnostic criteria based on reviewing the available literature.

CASE SCENARIO

A healthy, 30-year-old, female teacher presented with recurrent attacks of pulsatile bifrontal headache of two-week duration. Each attack lasts for more than one-hour and significantly impacted her daily activities. The headache is associated with profound dizziness and “dropping attacks”; assumed to be seizures by her general physician. The patient’s EEG and video EEG were both normal. She was referred to the neurosurgery outpatient clinic at our institution with a suspicious medial temporal lesion on a cranial CT scan. On examination, the patient was pale but fully oriented with no remarkable neurologic deficits. Her brain CT scan showed a small rounded heterogeneous lesion with calcification at the medial temporal area; there was no evidence of peri-lesional edema. Initially, the diagnosis of uncal cavernous malformation was pondered. (Fig.1). In order to confirm this diagnosis, brain MRI with T2-gradient echo and MRA studies were ordered. The T2-weighted MRI study revealed lesional flow-void, the T2-gradient echo was negative and the MRA showed an abnormal vascular loop of the MCA within the lesion. These findings excluded the diagnosis of cavernous malformation and strongly suggested MCA aneurysm or dolichoectasia (Fig.2). Next, a computed tomography angiography (CTA) of

the brain was obtained. The CTA revealed that the proximal part of the MCA was dilated, elongated, tortuous and formed a superior blind loop; findings that were consistent with the diagnosis of MCA dolichoectasia (Fig.3). Moreover, catheter cerebral angiography can be used to confirm the diagnosis in such situation but it is not feasible in our facility nor in many neurosurgical institutions around the world. Thereafter, patient was reassured that she had a “benign variation in the brain circulation rather than a critical pathology and that no intervention was indicated at the time”. Laboratory investigations normal except for iron deficiency anemia. The patient was discharged and a follow-up was scheduled with her physician. At 6-month follow-up, patient was generally well, had already resumed her normal daily activities and received treatment for anemia. The headache was both minimal and occasional at this stage. Both CTA and MRI revealed no new significant findings.

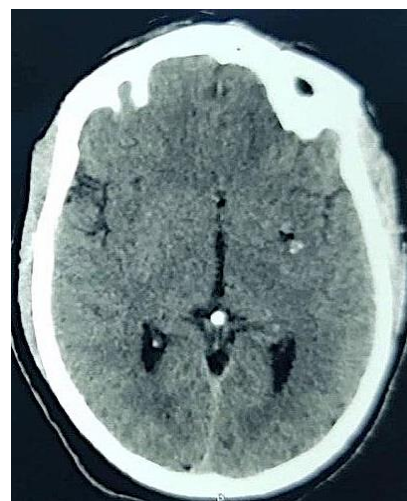


Figure 1. Cranial CT scan showing a heterogeneous, deep left-sided, temporal lesion of mixed density with no perilesional edema. Here, the initial diagnosis was cerebral cavernous malformation.

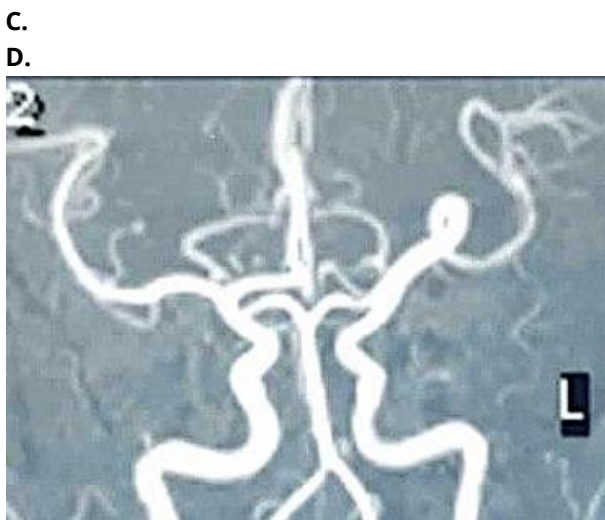
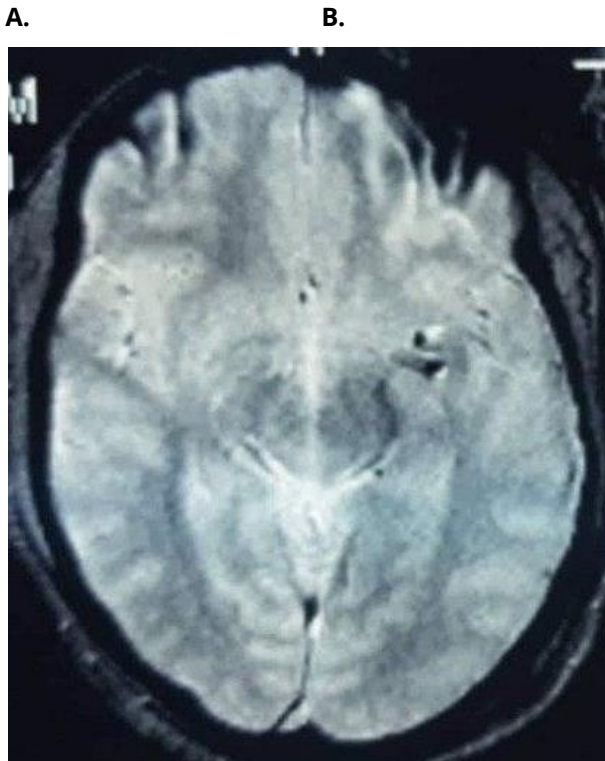
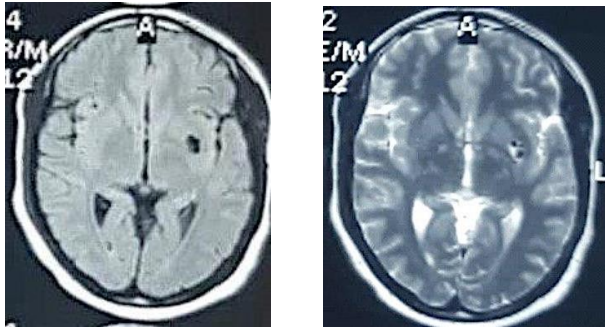


Figure 2. Brain MRI showed deep left temporal lesion. **A:** FLAIR axial section: The lesion is hypointense with no perilesional edema. **B:** T2 axial section: The lesion contains signal voids that denoted the presence of vessels within the lesion. **C:** T2-

Gradient Echo axial view showing the absence of blood clots. **D:** MRA showing an enlarged and tortuous left MCA (sphenoidal segment) as compared with the right MCA with a superiorly projecting loop or a possible aneurysm.

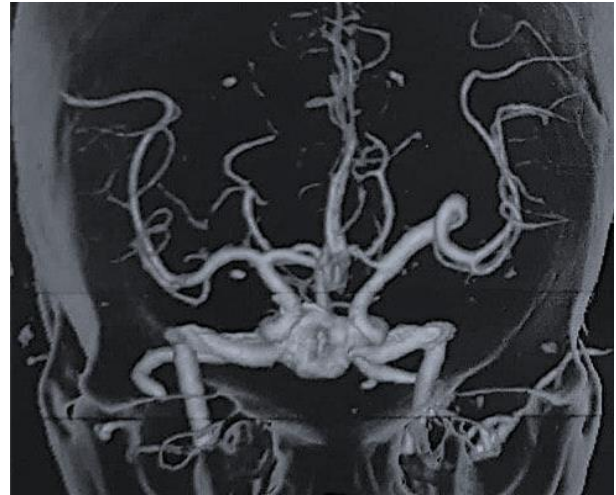


Figure 3. Brain CT angiography 3D reconstructed image showing an enlarged and tortuous left MCA (sphenoidal segment) as compared with the right MCA with a superiorly projecting loop, confirming the diagnosis of left MCA Dolichoectasia and excluding the presence of an aneurysm.

DISCUSSION

the vertebrobasilar system is the most common site of IADE followed by internal carotid artery. IADE is a disease of all ages although its presentation in the pediatric age group is rare. It affects females more than males [2]. IAED may be asymptomatic or masked by an array of inconclusive manifestations such as headaches, strokes, seizures and focal deficits [4]. In this report, a 30-year-old female presented with recurrent bouts of headache and dizziness. A brain CT-scan revealed a calcified lesion, leading to a provisional diagnosis of an uncus cavernous malformation. Further imaging studies including MRA and T2-gradient ECHO- provided a better visualization of the vasculature and the brain parenchyma narrowing the differential diagnosis to an aneurysm or a dolichoectasia. Finally, CTA images showed dilated, distended and tortuous vessels and excluded the differential of an aneurysm.

IADE is commonly mistaken with other vascular pathologies, such as dural fistulas or Arteriovenous malformations [7]. Therefore, multiple imaging modalities are often required to reach the definitive diagnosis of dolichoectasia especially if it is located distally in the anterior circulation. Nakahara et al

reported a case of MCA dolichoectasia, initially diagnosed as a terminal-ICA, saccular aneurysm using antero-posterior and lateral CTA views. However, the reverse waters view suggested the correct diagnosis of a dolichoectatic MCA rather than an ICA aneurysm; this study highlights the importance of multiple CTA views in the diagnosis of IADE [8]. Several efforts attempted to establish a solid platform for diagnosing anterior circulation dolichoectasia depending on a multi-modal diagnostic approach. Some authors have recommended the co-utilization of additional radiological techniques such as digital subtraction angiography to capture the real-time flow properties of the aberrant vessel [9,10]. Dolichoectatic MCA is a benign lesion in general. However, treatment is usually indicated when there is a co-existing pathology. Surgical manipulation of the enlarged vessel may lead to complications such as hemorrhage or ischemia [10]. In this study, we

treated the patient conservatively using simple analgesics which enabled her to resume her normal activities. Our approach is comparable to the one described in the literature of MCA dolichoectasia (Table 1). However, the initial false interpretation of medial temporal cavernous malformation, then MCA aneurysm rendered this case report to be of a critical value regarding differential diagnosis of MCA dolichoectasia [8,10]. Based on the aforementioned literature analysis, we suggest 3 features that can be considered as alarming criteria for the diagnosis of MCA dolichoectasia, these include: atypical clinical presentation, enlarged parent vessel and unusual location of the lesion.

We recommend a multi-modal diagnostic approach to determine the most appropriate management along with long-term clinical and radiological follow-up for monitoring of a less likely but possible lesion enlargement.

Table 1: Literature review of dolichoectatic middle cerebral artery

Author	Sex	Age, year	Presentation	Radiologic findings	Treatments
Brinjkji et al [11]	F	19	Asymptomatic, found incidentally	MCA dolichoectasia with superimposed multilobulated aneurysm, mild preceding stenosis	Conservative
Feliciano et al [12]	M	42	Headache associated with left-sided weakness and intermittent nausea and vomiting	MCA dolichoectasia and a cluster of aneurysms with right basal ganglia hemorrhage	Conservative
Abe et al [13]	M	32	Asymptomatic, found incidentally after a motor-vehicle accident	MCA dolichoectasia	—
Nakahara et al [8]	F	59	Left hyposmia and mild intermittent occipitalgia	MCA dolichoectasia	No surgery, no medication
Kanemoto et al [14]	F	41	Seizures and anxiety	MCA dolichoectasia with cavernous hemangioma	Cavernous hemangioma resection

Tokunaga et al [15]	F	58	Right hemiplegia, homonymous hemianopia, hypertension	Left putamen hematoma and bilateral MCA dolichoectasia	—
Puca et al [16]	F	32	Ischemic stroke at the age of 7 y	Old ischemic lesion and MCA dolichoectasia	No surgery, no medication
Maruya et al [17]	F	40	Subarachnoid hemorrhage	A saccular aneurysm on a dolichoectatic MCA	Surgical clipping of the aneurysm
Guo et al [10]	M	43	Ischemic stroke 3 y ago	MCA dolichoectasia	No surgery, antiaggregating therapy
Current study	F	30	Headache and dizziness	MCA dolichoectasia	Conservative
M = Male; F = Female; MCA = Middle cerebral artery					

CONCLUSION

MCA dolichoectasia is a rare and benign lesion. However, it can masquerade as cerebral cavernous malformation or intracranial aneurysm. Thus, careful radiological evaluation along with the suggested diagnostic criteria are of a paramount importance to prevent its misdiagnosis.

ABBREVIATIONS

IADE; Intracranial arterial dolichoectasia, EEG; electroencephalogram, CT; computed tomography, MRI; Magnetic resonance imaging, CTA; computed tomography angiography, MCA; Middle cerebral artery.

DECLARATIONS

Acknowledgements: None.

Authors' contributions: SA wrote the primary manuscript. ZA, SH participated in its coordination, supervision, and revision of the manuscript. SH conceived of the study and collected the data. ZA, AJ helped to draft the manuscript. SH, NA, NH diagnosed the case. All authors read and approved the final manuscript.

Funding: None.

Availability of data and materials: Not applicable.

Ethics approval and consent to participate: Not applicable.

Consent for publication: Not applicable.

Competing interests: The authors declare that they have no competing interests.

REFERENCES

- Jia ZY, Zhao LB, Lee DH. Localized marked elongation of the distal internal carotid artery with or without PHACE syndrome: segmental dolichoectasia of the distal internal carotid artery. *American Journal of Neuroradiology*. 2018 May 1;39(5):817-23.
- Baran, B., Kornafel, O., Guziński, M., & Sasiadek, M. Dolichoectasia of the circle of Willis arteries and fusiform aneurysm of basilar artery—case report and review of the literature. *Polish journal of radiology*. 2012;77(2):54-59.
- Yuan Y, Xu K, Luo Q, Yu J. Research Progress on Vertebrobasilar Dolichoectasia. *International Journal of Medical Sciences*. 2014;11(10):1039-1048.
- Kansal R, Mahore A, Dange N, Kukreja S. Dolichoectasia of vertebrobasilar arteries as a cause of hydrocephalus. *Journal of neurosciences in rural practice*. 2011 Jan;2(01):062-4.
- Del Brutto VJ, Ortiz JG, Biller J. Intracranial arterial dolichoectasia. *Frontiers in neurology*. 2017 Jul 17; 8:344.
- Smoker WR, Corbett JJ, Gentry LR, Keyes WD, Price MJ, McKusker S. High-resolution computed tomography of the basilar artery: 2. Vertebrobasilar dolichoectasia: clinical-pathologic correlation and review. *American journal of neuroradiology*. 1986 Jan 1;7(1):61-72.

7. Smith K, Bardenheier J. Aneurysm of the Pericallosal Artery Caused by Closed Cranial Trauma. *Journal of Neurosurgery*. 1968;29(5):551-554.
8. Nakahara I, Taki W, Tanaka M, Matsumoto K, Kikuchi H. Dolichoectasia of the Middle Cerebral Artery. *Neurologia medico-chirurgica*. 1995;35(11):822-824.
9. Sharawat IK, Kumar A, Goswami JN, Sankhyan N. Dolichoectasia of the anterior cerebral arteries: a rare cause of headache in a young child. *Child's Nervous System*. 2018 Mar 1;34(3):389-91.
10. Guo L, Zhang X, Ge J, Qiu Y. Middle Cerebral Artery Dolichoectasia With Radiologic Follow-Up. *Journal of Craniofacial Surgery*. 2014 May 1;25(3): e269-71.
11. Brinjikji W, Nasr DM, Flemming KD, Rouchaud A, Cloft HJ, Lanzino G, Kallmes DF. Clinical and imaging characteristics of diffuse intracranial dolichoectasia. *American Journal of Neuroradiology*. 2017 May 1;38(5):915-22.
12. Feliciano CE, Pamiás-Portalatin E, Mendoza-Torres J, Effio E, Moran Y, Rodríguez-Mercado R. Color-coded digital subtraction angiography in the management of a rare case of middle cerebral artery pure arterial malformation: A technical and case report. *Interventional Neuroradiology*. 2014 Nov;20(6):715-21.
13. Abe T, Singer RJ, Marks MP, Kojima K, Watanabe M, Uchida M, Hayabuchi N. Arterial vascular abnormality accompanying cerebral cortical dysplasia. *American journal of neuroradiology*. 1997 Jan 1;18(1):144-6.
14. Kanemoto Y, Hisanaga M, Bessho H. Association of a Dolichoectatic Middle Cerebral Artery and an Intracranial Cavernous Hemangioma—Case Report—. *Neurologia medico-chirurgica*. 1998;38(1):40-2.
15. Tokunaga T, Yamamoto T. Hemorrhage with dolichoectatic middle cerebral arteries. *Neurology*. 2003 Jul 22;61(2):E4.
16. Puca A, Marchese E, Esposito G, Calcagni ML, Di Lazzaro V. Middle cerebral artery dolichoectasia in a young woman with a previous stroke. *European journal of neurology*. 2007 Jan;14(1):109-11.
17. Maruya J, Nishimaki K, Minakawa T. Hyperperfusion syndrome after neck clipping of a ruptured aneurysm on a dolichoectatic middle cerebral artery. *Journal of Stroke and Cerebrovascular Diseases*. 2011 May 1;20(3):260-3.



The two stages surgery in the management of central neurocytoma. Case series of 10 patients

W. Bennabi, A. Khelifa, Y. Felissi, L. Houari, A. Morsli

Department of Neurosurgery. El Oued University Hospital, Algiers, ALGERIA

ABSTRACT

Central neurocytoma is an uncommon benign tumour of the central nervous system. The intraventricular location close to the Monro foramina and the attachment to septum pellucidum are characteristics for diagnosis. The encasement of vascular structures represents a surgical challenge. We report a series of 10 cases of central neurocytoma operated at our department 06 of those was operated in two stages intentionally in order to avoid post-operative complications and to obtain complete removal.

INTRODUCTION

Central neurocytoma (CN) is an extremely rare benign tumour of central nervous system accounting for only 0.1 to 0.5% of brain tumours [1]; although described for the first time by Hassoun et al in 1982 [2]; since then, we dispose poor data about these tumours in the literature [1]. The intraventricular location is the main site of development of these lesions [1,3]. The brain MRI is an important tool for diagnosis; however, the certainty is obtained by histological examination; in which the differential diagnosis is made with oligodendroglioma and ependymoma. Surgery represents the only effective option to deal with this kind of lesions, with usually good results, associated with conventional radiation or radiosurgery in case of atypical finding.

MATERIALS AND METHODS

We report a retrospective study of 10 cases of central neurocytoma treated in our department over a period extending from 2003 to 2019. All patients underwent computerized tomography (CT) scans and magnetic resonance imaging (MRI) on T1, T2, FLAIR, and T1 injected sequences.

RESULTS

The study includes 10 patients aged between 22-60 years old, with average age of 30.5 years. The sex ratio was 3F/2M.

Keywords

central neurocytoma,
ventricular tumour,
immunohistochemical
markers



Corresponding author:
Walid Bennabi

Department of Neurosurgery, El
Oued University Hospital, Algiers,
Algeria

walidneurosurgeon@gmail.com

Scan to access the online version



CLINICAL PRESENTATION

Increasing intracranial pressure (ICP) symptoms were the main clinical presentation observed in six patients, associated to visual disorder in seven patients; other symptoms were less frequent: seizures were found in two patients, cognitive disturbance in three patients, and decreased consciousness in one patient.

IMAGING

The computerized tomography (CT scan) showed in the majority of cases heterogeneous lobulated lesion, located frequently in the frontal horn of the lateral ventricle adherent to the septum pellucidum and frequently invading this one, the lesion was associated in most cases with biventricular dilation. The magnetic resonance imaging (MRI) showed the characteristic aspect of this lesion: isointense on T1 weighted imaging, iso or hyperintense on T2 weighted imaging with heterogeneous enhancement due to the cystic and calcic components after gadolinium injection; showing a "soap bubble" characteristic aspect.

TREATMENT

Hydrocephalus management

Six patients consulted with hydrocephalus treated with different modalities: ventriculo-peritoneal shunt (VP-shunt) was used in two patients; endoscopic third ventriculostomy (ETV) was performed in one patient; Rickham reservoir was placed in one patient (Table 1).

Method	Number of patients
VP-shunt	2
ETV	1
Rickham reservoir	2
Direct approach	1

VP-shunt: ventriculo-peritoneal shunt, ETV: endoscopic third ventriculostomy

Management of the lesion

All patients were operated with open approaches, the trans-frontal trans-ventricular approach was used in all patients combined to the trans-callosal approach in three patients. Six patients were operated intentionally in two stages. A complete resection was obtained in six (06) patients and subtotal resection in four (04) patients. The resection

was limited in the remaining four (04) cases because of the infiltration of the trigone and encasement of the major venous vessels.

Table 2: Surgical approaches

Patients	Approach		Outcome and Complications
	1 st stage	2 nd stage	
Patient 1	TFTV	TFTV	Recidivism
Patient 2	TFTV	TFTV	Worsening of the cognitive disturbance
Patient 3	TFTV	None	None
Patient 4	TFTV	Transcallosal	None
Patient 5	TFTV	TFTV	None
Patient 6	TFTV	None	None
Patient 7	TFTV	Transcallosal	None
Patient 8	TFTV	Transcallosal	None
Patient 9	TFTV	None	None
Patient 10	TFTV	None	None

TFTV: trans-frontal trans-ventricular

Pathological findings

The diagnosis of CN was based on microscopic examination and several immunohistochemistry markers such as synaptophysin, GFAP, Olig2, NSE, chromatogranin, Ps100. Patients with Ki-67 antigen (Mib1) $\geq 8\%$ was considered as atypical CN. This finding was observed in three patients.

Adjuvant therapy

Conventional radiotherapy was used for the three patients with atypical CN whereas surgery was preferred in recurrence with low grade lesion. We didn't experience stereotactic radiosurgery in our series as well as chemotherapy.

Mortality and morbidity

We noted that one patient presented a worsening of his cognitive disturbance (memory loss) while we didn't observe any death in our series. Although we reoperated one patient for recidivism three years later. (table2)

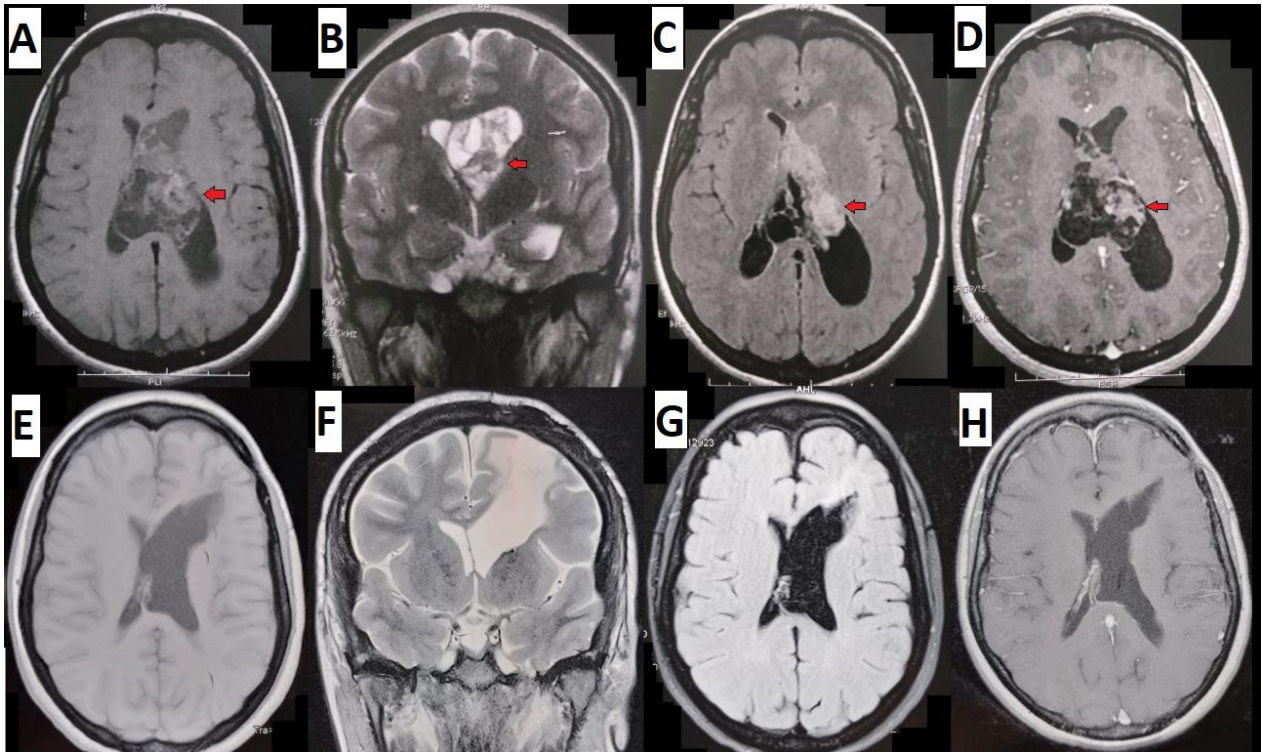


Figure 1. 30 years old female, with six months history of headache vertigo and visual disturbance with progressive worsening, at the admission the patient was conscious presenting visual acuity at 1/10 and 5/10, there was also a stage III papilledema in both eyes. Brain MRI objectified a 55 mm intraventricular process located on the left lateral horn, isointense on T1 WI, hyperintense on T2 and FLAIR sequences, with heterogeneous enhancement due to those images were defined a “soap bubble” aspect characteristic for neurocytoma (A, B, C, and D). The patient was operated and the lesion was totally removed through a left trans-frontal trans-ventricular approach. Pathological study confirmed the diagnosis of benign neurocytoma in post-operative there was a disappearance of headache and vertigo; the control imaging performed four years later showed no recidivism (E, F, G, and H). (A and E: T1 WI; B and F: T2 WI; C and G: FLAIR sequences; D and H: T1 injected images).

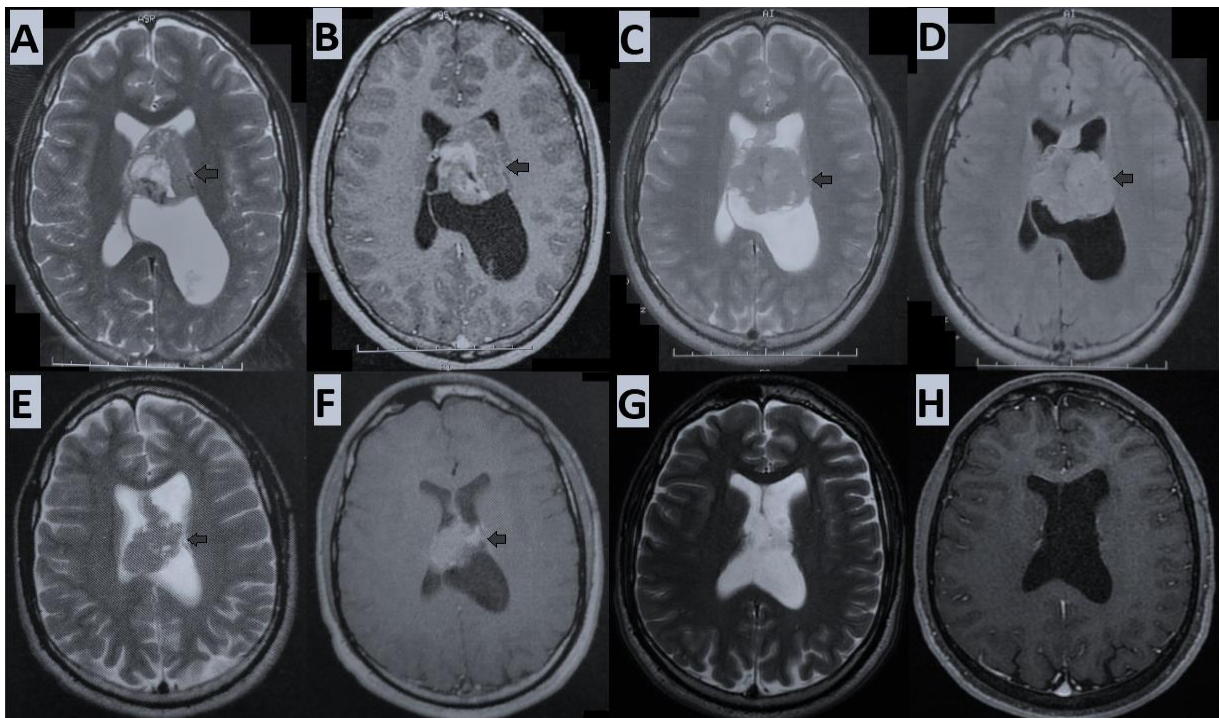


Figure 2. 22 years old male with one-month history of severe headache clinical exam at the admission found conscious patient without neurologic deficit there was no papilledema. Brain MRI objectified a process in the left ventricular frontal lateral horn measuring 33 X 45 mm with heterogeneous isosignal in T1WI, T2 WI, and FLAIR sequences with heterogeneous enhancement after gadolinium injection (A, B). The patient was operated and the lesion was subtotally removed through a left Trans frontal Trans ventricular approach. One year later a control brain MRI objectified a re-expansion of the lesion it measured 50 X 50 X 42 mm (C, D), this time a total removal of the tumour was planned to be performed in two stages first a subtotal removed was performed through the same approach. Three years later the brain MRI objectified the persistence of the residual amount of the tumour measuring 23 X 34 mm (E, F) so the second stage of the removal was lunched and as plained the total removal obtained through the same approach. The brain MRI control images performed four later objectified no evidence of recurrence (G, H). A, C, E, and G axial T2 WI b; B, F, and H injected sequences; and C: FLAIR sequence).

DISCUSSION

The central neurocytoma represents a very small proportion of brain tumours (0.1-0.5%), mostly in the lateral ventricle (77%),^[2] with sometimes extension to the third ventricle (26%)^[6] and rarely an exclusive localization in the third ventricle. As in our series it occurs frequently at the third decade with extremities ranging from (8 to 67) years old^[7,8]. Most studies attest that there is no correlation between gender and incidence of central neurocytoma^[5,9,10,11]; a slight female predominance was noted in our study, also higher incidences of this lesion was mentioned in some studies in Japan, Korea and India^[8,12,13]. The clinical presentation is dominated by increasing intracranial pressure signs due to obstructive hydrocephalus by obliteration of the foramen of Monro associated to cognitive disturbance. Seizures, decreased consciousness and vision problems are less frequent. We consider that the cognitive disturbance is due to the close relation of the tumour to the trigone which is frequently infiltrated by the lesion (..). In radiological findings this lesion is mostly located in the anterior half of lateral ventricle appears to be isodense in computerized tomography (CT) scans associated to hyperdensities indicating calcifications which occur in up to 50% of all cases^[5, 14]. In magnetic resonance imaging (MRI) the central neurocytoma appears isointense on T1 weighted imaging, iso-hyperintense on T2 weighted imaging; and with heterogeneous moderate enhancements after contrast agent injection which is the classic "soap bubble" aspect^[15]. Surgery is the only effective treatment for this kind of lesions and complete resection is associated with better rates of survival and local control, with five-year survival rate of 99% for gross total resection (GTR) and 86% for subtotal resection (STR)^[19].

The trans-frontal trans- ventricular approach as well as the anterior trans-callosal approach offers the best surgical corridor to all lesions located in the

frontal horn of the lateral ventricle^[20]. We noted in patients operated in two stages that the resection was safer and easier comparing with those operated in single stage, this can be explained by the devascularization of the lesion in the first stage. Due to its histological similarities with other ventricular tumors such as ependymoma or oligodendroglioma the CN is frequently not easy to diagnose, the immunohistological markers are very useful in the diagnosis of this lesion and synaptophysin is the most specific one^[13]. Adjuvant therapies are indicated in case of atypical, incomplete resection or inoperable recurrence neurocytoma; tow modalities are used conventional radiotherapy and stereotactic radiosurgery; with no statistically difference between both therapies.^[16, 18]

CONCLUSION

The CN is usually a benign tumour of the central nervous system in which the surgical treatment is the only efficient option with very good results in term of survival rates and local control. Conventional radiotherapy or stereotactic radiosurgery can be considered in cases of atypical neurocytoma. The two stages surgery adopted in our department can be a good and safe strategy to deal with this kind of haemorrhagic tumours.

REFERENCES

1. Waters JD, Gonda D, Chen CC, Carter BS. Evidence-Based Management of Central Neurocytoma (Gross Total Resection versus Subtotal Resection and the Role of Adjunctive Therapies). In: Alfredo Quinones-Hinojosa, Shaan M.Raza, editors. Best Evidence Medicine for Brain Tumor Surgery, 1st edition. New York, Stuttgart: Thieme Medical Publishers; 2014. p. 155-61.
2. Hassoun, J., Gambarelli, D., Grisoli, F., et al. Central neurocytoma. An electronmicroscopic study of two cases. Acta Neuropathol 1982; 56, 151-156.
3. Peltier J, Baroncini M, Le Gras D, Lejeune JP. Central neurocytoma of the lateral ventricle. A series of 35

- cases with review of the literature. *Neurochirurgie* 2011; 57: 215-9.
4. Kerkeni A, Benlakhder Z, Rkhami M, Sebai R, Belguith L, Khaldi M, et al. Central neurocytoma: study of 32 cases and review of the literature. *Neurochirurgie* 2010; 56: 408-14.
 5. Hassoun, J., Söylemezoglu, F., Gambarelli, D., et al. Central neurocytoma: a synopsis of clinical and histological features. *Brain Pathol* 1993; 3, 297-306.
 6. Moussa R, Abadjian G, Nader M, Rizk T, Samaha E, Nohra G, et al. Central neurocytoma. Four patients. *Neurochirurgie* 2004 ; 50 n6: 639-46.
 7. Figarella-Branger D, Soylemezoglu F, Kleihues P, Hassoun J. Central neurocytoma. In: Kleihues P, Cavenee WK. *Pathology and genetics of tumors of the nervous system*. Lyon: IARC Press; 2000.p.107-9.
 8. Sharma MC, Deb P, Sharma S, Sarkar C. Neurocytoma: a comprehensive review. *Neurosurg Rev* 2006;29:270-85; discussion 285.
 9. Maiuri F, Spaziante R, De Caro ML, Cappabianca P, Giamundo A, Iaconetta G. Central neurocytoma: clinicopathological study of 5 cases and review of the literature. *Clin Neurol Neurosurg* 1995; 97:219-28.
 10. Patel DM, Schmidt RF, Liu JK. Update on the diagnosis, pathogenesis, and treatment strategies for central neurocytoma. *J Clin Neurosci* 2013; 20: 1193-9.
 11. Vasiljevic A, François P, Loundou A, et al. Prognostic factors in central neurocytomas: a multicenter study of 71 cases. *Am J Surg Pathol* 2012; 36:220-7.
 12. Kim DG, Chi JG, Park SH, et al. Intraventricular neurocytoma: clinicopathological analysis of seven cases. *J Neurosurg* 1992; 76:759-65.
 13. Lee SJ, Bui TT, Chen JHC, Lagman C, Chung LK, Sidhu S et al. Central Neurocytoma: A review of clinical management and histopathological features. *Brain Tumor Res Treat* 2016; 4(2):49-57.
 14. Goergen SK, Gonzales MF, McLean CA. Intraventricular neurocytoma: radiologic features and review of the literature. *Radiology* 1992 ; 182:787-92.
 15. Chen, C.L., Shen, C.C., Wang, J., et al., 2008. Central neurocytoma: a clinical, radiological and pathological study of nine cases. *Clin Neurol Neurosurg* 110, 129-136.
 16. Barani, Igor J., Raleigh, David R., Et Larson, David. The management of central neurocytoma: radiotherapy. *Neurosurgery Clinics*, 2015, vol. 26, no 1, p. 45-56.
 17. Garcia RM, Evan MI, Oh T, Barani I, Parsa AT. Intraventricular Neurocytoma: A systematic review of stereotactic radiosurgery and fractionated conventional radiotherapy for residual or recurrent tumors. *Clinical Neurology and Neurosurgery* 2014; 117: 55-64
 18. Rades, D., & Schild, S. E. (2006). Value of postoperative stereotactic radiosurgery and conventional radiotherapy for incompletely resected typical neurocytomas. *Cancer: Interdisciplinary International Journal of the American Cancer Society*, 106(5), 1140-1143.
 19. Rades D, Fehlaue F. Treatment options for central neurocytoma. *Neurology* 2002; 59:1268-70.
 20. Mortazavi MM, Adeeb N, Ellenbogen RG. Microsurgical removal of intraventricular tumors. In: Sekhar LN, Fessler RG, editors. *Atlas of Neurosurgical Techniques*, 2nd edition. New York, Stuttgart, Delhi, Rio de Janeiro: Thieme Medical Publishers; 2016.p.154-71.



Multilocular hydrocephalus

**Harold Vasquez^{1,5}, Ezequiel García-Ballestas²,
Luis Rafael Moscote-Salazar³, Sergio A Serrato⁴,
William A Florez⁵, Amit Agrawal⁶**

¹ Facultad de Ciencias de la Salud, Universidad del Sinu Elias
Bechara Zainum, Cartagena de Indias, COLOMBIA

² Center for Biomedical Research (CIB). Faculty of Medicine -
University of Cartagena, COLOMBIA

³ Neurosurgeon. Critical Care. Center for Biomedical Research (CIB).
Director of Research Line Cartagena Neurotrauma Research Group.
Faculty of Medicine - University of Cartagena, COLOMBIA

⁴ Uros Clinic, Neiva, COLOMBIA

⁵ Latin-American council of neurointensivism - ClaNi, Cartagena,
COLOMBIA

⁶ Department of Neurosurgery, All India Institute of Medical
Sciences, Saket Nagar, Madhya Pradesh, INDIA

ABSTRACT

Multilocular hydrocephalus is an entity that occurs relatively frequently in neurosurgical practice. We are present an editorial letter with a mini-review of the pathophysiology, surgical, and medical treatment.

Multiloculated hydrocephalus (MH) has also been termed as a multiseptate hydrocephalus, polycystic hydrocephalus, interventricular septum and can be unilocular or multiloculated.^{5,6,9} MH is characterized by the presence of septations or obstructions within the normal ventricular system, leading to cerebrospinal fluid (CSF) accumulation due to a lack of communication between ventricles^{4,6,8,10,11}. Although the etiology and pathogenesis not clearly known, the presence of septations has been considered to be caused by a fibrous adhesion within the ventricles or by inflammation leading to sub ependymal gliosis leading to glial bumps and septations leading to Ventricular obstruction^{4,8,9}.

Many etiological factors have been shown to associate with multiloculated hydrocephalus such as many intracranial processes as infection, intracranial hemorrhage, bacterial or fungal meningitis, congenital malformations, birth trauma, tumors, intracranial surgery, among others^{2, 6, 8,10,11}

Histologically, ventricular septum it is origins from a glial protrusion

Keywords

multilocular hydrocephalus,
hydrocephaly,
endoscopic neurosurgery,
operative approach



Corresponding author:
William A Florez

Latin-American council of
neurointensivism - ClaNi,
Cartagena, Colombia

william-florez@hotmail.com

Scan to access the online version



in ventricles⁴. The clinical presentation is determined by the most frequent manifestations of complicated hydrocephalus, such as: enlargement of the head, convulsions, neurological impairment, sign of the setting sun (inability to look upwards, observed with higher frequency in infants), headache or mental retardation^{3,7}. On the other hand, in the worst scenario, many patients may have the intracranial pressure (ICP) increased, presented as a consequence of the expansion or enlargement of the ventricles (ventriculomegaly)^{3,10}. Computed tomography (CT) and magnetic resonance imaging (MRI) allow visualization of the multiple cavities with CSF and irregular dilations with multiple septations (Figure -1)^{2,4,9,10}. The complications may be obtained by catheters and interventions to relieve the symptoms caused by raised intracranial pressure, however, the primary goal is to establish communication between existing compartments

and thereby achieve the diversion of the CSF^{8,10}

Treatment seeks to restore communication between isolated intraventricular compartments, in order to create a single cavity and implement a single bypass¹¹. Treatment options include placement of multiple bypass systems, endoscopic fenestration of localized compartments, septostomy, third endoscopic ventriculostomy, stereotactic aspiration, or craniotomy for the microsurgical fenestration of localized compartments or combination of several surgical principles.^{2,3,4,10} This mentioned open surgical and endoscopic approach effective at improving adequate function of CSF derivation. Furthermore, endoscopic techniques have the advantage in decrease time of surgery, need of transfusion and length hospital stay¹. The craniotomy and open surgical approach show a better success rate in severity and/or refractory cases^{1,2}

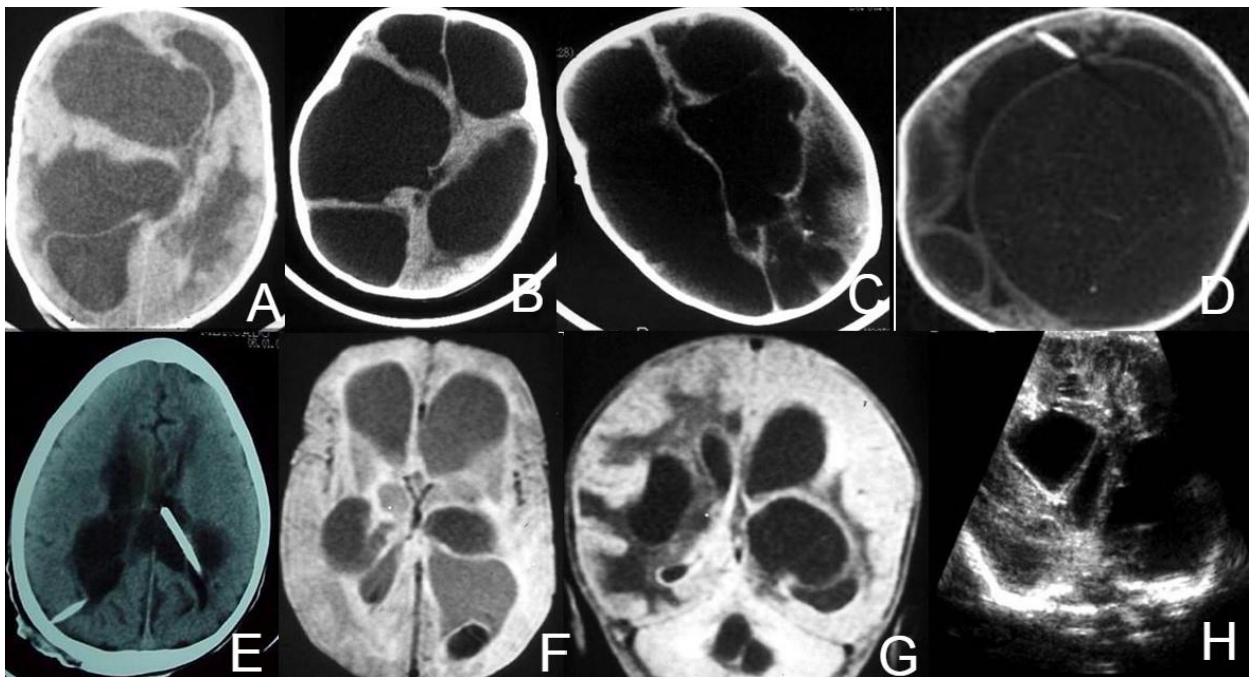


Figure 1. CT scan (A-E), MRI (F and G) and USG images showing characteristic imaging appearance of multiloculated hydrocephalus i.e., dilated ventricle and multiple septations.

REFERENCES

1. Akbari SHA, Holekamp TF, Murphy TM, Mercer D, Leonard JR, Smyth MD, et al. Surgical management of complex multiloculated hydrocephalus in infants and children. *Child's Nerv Syst.* 2015;31(2):243-9.
2. Andresen M, Juhler M. Multiloculated hydrocephalus: a review of current problems in classification and treatment. *Child's nervous system: ChNS : official journal of the International Society for Pediatric Neurosurgery* 2012;28:357-362.
3. Chamilos C, Sgouros S. Intrauterine grade IV intraventricular hemorrhage in a full-term infant leading to hydrocephalus. *Child's nervous system: ChNS: official journal of the International Society for Pediatric Neurosurgery* 2013; 29:861-865.
4. El-Ghandour NM. Endoscopic cyst fenestration in the treatment of multiloculated hydrocephalus in children.

- Journal of neurosurgery Pediatrics 2008;1:217-222.
5. Eshra MA. Endoscopic management of septated, multiloculated hydrocephalus. Alexandria Journal of Medicine 2014;50:123-126.
 6. Jamjoom AB, Mohammed AA, al-Boukai A, Jamjoom ZA, Rahman N, Jamjoom HT. Multiloculated hydrocephalus related to cerebrospinal fluid shunt infection. Acta neurochirurgica 1996;138:714-719.
 7. Kirkpatrick M, Engleman H, Minns RA. Symptoms and signs of progressive hydrocephalus. Archives of disease in childhood 1989;64:124-128.
 8. Lee YH, Kwon YS, Yang KH. Multiloculated Hydrocephalus: Open Craniotomy or Endoscopy? J Korean Neurosurg Soc 2017;60:301-305.
 9. Lewis AI, Keiper GL, Jr., Crone KR. Endoscopic treatment of loculated hydrocephalus. Journal of neurosurgery 1995;82:780-785.
 10. Sandberg DI, McComb JG, Krieger MD. Craniotomy for fenestration of multiloculated hydrocephalus in pediatric patients. Neurosurgery 2005;57:100-106; discussion 100-106.
 11. Zuccaro G, Ramos JG. Multiloculated hydrocephalus. Child's nervous system : ChNS : official journal of the International Society for Pediatric Neurosurgery 2011;27:1609-1619.



Safety of metoclopramide in traumatic brain injury patients. A systematic review of literature

Said Al Jaadi¹, Yahya Al Kindi¹, Tariq Al-Saadi^{1,2}

¹ College of Medicine and Health Sciences, Sultan Qaboos University, OMAN

² Neurosurgeon. CANADA

ABSTRACT

Background: One in every three related-injury deaths in United State are linked directly to traumatic brain injury (TBI), for which it is considered as a leading cause of death. Traumatic brain injury took place due to severe head assault to a hard object, with headache and vomiting being amongst the most common presenting symptoms. Metoclopramide is an old antiemetic agent that has been used widely for nausea and vomiting in TBI patients.

Aim: A systematic review of the literature to investigate the safety of metoclopramide in treating traumatic brain injury patients.

Methods: A literature review was conducted in 6 databases, we determine the pertinence of a study to the inclusion criteria by assessing the title, keywords, and abstracts. Five studies were found to be relevant. Data were extracted using multiple variables that were formulated incongruent with the study aim and then further analyzed.

Results: The collective sample size was 93 patients with an average of age 38.5 years. 51.6 % were male and 48.6% were females. Most patients received 10 mg metoclopramide IV with a percentage of 77.4%. While only 22.5% received 20 mg IV metoclopramide. Seventy-one patients received metoclopramide alone and 22 received combination therapy. Headache was the most common reported side effect (46.2 %), followed by anxiety and drowsiness with (39.7%) and (27.9 %); respectively. Fatigue reported in (24.7%), while dystonia was the least common and developed only in 5.3%.

Conclusion: Metoclopramide is a common medication used to treat TBI patients in the emergency department. However, the review demonstrated that the central nervous system (CNS) side effect is excepted. Alternative options with lower CNS side effects may be better tried.

BACKGROUND

One in every three related-injury deaths in the US are linked directly to TBI, for which it is considered as a leading cause of death (1). As for paediatric cases the prevalence across countries varies from 47 and 280 per 100,000 children, more than 80% of which are minor head injuries with GCS of 14-15(2). Traumatic brain injury took place due to

Keywords

traumatic head injury,
metoclopramide,
safety,
side effect,
headache,
vomiting



Corresponding author:
Tariq Al-Saadi

Neurosurgeon. Canada

tariq.dh.95@gmail.com

Scan to access the online version



severe head assault to a hard object, which then can be classified into mild, moderate, and severe using GCS (3). Moreover, the main causes of TBI are road traffic accidents (RTA), falling, physical violence, exercise-related head injuries among others (1,3). Patients with TBI usually present to the emergency room (ER) with headache, nausea, and vomiting (4). Other common presentations are dizziness, blurred vision, loss of consciousness, amnesia, and disturbance in concentration (1,2,4). As for headache, 1 in every 4 patients reported persistent headache syndrome (4). TBI patients were treated with antiemetic agents for their symptoms. Metoclopramide (4-amino-5-chloro-2-methoxy-N-(2-dimethylamino methyl benzamide) is an old antiemetic agent that has been used widely for nausea and vomiting as well as other gastrointestinal disorders (2). It is an antidopaminergic agent, centrally and peripherally acting, in order to enhance upper gastrointestinal motility without affecting its secretion (3). Metoclopramide administration through PO takes about 1-2 hours for maximum plasma concentration while it takes only 15min on an IV route (2,3). It is metabolized by the hepatic Cytochrome P450 CYP2D6 enzyme (2). The drug has multiple side effects such as; dystonia, restlessness or anxiety, fatigue, drowsiness, confusion, insomnia, and flushing (2,3). Our main aim is to study the safety of metoclopramide in treating TBI cases by reviewing the literature.

METHODOLOGY

Literature search and formulating selection criteria

This study is a literature review with the main aim being to study the safety of metoclopramide in treating TBI cases. We searched Pubmed, EBSCO, Proquest, ScienceDirect, Wiley Online, and Springer for pertinent studies. Moreover, we determined the pertinence of a study to the inclusion criteria by assessing the title, keywords, and abstracts. The keywords we used were; Traumatic Head Injury, Head Injury, Brain Injury, Subdural Injury, Epidural Injury, Metoclopramide, Safety of Metoclopramide, and Metoclopramide side effect. Furthermore, the inclusion criteria were; all English literature and articles about TBI that used metoclopramide and reported drug side effects while we excluded any articles that are non-completed, repeated, or did not meet any of the aforementioned criteria.

Data Extraction

Data were extracted using multiple variables that were formulated incongruent with the study aim. The variables are; article type and author's name, number of patients, the average age, gender, the dose of metoclopramide, drug combination, drug side effects, mechanism of injury, GCS, and duration of follow up. All of which were gathered in a table and were set for analysis.

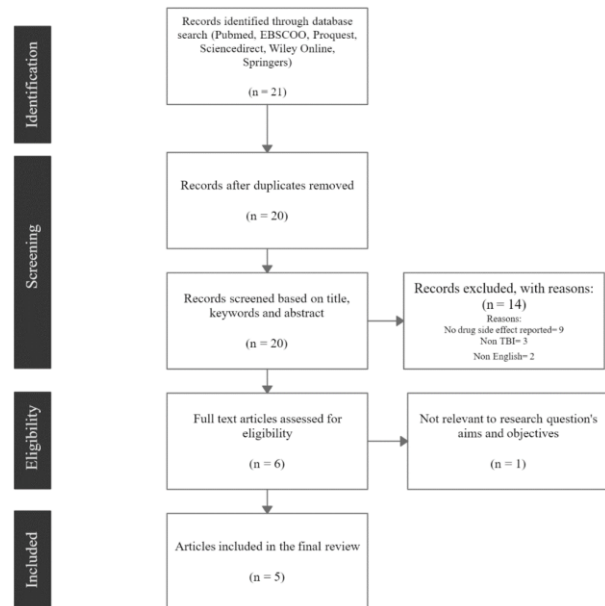


Figure 1. PRISMA flow diagram show Methodology characteristic of included study

Figure 1 represents flow chart depicting the study selection process. Of 21 relevant studies, one of them was found to be a repetition, 14 were not eligible and one was irrelevant to the research aim. 5 pertinent literature were studied thoroughly for data extraction.

Data Analysis

Data were collected in an EXCEL sheet, formula builder was used to calculating simple mathematic, including the total number of patients, the number of females and males, and the percentage of each, total number of side effects reported. SPSS has been used to calculate the mean of age and the days of follow up using a bar of weight cases.

RESULT

Our study included 5 articles, as shown in Table 1. Two studies were randomized controlled, one was

prospective, and two case reports. There were variations in the drug side effects reported in each study. Two studies used Diphenhydramine 25mg and Cisapride as a combination thereby, while the remained used metoclopramide alone. All the studies used 10 mg IV metoclopramide except one study used 20 mg IV. Headache was the most common reported side effect by 2 studies. There was some missing data especially on the mechanism of injury.

Our sample size was 93 patients with an average of age 38.5 years. 51.6 % were male and 48.6% were female (Table 2). Most patients received 10 mg metoclopramide IV with a percentage of 77.4%. While only 22.5% received 20 mg IV metoclopramide. Seventy-one patients received metoclopramide alone and 22 received combination therapy. Headache was the most common reported side effect (46.2 %), followed by anxiety and drowsiness with (39.7%) and (27.9 %); respectively. Fatigue reported in (24.7%). While dystonia was the least common and developed only in 5.3%.

DISCUSSION

This is the first systemic review study of metoclopramide side effects on patients with TBI. There is a lack of clinical trial which study the side effect of metoclopramide in patients with TBI. Our study identified 93 patients who received metoclopramide after TBI. The average age of patients was 6.9 years (4-69). Male was relatively higher than female in our sample size as 51.6% of our sample size were male compared to 48.4% female. Comparing done to identify the incidence and management of moderate to a severe head injury which showed that male to female ratio is 2:1(5). This might be due to the type of our research as it is a systemic review and most of our data were collected from prospective and clinical trial research. A previous study on the identification of the efficacy of metoclopramide in TBI, showed that the leading causes of TBI were RTA, followed by fall (6). In comparison to our study fall and trip were the highest.

In our review, 77.4% received 10 mg metoclopramide intravenously, and 22.5% received 20 mg intravenously. This dose was supported by the recommendation of the European Medicines Agency that the maximum daily dose of Metoclopramide is between 10 mg to 30 mg in order to decrease the risk

of neurological and other adverse effect (7). Metoclopramide is a prokinetic agent that have been widely used in critically ill patient to improve gastric motility and the symptoms of head concussion, nausea, and vomiting (8). However, the concerns of metoclopramide's safety have been raised (9). One of the studies included in our review showed that the effectiveness of metoclopramide and ondansetron was similar. However, because of the incidence of the complications in patients treated with metoclopramide were higher than ondansetron, they concluded with the suggestion to use ondansetron instead of metoclopramide inpatient with TBI (10). In TBI patient with an enteral feeding problem, the use of erythromycin instead of metoclopramide in some situation has been studied which show there is a significant decrease in high gastric aspirate volume with the use of erythromycin compared to metoclopramide (11).

In the current systemic review, the most common symptom was the headache as it is presented in 45.2% of the sample size^(10,12). In contrast to a survey study done by *Hale.T* which showed that among 32 participants in the study, 1-7% of participants complained of some central side effects ranging from dizziness and headache. We can see that patients with TBI are more susceptible to develop a headache and other neurological side effects, including extrapyramidal side effects, from metoclopramide compared to others (13). In our review, the incidence of anxiety and drowsiness were 37 patients (29.0%) and 26 patients (27.9%), respectively. Fatigue was only represented in 23 patients (24.7%)(10)(12). While another systemic review study done to study the use of metoclopramide in diabetic gastroparesis, showed that fatigue, drowsiness and lethargy were presented in 10% of patients (14). Dystonia was represented in 5 patients (5.3%). The incidence of dystonia in the previous systemic review was in an approximately 0.2–6% of patients who received metoclopramide (14). These side effects may explain by the ability of metoclopramide to cross the blood-brain barrier easily (15).

The early signs of an increased ICP are headache, vomiting or nausea, ocular palsies, and altered level of consciousness. Side effects of metoclopramide overlap with raised ICP symptoms, since it is subtle it is difficult to recognize a rise in ICP unless you investigate it. In our literature review, a case report

identifies an increased in ICP from baseline of 15 - 20mmHg to 36mmHg following a 10mg intravenous metoclopramide and the same dose in the following day reports another increases to 34 mmHg (16). Such side effects raise a question of the safety of the metoclopramide in patients with TBI. Inconsistent with our results that found an increased susceptibility for neurological side effects after

metoclopramide administration in TBI patients. A controlled randomized clinical trial is recommended to exploit the relationship between raised ICP and metoclopramide.

Limitations:

The limitation of the study includes the lack of high evidence studies as there were only two randomized controlled trials and one prospective study. publication bias was not done because of the same reason. In addition, the lack of long term follows up was also noticed. In addition, in 75.2% of cases, the mechanism of injury was not mentioned.

CONCLUSION

Metoclopramide is a common medication used to treat TBI patients in the emergency department. However, the review demonstrated that the CNS side effects are excepted. Alternative options with lower CNS side effects may be better tried.

Table 1. Summary of Metoclopramide and TBI studies

Article type	Author Year of publication	No. of patients	Age	Gender		Dose of metoclopramide	Combination	Side effect	Mechanism of injury	GCS	Duration of Follow up
Controlled, randomize, double blind clinical trial	Majid Zamani et al. 2015	60	36.1	M	33	10 mg, IV	NA	- Headache 30/60(30%) - Drowsiness 26/60(43.3%) - Fatigue 23/60(38.3%) - Anxiety 37/60(61.7%) - Dystonia 5/60 (8.3%)	NA	14-15	NA
				F	27						
Prospective, randomize, controlled, double-blind	Tarik Zafer Nursal 2007	10	43	M	8	10 mg, IV	NA	5/10 develop complication *	TBI not defined	11-6	5 days
				F	2						
Prospective	Benjamin W 2018	21	45	M	5	20 mg, IV	Diphenhydramine 25mg	headache 12/19 (63%)	- Trip/fall 9 - Impacted stationary object 4. - Projectile 4 - Assault 3 - RTA 1	NA	5 days
				F	16						
Case report	Simon Deehan 2002	1	22	M	1	10 mg, IV	NA	- Increase ICP - Raised MAP	RTA	3	4 days
Case report	Thomas Altmayer, 1996	1	22	M	1	10mg, IV	Cisapride	None	RTA	9	69 days

GCS: Glasco coma scale

RTA: road traffic accident

*Not defined but none of which were extrapyramidal symptoms

Table 2. Summary of Metoclopramide and TBI studies findings

Number of patients		93
Average of age		38.5
Gender	Male	48(51.6%)
	Female	45(48.4%)
Treatment	Metoclopramide only	71(76.3%)
	Metoclopramide and Diphenhydramine	21(22.5%)
	Metoclopramide and Cisapride	1(1.1%)
Dose of metoclopramide	10 mg, IV	72(77.4%)
	20 mg, IV	21(22.5%)
Side effect	Headache	42(45.2%)
	drowsiness	26(27.9%)
	Fatigue	23(24.7%)
	Anxiety	37(29.0%)
	Dystonia	5(5.3%)
	Increase ICP Increase MAP	1(1.1%)
Mechanism of injury	Not defined	70(75.2%)
	RTA	3(3.2%)
	Trip/fall	9(9.7%)
	Impacted stationary object, assault	7(7.5%)
	Projectile	4(4.3%)
	Undefined complication	5(5.3%)
Average of the follow up		6.9(4-69)

ABBREVIATION

TBI: Traumatic brain injury
 ICP: Intracranial pressure
 CNS: Central nervous system
 GCS: Glasgow Coma Scale
 ER: Emergency Room
 RTA: Road Traffic Accident
 MAP: Mean Arterial Pressure

REFERENCES

- Report MW. Surveillance for Traumatic Brain Injury – Related Deaths — United States, 1997 – 2007. *CDC*. 2011;60(5):1997–2007.
- Moezzi M, Delirrooyfard A, Motamed H, Mortazavi MK, Specialist EM. Antiemetic effects of metoclopramide with and without dexamethasone in children with minor head trauma: a single blind randomized clinical trial. 2018;188(December):7307–13.
- Majid Zamani, Behnam Namdar, Reza Azizkhani, Omid Ahmadi MED. Comparing the Antiemetic Effects of Ondansetron and Metoclopramide in Patients with Minor Head Trauma. In 2015. p. 137–40.
- Friedman BW, Babbush K, Irizarry E, Gallagher EJ, Health M. An exploratory study of IV metoclopramide + diphenhydramine for acute post-traumatic headache. 2019;36(2):285–9.
- Maegele M, Lefering R, Sakowitz O, Kopp MA, Schwab JM, Steudel WI, et al. Inzidenz und Versorgung des mittelschweren bis schweren Schädel-Hirn-Traumas. *Dtsch Arztebl Int*. 2019 Mar 8;116(10):167–73.
- Dickerson RN, Mitchell JN, Morgan LM, Maish GO, Croce MA, Minard G, et al. Disparate response to metoclopramide therapy for gastric feeding intolerance in trauma patients with and without traumatic brain injury. *J Parenter Enter Nutr*. 2009 Nov;33(6):646–55.
- Medical Science News: Fda Requires Boxed Warning and Risk Mitigation Strategy for Metoclopramide-Containing Drugs [Internet]. [cited 2020 Apr 20]. Available from: <https://elbiruniblogspotcom.blogspot.com/2009/02/fda-requires-boxed-warning-and-risk.html>
- Nursal TZ, Erdogan B, Noyan T, Cekinmez M, Atalay B, Bilgin N. The effect of metoclopramide on gastric emptying in traumatic brain injury. *J Clin Neurosci*. 2007 Apr;14(4):344–8.

9. van der Meer YG, Venhuizen WA, Heyland DK, van Zanten ARH. Should we stop prescribing metoclopramide as a prokinetic drug in critically ill patients? *Crit Care*. 2014 Sep 23;18(5).
10. Zamani M, Namdar B, Azizkhani R, Ahmadi O, Esmailian M. Comparing the Antiemetic Effects of Ondansetron and Metoclopramide in Patients with Minor Head Trauma. *Emerg (Tehran, Iran)* [Internet]. 2015 [cited 2020 Apr 20];3(4):137–40. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26495402>
11. Makkar JK, Gauli B, Jain K, Jain D, Batra YK. Comparison of erythromycin versus metoclopramide for gastric feeding intolerance in patients with traumatic brain injury: A randomized double-blind study. *Saudi J Anaesth*. 2016 Jul 1;10(3):308–13.
12. Friedman BW, Babbush K, Irizarry E, White D, John Gallagher E. An exploratory study of IV metoclopramide + diphenhydramine for acute post-traumatic headache. *Am J Emerg Med*. 2018 Feb 1;36(2):285–9.
13. Hale TW, Kendall-Tackett K, Cong Z. Domperidone versus metoclopramide: Self-reported side effects in a large sample of breastfeeding mothers who used these medications to increase milk production. *Clin Lact*. 2018;9(1):10–7.
14. Shakhatreh M, Jehangir A, Malik Z, Parkman HP. Metoclopramide for the treatment of diabetic gastroparesis. *Expert Rev Gastroenterol Hepatol*. 2019 Aug 3;13(8):711–21.
15. Jolliet P, Nion S, Allain-Veyrac G, Tilloy-Fenart L, Vanuxeem D, Berezowski V, et al. Evidence of lowest brain penetration of an antiemetic drug, metopimazine, compared to domperidone, metoclopramide and chlorpromazine, using an in vitro model of the blood-brain barrier. *Pharmacol Res*. 2007 Jul;56(1):11–7.
16. Deehan S, Dobb GJ. Metoclopramide-induced raised intracranial pressure after head injury. *J Neurosurg Anesthesiol*. 2002;14(2):157–60.



Pre-hospital care: demography, current profile and future trends. Improving the health of traumatic brain injury patients

Sateesh Chandra Verma, Abhijeet Singh Sachan,
Surjeet Singh, Prakrati Sachan

Department of Neurosurgery, Sawai Man Singh Medical College,
Jaipur, INDIA

ABSTRACT

Introduction. Traumatic brain injury (TBI) is a major public health problem throughout the world. It is one of the leading causes of mortality and disability as a consequence results in a great financial burden on societies. Damage to the brain following trauma does not occur only at the moment of injury but also develops over a period of hours to days with the further secondary insult of the brain.

Methods. This was a prospective study done between April 2017 to March 2019. A total of 2134 patients were enrolled for this study with a collection of data in a formatted proforma. All the patients of trauma with clinical or radiological evidence of head injury coming to the trauma centre were included.

Results. In our study patient, mortality was 6.79% in patients receiving pre-hospital care compared to 12.03% in patients not receiving adequate pre-hospital care. 29.42% were in the age group of 21–30 years. RTA (overall 64.45%) was the most common mode of injury in the age group 21–30 years with 81.36% cases. Mortality in first emergency care provider by ambulance paramedics was 5.69% and member of the public was 10.10%.

Conclusion. It was observed that mortality was higher in patients not receiving adequate pre-hospital care. Early resuscitation facilities at the site of the accident have to be introduced and improved with the execution of rapid transportation to trauma care centres.

INTRODUCTION

Traumatic brain injury (TBI) is a major burden on the health care system in developing countries like India. It is one of the leading causes of mortality and disability worldwide as a consequence results in a great financial burden on societies. Research in the area of neurological trauma has shown that the totality of damage to the brain following trauma does not occur at the moment of injury but develops over a period ranging from hours to days. Brain injury occurs with further insult from secondary causes like hypotension, hypoxia, cerebral

Keywords

pre-hospital care,
hypoxia,
hypotension,
ambulance,
intubation,
traumatic brain injury



Corresponding author:
Surjeet Singh

Department of Neurosurgery,
Sawai Man Singh Medical College,
Jaipur, India

sujitgmc35@gmail.com

Scan to access the online version



edema, raised intracranial pressure, and expansion of the mass lesion. The incidence of TBI has increased significantly in the last 30 years but the mortality has decreased as a result of better management and availability of health care services.^{1,2} In developing countries there is a large number of lives lost due to lack of pre-hospital care whereas in developed countries life expectancy has increased³ due to advancements in pre-hospital and better understanding of pathophysiological processes in TBI.

To achieve better outcomes an early critical intervention in delaying or preventing secondary brain insults and maintaining cerebral perfusion is of paramount importance. This can be done with simple measures done just after trauma following ATLS guidelines with the prevention of hypotension and hypoxia. Evidence-based guidelines have been developed for the management of traumatic brain injury and implemented over the past decade, particularly within the intensive care unit (ICU) environment. However, the uncertainty of the efficacy of pre-hospital advanced life support interventions remains as such. In pre-hospital care, the standard management procedure for severe traumatic brain injury varies from case to case due to divergent scene conditions and characteristics. Multiple factors such as mechanism of injury, severity, and pattern, location of the accident, mode of transport, the time interval between trauma and first care and experience and skill level of paramedic contribute to this varied response.⁴

As a consequence of this uncertainty in the efficacy, further investigations and researches are the need of the hour. While pre-hospital management of severe TBI has become progressively more advanced, many challenges are remaining especially in the early recognition and treatment of severe brain trauma by ambulance paramedics. The expeditious transport of patients with brain injuries to an appropriate facility and the prevention of secondary insult is of increasing importance in the reduction of mortality and morbidity in brain trauma patients.⁵ It is crucial that the first health care provider must be familiar with the complex presentation of severe traumatic brain injury patients in the initial stages of injury. Early recognition and response to traumatic brain injury can significantly impact on neurological outcome. Paramedics must have a sound knowledge of the

interventions which may minimize secondary insult with the pre-hospital treatment of hypoxemia and hypotension being crucial components of traumatic brain injury management.

This study can be used to formulate new guidelines and plans to tackle the delay in first care to patients with TBI.

METHODOLOGY

The study was conducted at a level 1 trauma center of SMS medical college, Jaipur, India between April 2017 to march 2019. Overall, 2134 patients were enrolled for this study with a collection of data in a formatted proforma from admission to discharge. The data was collected from patients and their relatives. The ethical committee clearance was obtained prior to the commencement of the study. All the patients of trauma with clinical or radiological evidence of head injury or associated other injury coming to the trauma center were included.

It was a prospective observational study. Data of individual patients were collected in the form of age, sex, mode of injury, mode of transportation, distance from the hospital, Care providers, Safety equipment used by the vehicle, duration in reaching the hospital, pre-hospital care, Glasgow Coma Scale (GCS), saturation of peripheral oxygen (SpO₂), systolic blood pressure (SBP) at admission and Glasgow Outcome score (GOS) at time of discharge. Based on GCS, TBI cases were graded as mild (13-15), moderate (9-12), and severe (<8). This neurosurgical center is one of the leading institutes of India and Asia catering to both urban and rural populations.

After researching various literature published, we could conclude that this study is one of the largest in the world and is unique with maximum variations in population.

RESULTS

During the period from April 2017 to March 2019 data from 2134 TBI patients was collected. The mean age was 31.65± 15.1 years. In our study 69.89% were males and 31.11% were females (**Table 1**). Males were 2.21 times more common than females. Most patients affected were in the age group of 21–30 years (29.42%) followed by 31–40 years (22.68%). Road traffic injury (64.45%) was seen as the most common mode of injury in the age group 21–30 years (81.36%) followed by injury due to fall (21.41%) which mostly affected the age group of 0–10 years

(71.44%) and above 60 years (33.80.%) (Table 2). Most of the patients were attended by the members of public as a first responder (77.41%) (Table 3) and transported to definitive treatment centers in ambulances (66.82%) (Table 4) but most of them not received care in the form of vitals monitoring, intravenous (IV) fluid administration and airway protection at the site of trauma and during transportation. Safety devices such as helmets, seat belts, and child restraint were used in 27.03% patients only (Table 5). Alcohol consumption while driving is 14.53% (Table 6). Time duration to reach definitive treatment centers was <1 hour in 3.13% of patients, between 1 and 4 hours in 16.16% of patients, between 4 and 12 hours in 56.04% and >12 h in 24.65% of patients (Table 7). 32.29%, patients were primary referrals, and 67.71%, patients were secondarily referred to our study center (Table 8). The overall mild injury was seen in 49.11% cases, moderate in 31.02%, and severe in 19.87% (Table 9).

Table 1. Different age groups and outcome

Age in years	The total no. of cases n (%)	Out come Alive Death n=1901(%) n=233 (%)	
Age yrs.(mean)	31.65± 15.1	33.24 ± 14.5	41.36 ± 17.8
0-10	191(8.95)	183 (8.58)	8(4.18)
11-20	233(10.91)	221 (10.36)	12(5.15)
21-30	628(29.42)	554 (25.96)	74(11.78)
31-40	484(22.68)	428 (20.06)	56(11.57)
41-50	232(10.87)	192 (8.99)	40(17.24)
51-60	153(7.17)	139 (6.51)	14(9.15)
>60	213(9.98)	184 (8.62)	29(13.61)
Total Male	1470(68.89)	1311(89.19)	159(10.81)
Female	664(31.11)	590(88.85)	74(11.14)

Table 2. Incidence of mode of injury in different age groups

Age (years)	Total cases n(%) n=2134	mode of injury				
		RTA n(%)	Fall n(%)	Assault n(%)	Sports n(%)	Others n(%)
0-10	191 (8.95)	41 (21.47)	130 (68.06)	Nil	12 (6.28)	8 (4.19)
11-20	233 (10.92)	128 (54.93)	54 (23.17)	15 (6.43)	24 (10.3)	12 (5.15)
21-30	628 (29.43)	511 (81.36)	43 (6.85)	29 (4.61)	5 (0.79)	40 (6.36)
31-40	484 (22.68)	357 (73.76)	69 (14.26)	34 (7.02)	Nil	24 (4.96)
41-50	232 (10.87)	144 (62.06)	54 (23.27)	26 (11.20)	Nil	8(3.44)
51-60	153	71	35	45	Nil	2(1.31)

	(7.17)	(46.41)	(22.87)	(29.41)		
>60	213 (9.98)	124 (58.21)	72 (33.80)	13 (6.10)	Nil	4 (1.88)
Total	2134 (100)	1376 (64.48)	457 (21.41)	162 (7.59)	41 (1.92)	98 (4.60)

Table 3. First emergency care provider

Care providers	No of patient n (%)	Outcome Alive Death n(%) n (%)	
Member of public	1652 (77.41)	1485 (89.89)	90 (80.35)
Ambulance officer or paramedic	123 (5.76)	116 (94.30)	7(5.69)
Relatives	247 (11.57)	210 (85.02)	37 (14.98)
Medical retrieval team	Nil	Nil	Nil
Unknown	112 (5.24)	90 (80.35)	22 (19.64)

Table 4. Mode of transportation

Mode	First Hospital Total no of cases N=1445(%)	Study center Total no of cases n(%)	Outcome Alive Death n(%) n(%)	
Ambulance	432 (29.90)	1426 (66.82)	398 (92.13)	34 (7.8)
Private vehicle	1013 (70.10)	708 (33.18)	1503 (88.30)	199 (11.69)

Table 5. Safety equipment used

Equipment	No of patient n(%)	Outcome Alive Death n(%) n(%)	
Helmet- Urban	204(20.90)	189(92.64)	15(7.35)
Rural	139(68.13)	131(94.24%)	8(5.76%)
Seatbelt	65(31.87)	58(89.23%)	7(10.77%)
Seatbelt	168(78.50)	157(93.45)	11(6.54)
Child restraint	Nil	nil	Nil
Unknown	495(23.20)	447(9.03)	48(96.97)

Table 6. Substance abuse

	No of patient n(%)	Outcome Alive Death n(%) n(%)	
Alcohol involvement	310(14.53)	243(78.39)	67(21.61)
Alcohol breath on admission	213(10.00)	184(86.38)	29(13.62)

Drug involvement	10(0.47)	8(80.00)	2(20.00)
Using mobile phone at time of accident	43(2.00)	35(81.40)	8(18.60)
Prior head injury	43(2.00)	33 (76.74)	10(23.25)
Multiple addiction	46(2.16)	33(71.74)	13(28.26)
None	1469(68.84)	1365(92.92)	104(7.08)

Table 7. Time to arrival at hospital

Time to arrival at hospital	First hospital n (%)	Study center n (%)	Outcome	
			Alive, n(%)	Death, n(%)
-				
<1 hrs	1364(63.92)	67 (3.13)	59 (88.05)	8 (11.94)
1-4 hrs	585 (27.41)	345 (16.16)	328 (95.07)	17 (4.92)
4-12 hrs	123 (5.76)	1196(56.04)	1040 (86.96)	156 (15.00)
>12 hrs	62 (2.91)	526 (24.65)	474 (90.11)	52 (09.89)

Table 8. Correlation of SBP and SpO2 and outcome

Systolic blood pressure	No of patient (%)	Outcome	
		Alive, n(%)	Death, n(%)
>90 mmHg	1885(88.33))	1745(92.57)	140(7.43)
<90 mmHg	249(11.69)	156(8.20)	93(37.35)
SpO2 -			
<90%	339(15.89)	216(63.72)	123(36.28)
>90%	1785(84.11)	1675(93.84)	110(6.16)
First CT			
Primary hospital	456(21.36)	425(93.20)	31(6.79)
Study center	1678(78.63)	1476(87.96)	202(12.03)
Referral -			
Primary	689(32.29)	632(91.73)	57(8.27)
Secondary	1445(67.71)	1269(87.82)	76(12.18)

Table 9. Severity of injury

GCS on admission	Total no of cases, n (%)	Outcome	
		Alive, n (%)	Deaths, n (%)
Mild (13-15)	1048 (49.11)	1036(98.85)	12 (1.1)
Moderate (9-12)	662(31.02)	608(91.84)	54 (8.15)
Severe (<8)	424 (19.87)	257(60.61)	167(39.38)

DISCUSSION

With rapid industrialization, the cases of TBI are rising, and so does its severity. But the advancement

in pre-hospital care is lacking in developing countries. Different studies have shown that early resuscitation and pre-hospital care are cardinal to better outcomes in TBI. Mortality and morbidity of the severely injured patient can be reduced significantly by directly transporting them from the scene to Level I trauma centers. Early identification and prompt management lead to a better survival rate in cases of TBI. This can be achieved through pre-hospital care which was non-existent in India.⁶⁻⁸

In our study, the incidence of head injury was highest in the age group 21-30 years i.e. 29.42% and commonest mode of injury were as RTA in 64.45% cases followed by fall from height in 21.41%. Similar studies conducted by Meena et al.⁹ and Phonprasert et al.¹⁰ showed 69.52% and 58% of cases were due to RTA respectively. Gururaj et al.¹¹ in his study claimed 60% of cases were due to RTA and 20-25% cases were of falls. Thus, RTA was found to be the most common mode in almost all studies.⁹⁻¹¹ It was most probably due to excessive congestion of traffic on roads, less traffic sense, poor conditions of the road, not using helmet by bike riders, and not following the road traffic rules.

Alcohol consumption while driving is also a contributing factor for increasing RTAs in young adults. In studies by Esser et al.¹² and Gururaj¹³ the percentage of alcohol consumption was 17.9% and 14.50% respectively which is comparable to our study which is 14.53%. The patient using a helmet more often sustain milder head injuries, whereas, a patient without a helmet was having more severe injuries. Alcohol consumption was associated with more severe head injuries and high mortality of 21.61% compared to 7.08% in patients not using any drug and alcohol.

In our study private vehicle was the most common mode of transport at the first hospital while the ambulance was the most common mode at the study center. There was clearly a decrease in mortality of patients transported by ambulance (7.80%) than by private vehicle (11.69%), the difference was due to early identification and less time taken to reach the hospital and early treatment resulting in decreased secondary insults.

Prevention of hypoxia and hypotension is of utmost importance with the maintenance of cerebral perfusion. The presence of leads to multiple cascades of events leading to increased cerebral edema decreased cerebral perfusion, decreased

tissue, and vital organ perfusion. These all contribute to poor outcomes. In our study patients with SBP, less than 90 mmHg on admission had a mortality of 37.35% than patients with SBP, more than 90 mmHg 7.43 % mortality. The mortality in patients with SPO2 less than 90% was 36.28% compared to 6.16% in patients with SpO2 above 90%. Our study suggested that most of the primary or first hospitals overlooked the importance of monitoring oxygen saturation and blood pressure with increased chances of missing hypoxia, hypotension, thereby undervaluation of important secondary changes in the brain ultimately increasing the risk of worse outcomes. In the primary hospital CT scan had done in 21.36% and mortality 6.79% and study center 78.63% and mortality 12.03 %. Patients with their CT brain done at the first hospital within 4 hours after injury performed better. Early CT brain is a critical step in managing TBI cases with early information about operative intervention required, thus preventing further insult to the brain. Thus it is very critical for the emergency staff to be well versed with an indication of CT brain in trauma patients. For providing good pre-hospital care there are needs for intensive training of medical personnel and adequate resources at primary and secondary level health care facilities.

Time lapsed in reaching the hospital is also a significant factor determining the outcome. There is a major part of critical time lost in transportation. The prognosis of TBI is excellent if the patients get appropriate treatment in the golden hour. Our study noted that around 3.13%, 16.16%, 56.04%, and 24.65% of patients reached the hospital in less than 1 hour, 1-4 hour, 4-12 hour, and more than 12 hours respectively. In a comparative study by Gururaj,¹³ only 25% reached hospital within 3 hours and 20% reached after 24 hours. The time interval between the time to arrive at the injury site and the hospital is one of the deciding factors between life and death. The overall mortality was found to be 10.92% as compared to 16% by both Phonprasert et al.¹⁰ and Narwade et al.¹⁴

The maximum severity of the injury was shifted to the hospital by private vehicle, without any vital monitoring. It was observed that mild, moderate, and severe TBI cases were 49.11%, 31.02%, and 19.87% respectively. A study by Natarajan et al.¹⁵ showed the total number of mild, moderate, and severe injuries were 42%, 30%, and 28%, respectively. In our study, it was observed that

mortality was highest in severe TBI (39.38%) and 1.1% in mild TBI.

In our study patient, mortality was 6.79% in patients receiving pre-hospital care compared to patients 12.03% in patients not receiving adequate pre-hospital care. This clearly signifies that pre-hospital care is a crucial step in managing TBI patients.

Chennai had 8.16% mortality, Bangalore had 8.6% and 5.5% mortality rate in 2002 and 2005 respectively whereas the mortality rate in Delhi was 10.49%. In recent years the mortality has decreased due to the availability of better health care facilities. With intensive studies and data registry in the USA and other western countries, they have formed better pre-hospital guidelines for trauma patients thus are able to avoid preventable deaths and disability.

Our study showed that patient with TBI need aggressive management in the form of, victims reaching the hospital in the shortest possible time, taking care of airway by use of laryngeal mask/endotracheal tube intubation, oxygenation and iv infusion for maintaining perfusion pressure for prevention of secondary brain injuries like hypoxia, hypotension, and cerebral edema. We can apply this data to develop new action plans and public awareness programs and developing adequate neurotrauma care protocols for aggressive management of patients with poor admission GCS score.

CONCLUSION

It is recommended that essentially, the outcome in TBIs can be improved by attending to priorities of reaching the victims in the shortest possible time, and evacuating them to hospital, taking care of airway, oxygenation and maintaining total perfusion pressure through judicious IV infusions. Depending upon the skills of Emergency Medical Technician / Paramedic, the use of Laryngeal Mask Airway / Endotracheal Tube can be considered. Infrastructure in the form of dedicated trauma centers, well-equipped ambulances with trained trauma staff, should be developed.

ABBREVIATION

TBI- Traumatic brain injury, ICU- intensive care unit, GOS- Glasgow Outcome Score, GCS- Glasgow Coma Scale, SBP- systolic blood pressure, SpO2 - saturation of peripheral oxygen.

FINANCIAL SUPPORT AND SPONSORSHIP

Nil

CONFLICTS OF INTEREST

There are no conflicts of interest.

REFERENCES

1. WHO. World Report on the road Traffic Injury Prevention. Geneva: World Health Organization; 2004.
2. Maas AI, Stocchetti N, Bullock R. Moderate and severe traumatic brain injury in adults. *Lancet Neurol*. 2008;7:728-41.
3. Stocchetti N, Paterni R, Citerio G, Beretta L, Colombo A. Traumatic brain injury in an aging population. *J Neurotrauma*. 2012;29:1119-25.
4. Boulger, C. T., & Werman, H. A. (2010). Controversies in emergency medical services. *Emergency Medicine Reports*, 31(7), 77-87.
5. Badjatia, N., Carney, N., Crocco, T. J., Fallat, M. E., Hennes, H. M. A., Jagoda, A. S., Wright, D. W. (2007). Guidelines for the prehospital management of traumatic brain injury. *Prehospital Emergency Care*, 12(1), S1-S52.
6. Sampalis JS, Denis R, Fré Chette P, Brown R, Fleischer D, Mulder D. Direct transport to tertiary trauma centers versus transfer from lower level facilities: impact on mortality and morbidity among patients with major trauma *J Trauma* 1997; 43:288-95.
7. Dash HH. Pre-hospital care of head injured patients. *Neurol India* 2008; 56:415-9.
8. Saxena MK, Sahoo S, Vibha P, Rahman A. Pre-hospital determinants of outcome in traumatic brain injury: Experiences from first comprehensive integrated prehospital care providers in India: GVK - EMRI experience. *Indian J Neurotrauma*. 2010;7:129-34.
9. Meena US, Gupta A, Sinha VD. Prehospital Care in Traumatic Brain Injury: Factors Affecting Patient's Outcome. *Asian J Neurosurg*. 2018;13(3):636-639.
10. Phonprasert C, Suwanwela C, Hongsaprabhas C, Prichayudh P, O'Charoen S. Extradural haematoma: analysis of 138 cases. *J Trauma*. 1980;2:679-83.
11. Gururaj G. Road traffic deaths, injuries and disabilities in India: Current scenario. *Natl Med J India*. 2008;21:14-20.
12. Esser MB, et al. Characteristics associated with alcohol consumption among emergency department patients presenting with road traffic injuries in Hyderabad, India. *Injury* (2015).
13. Gururaj G. Epidemiology of traumatic brain injuries: Indian scenario. *Neurol Res*. 2002;24:24-8.
14. Narwade N, Narwade P, Ghosalkar M, Shaikh TP, Sharma Y, Khan N, Ansari S. Clinical profile and management of head injury at tertiary health care center in rural area, India. *Int J Res Med Sci* 2015;3:3137-40.
15. Natarajan M. Adjustmental Problems of Head Injured Patients, Indian Council of Medical Research, 1987.



Encephalitic syndrome revealing cerebral gliomatosis in an adolescent

Si Ahmed Hakim, Daoudi Smail

Department of Neurology. CHU Tizi-Ouzou. ALGERIA

ABSTRACT

Cerebral gliomatosis is a rare glial tumour which is defined by a diffuse and not very destructive infiltration of the encephalon by the glial neoplastic cells in the absence of individualizable tumour mass (Sanson et al., 2005).

The clinical and radiological presentation is often misleading and not very specific, and the diagnosis is rarely mentioned. Histological diagnosis remains difficult. Finally, gliomatosis poses a specific therapeutic problem compared to other glial tumours due to the toxicity of panencephalic radiotherapy and the impossibility of achieving surgical reduction of the tumour (Sanson et al., 2005).

Data from the literature show a median overall survival of 14.5 months, a higher frequency of oligodendroglial forms. The prognosis is linked to age, functional status, histological grade, oligodendroglial differentiation (Sanson et al., 2005).

We report the observation of a gliomatosis occurring in a 14-year-old boy, having presented focal subintra epileptic attacks accompanied by hemiparesis. Flair sequence brain MRI showed a left fronto-temporo-insular hyper signal. The brain biopsy revealed gliomatosis. The evolution was favourable after radiotherapy. Gliomatosis is a diagnosis to be systematically evoked in the presence of a diffuse cerebral affection. Its etiopathogenic mechanism is unknown, and evolution is unpredictable (Millan. BS et al., 2010).

INTRODUCTION

Cerebral gliomatosis is a condition initially described by Nevin in 1938 (Nevin et al., 1938), characterized by diffuse infiltration of glial tumor cells invading a large part of the brain, bilaterally (possibility also of the marrow), with absence of individualizable tumor mass (Nevin et al., 1938).

It is a rare neurosurgical pathology, since less than 300 cases are reported in the literature (Sanson et al., 2005), which can occur at any age, more frequently in adults between 40 and 50 years (MILLAN. BS et al., 2010). The clinical signs are non-specific and the imagery is often misleading, which can simulate a large number of non-neoplastic neurological medical pathologies (inflammatory or infectious encephalitis, angeitis, leukodystrophies) (Sanson et al., 2005). Its radiological and histological diagnosis is difficult because of the absence of identifiable tumor mass and its diffuse character. (MILLAN. BS et al., 2010). Gliomatosis also poses a problem of specific therapeutic

Keywords

encephalitic syndrome,
cerebral gliomatosis,
adolescent



Corresponding author:
Si Ahmed Hakim

Department of Neurology. CHU Tizi-
Ouzou, Algeria

siahmed-hakim@hotmail.fr

Scan to access the online version



management by comparing them to other glial tumors (its diffuse nature, surgery is excluded, radiotherapy is poorly tolerated since it often involves the entire brain, chemotherapy is possible unlike other gliomas) (Sanson et al., 2005).

We report a case of gliomatosis in a 14-year-old boy, diagnosed in pre-mortem using MRI and brain biopsy data, the clinical and radiological picture of which was misleading, simulating an acute limbic encephalitis picture.

OBSERVATION

A 14-year-old boy immediately developed serial, drug-resistant focal seizures with temporal spread, and then developed right hemiparesis. The examination showed right hemiparesis, with no disturbance of consciousness, no signs of intracranial hypertension, or meningeal syndrome.

Magnetic resonance imaging (MRI) revealed a hyper signal on the Flair and T2 sequences, without contrast enhancement, unilateral, on the left, touching the fronto-temporo-insular white matter (Fig. 1). The GES highlighted left hemispherical brain pain, without paroxysms (Figure 2). The cytochemical study of the CSF revealed a slight hyperproteinorachia at 0.5 g / l, as well as a lymphocytosis at 30 elements / mm³, and the immunological study did not show a chronic inflammatory process. All serologies were negative (Herpes, HTLV1, syphilis, HIV, Lyme ...), and the autoimmunity balance was also negative.

The patient received Methylprednisolone IV (1g / day for 5 days) with an oral relay (1mg / kg / day), combined with anti-epileptics (Levetiracetam 3g / day, Lamotrigine 200mg / day). The evolution was marked by a persistence of the epilepsy attacks, an appearance of headache and oculomotor disorders (diplopia, left exophthalmia), see obnubilation. Control MRI showed an aggravation of the lesions with mass effect and bilateralization of the hyper signal (Figure. 3). The brain biopsy was done urgently and returned in favor of a gliomatosis (oligodendrogiale). The child was treated with radiotherapy, with disappearance of disturbances of consciousness and seizures, and persistence of hemiparesis.

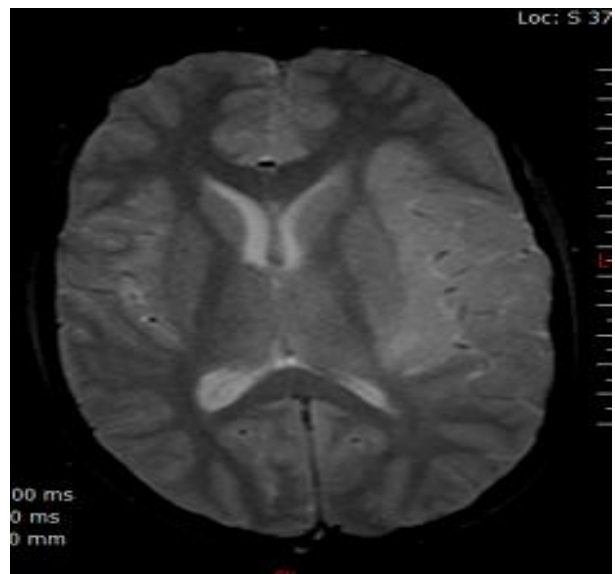
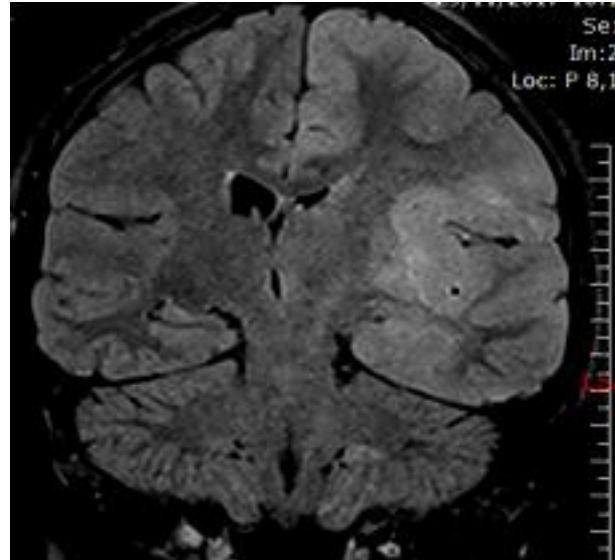


Figure 1. Cerebral MRI: a: coronal section, Flair sequence / b: transverse section, T2 sequence: left fronto-temporo-insular hyper signal.

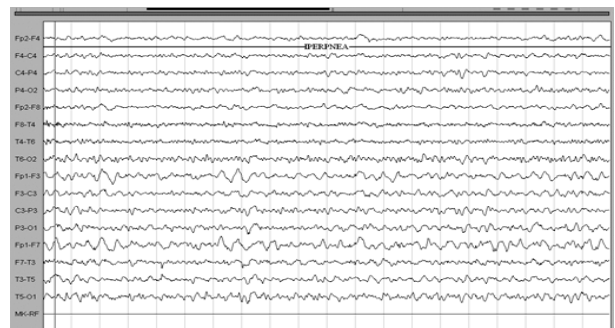


Figure 2. EEG. Left hemispherical pain (theta delta waves more marked on the left anterior regions).

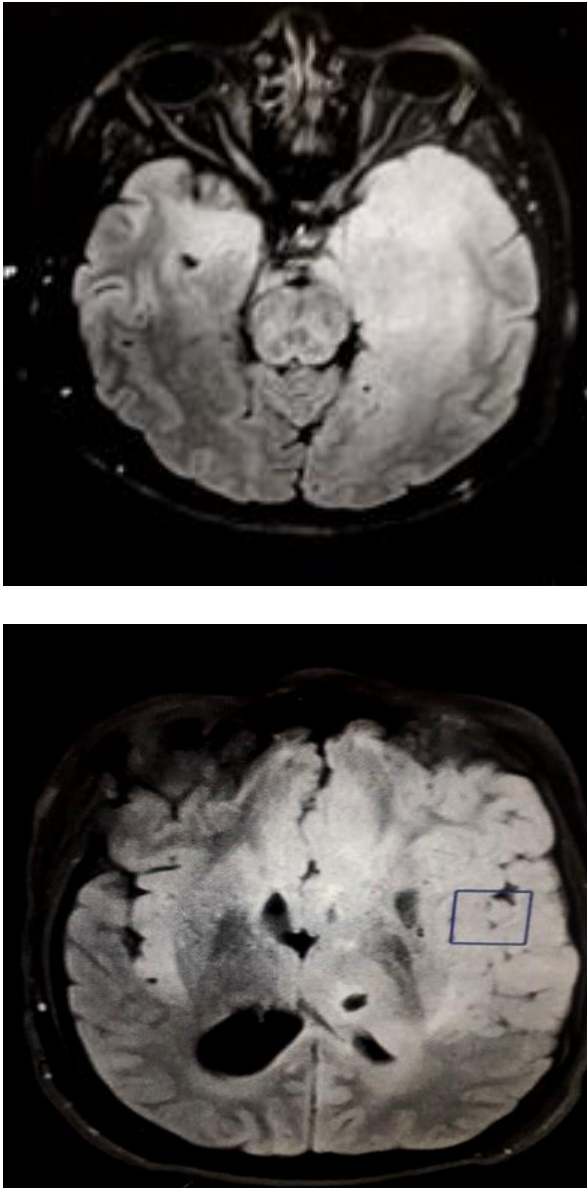


Figure 3. Control brain MRI (FLAIR sequences, cross section): extensive hyper signal affecting the fronto-temporo insular white matter, bilaterally, with mass effect.

DISCUSSION

We report a case of cerebral gliomatosis, the diagnosis of which was based on imaging and brain biopsy data and whose evolution was favorable with disappearance of epilepsy attacks, improvement in disorders of consciousness and hemiparesis.

Primary gliomatosis often poses diagnostic difficulties because its clinical presentation is not very specific. The most frequent modes of revelation were epilepsy, the occurrence of cognitive disorders, intracranial hypertension (headache), the presence of focal deficits (ARTIGAS. J, et al., 1985, Sanson et al.,

2005). It was in 1986 that the first premortem diagnosis of gliomatosis was made on the combined brain biopsy and MRI data (Troost D, et al., 1987). The incidence is higher in humans (in fact common to all gliomas) (Sanson et al., 2005) and, more specifically in gliomatosis, a younger age of onset in humans (Jennings et al., 1995).

In MRI, the Flair and T2 sequences are essential, they show an extended bilateral hyper signal of white matter and gray nuclei, which can extend to the brainstem and the spinal cord (Peretti-Viton P, et al., 2002), and gadolinium intake is generally absent (Sanson et al., 2005). It is defined as "an infiltrating process, encompassing at least three lobes, without contrast enhancement or less than 1 cm" (Sanson et al., 2004). The brain scan, including with injection, may be normal, but a careful examination may show suggestive abnormalities (discrete ventricular asymmetry, discrete poorly limited hypodensity, appearance of diffuse cerebral edema with small ventricles, and diffuse erasure of the furrows, or, in an elderly patient, the absence of atrophy of the brain scanner) (Sanson et al., 2005). The diagnoses most often mentioned were: multiple sclerosis, leukoencephalopathy of unknown cause, encephalitis, progressive multifocal leukoencephalitis, vasculitis, Behçet's disease (Sanson et al., 2005). Although not specific, certain aspects are suggestive of gliomatosis: the presence of a discrete mass effect, the thickening of the corpus callosum, the asymmetrical character of the hypersignal, the heterogeneous and "flaky" character of the hypersignal, better visible in T2 as in FLAIR, the associated impairment of the gray matter, in particular of the thalamus and the loss of the boundaries between the white matter and the gray matter (Sanson et al., 2005).

The clinical and radiological differential diagnosis includes all diffuse encephalopathies of various causes (infectious, vascular metabolic and tumor) (Peretti-Viton P, et al., 2002). This is the case of our patient who presented a misleading picture with clinical and para-clinical signs (MRI, EEG, CSF) of acute limbic encephalitis.

The diagnosis by histological study by biopsy is still essential, but often proves difficult, and sometimes non-contributory due to the low cell density, and the preservation of the normal architecture (Sanson et al., 2005). The histological grade is sometimes difficult to determine (Sanson et

al., 2004). (astrocytic, oligodendroglial, polymorphic aspect...). According to the literature, oligodendroglial gliomatosis is considered rare (Balko et al., 1992), unlike some authors where the majority of gliomatosis is of oligodendroglial type (Sanson et al., 2005), as was observed in our patient. The extremely diffuse aspect of tumor infiltration could explain the fact that the brain biopsy is sometimes not very contributory. Glioma cells do not have the capacity to cross the vascular basement membrane (limiting metastases by hematogenous or lymphatic route) (Tonn et al., 2003), but they have the capacity to migrate very far into the neuron (Tonn et al., 2003; Bellail et al., 2004).

Spontaneous evolution is extremely variable ranging from less than 1 month to 16 years (Artigas, 1985, Cervos-Navarro, 1987, Louis. DN, et al., 2007). Survival appears to be linked primarily to clinical factors: gender, age and Karnofsky's functional index. The prognosis also appears to be linked to histological characteristics (Sanson et al., 2005). Our case had a favorable evolution with follow-up for 08 months, marked by a regression of clinical signs (epilepsy attacks, disturbances of consciousness, oculomotor disorders). The criteria which seem in favor of a good evolution are criteria of clinical response (disappearance of convulsions, regression of cognitive disorders and headache) or radiological (reduction of the range of the hyper signal, regression of the mass effect) (Sanson et al., 2004, 2005).

Exeresis is not possible because of the extent of gliomatosis (Sanson et al., 2005), and radiotherapy has a major neurotoxicity, since it often involves the entire brain (Crossen et al., 1994). This is why some authors have proposed treating these patients with chemotherapy alone as first-line treatment, which has the advantage of better tolerance (Sanson et al., 2004).

REFERENCES

1. Artigas. J, Cervos-Navarro. J, Iglesias. Jr, et al. Gliomatosis cerebri: clinical and histological findings. *Clin Neuropathol* 1985;4:135—48.
2. Balko. Mg, Blisard. Ks, Samaha. Fj. (1992). Oligodendroglial gliomatosis cerebri. *Hum Pathol*, 23: 706-707.
3. Bellail. Ac, Hunter. Sb, Brat. Dj, Tan. C, Van Meir. Eg. (2004). Microregional extracellular matrix heterogeneity in brain modulates glioma cell invasion. *Int J Biochem Cell Biol*, 36: 1046-1069.
4. Cairncross. Jg, Ueki. K, Zlatescu. Mc et al. (1998). Specific genetic predictors of chemotherapeutic response and survival in patients with anaplastic oligodendrogliomas. *J Natl Cancer Inst*, 90: 1473-1479.
5. Galanaud. D, Chinot. O, Nicoli. F et al. (2003). Use of proton magnetic resonance spectroscopy of the brain to differentiate gliomatosis cerebri from low-grade glioma. *J Neurosurg*, 98:269-276.
6. Hoang-Xuan. K, He. J, Huguet. S et al. (2001). Molecular heterogeneity of oligodendrogliomas suggest alternative pathways in tumoral progression. *Neurology*, 57: 1278-1281.
7. Jennings. Mt, Frenchman. M, Shehab. T, Johnson. Md, Creasy. J, Laporte. K, Dettbarn. Wd. (1995). Gliomatosis cerebri presenting as intractable epilepsy during early childhood. *J Child Neurol*, 10: 37-45.
8. Lantos. Pl, Bruner. Jm. (2000). Gliomatosis cerebri in Tumours of the Nervous system. Kleihues and Cavenee Ed, IARC Lyon, pp. 92-93.
9. Louis. DN, Ohgaki. H, Wiestler. OD, Cavenee. WK, editors. Gliomatosis cerebri. Lyon; 2007, p. 50—2.
10. Millan. Bs, Kaci. R, Polivka. M, Robert. G, Heran. F, Gueguen. A, Mokhtari. K, Gray. F. Gliomatose cérébrale diffuse : étude biopsique et autopsique d'un cas. *Annales de pathologie* (2010) 30, 25—29.
11. Nevin. S. (1938). Gliomatosis cerebri. *Brain*, 61: 170-191.
12. Peretti-Viton. P, Brunel. H, Chinot. O, et al. Histological and MR correlations in Gliomatosis cerebri. *J Neurooncol* 2002;59:249—59.
13. Sanson. M, Cartalat-Carel. S, Taillibert. S et al. (2004). Initial Chemotherapy in Gliomatosis Cerebri. *Neurology*, 63: 270-275.
14. Sanson. M, Napolitanon. M, Cartalat-Carel. S, Taillibert. S. La gliomatose cérébrale. *Rev Neurol (Paris)* 2005; 161: 2, 173-181.
15. Tonn. Jc, Goldbrunner. R. (2003). Mechanisms of glioma cell invasion. *Acta Neurochir Suppl*, 88: 163-167.
16. Troost. D, Kuiper. H, Valk. J, et al. Gliomatosis cerebri, report of a clinically diagnosed and histologically confirmed case. *Clin Neurol Neurosurg* 1987;89:43—7.1987.



Brain radionecrosis after radiation therapy for atypical meningioma. An unexpected treatment outcome. Case report

Ebtesam Abdulla¹, Harleen Luther², Tejal Shah³, Nisha Chandran⁴

¹ BSc, MD Neurosurgery Resident, Department of Neurosurgery, Salmaniya Medical Complex, Manama, BAHRAIN

² M.S, M.Ch, Neurosurgery Consultant, Department of Neurosurgery, Salmaniya Medical Complex, BAHRAIN

³ MD, Radiology Consultant, Department of Radiology, Salmaniya Medical Complex, Manama, BAHRAIN

⁴ MD, Histopathology Specialist, Department of Anatomical Pathology, Salmaniya Medical Complex, Manama, BAHRAIN

ABSTRACT

Introduction. Atypical Meningioma (AM) is at high risk of local failure. The role of radiation therapy (XRT) as an adjuvant to surgical resection is incompletely defined. The most deleterious consequence of brain-directed XRT is radiation necrosis. Brain radionecrosis (BRN) after AM has been rarely reported. The relevant literature is reviewed, highlighting its diagnostic challenges.

Case presentation. We report a 25-year-old male with a BRN after adjuvant XRT for AM, which has been misdiagnosed as a recurrent neoplastic lesion upon magnetic resonance spectroscopy (MRS) examination. Surgery and histopathological description were made and yielded a definitive diagnosis of BRN. The patient was treated by dexamethasone with concomitant hyperbaric oxygen therapy (HBO2). The patient showed a further progression of the disease. Therefore, he was elected to receive bevacizumab. However, the patient finally died for refractory brain edema.

Conclusion. BRN is a relatively rare instance after XRT for AM. There is no single modality that can reliably distinguish BRN from tumour recurrence. Therefore, reaching an early prompt treatment decision is challenging.

INTRODUCTION

Meningiomas are extra-axial tumors that represent 30% of all primary brain tumors (1). The most common locations are along the cerebral falx and over the cerebral convexity, such in the case reported here (2). AM falls under the World health organization (WHO) Grade II tumors, accounting for 20% of all meningiomas (1-3). The distinction of AM is given to the meningeal tumor that exhibits high mitotic rate and brain invasion (1, 3). The median age for AM patients at diagnosis is 56 years (3). AM has a female predominance and a high predilection for recurrence (1-3).

Keywords

atypical,
meningioma,
radiation necrosis,
radiotherapy,
resection,
spectroscopy



Corresponding author:
Ebtesam Abdulla

Department of Neurosurgery,
Salmaniya Medical Complex,
Manama, Bahrain

Dr.Ebtesam@hotmail.com

Scan to access the online version



Currently, AM's treatment guideline entails the combination of maximum safe surgical resection and XRT (1-3). Despite the absence of solid evidence to support XRT for AM, several studies have reported encouraging results (1, 2). XRT has been shown to improve AM prognosis with a median 5-year progression-free survival of 54.2% ranging from 38% to 100% after XRT (1). Nevertheless, XRT carries a risk of radiation necrosis (1, 4-16).

Herein, we report a case of BRN after adjuvant XRT for AM, which has been misdiagnosed as a recurrent neoplastic lesion upon the MRS examination.

CASE PRESENTATION

A 25-year-old male presented with a nine-month history of intermittent headache, described as 'generalized pressure' and dizziness. The symptoms had become more severe, and weakness on the left side extremities started to progress over the last week. The vital signs were stable, and the patient was fully conscious. Neurological examination showed no abnormality aside from mild left hemiparesis (Grade 4/5 Medical Research Council).

Cranial computed tomography (CT) scan revealed an enhancing extra-axial mass in the right frontal region, which contained multiple foci of calcification. There was significant peritumoral edema. Cranial magnetic resonance imaging (MRI) showed an iso-intense mass, with an area of low-intensity corresponding to the calcification observed on the CT scan (**Fig. 1**). Magnetic resonance arteriogram and magnetic resonance venogram showed multiple feeding arteries mainly from the anterior cerebral arteries and, to a lesser extent, from the distal right middle cerebral arteries with multiple, prominent draining veins. Based on the radiographic appearance, a diagnosis of right frontal convexity meningioma was made.

The patient underwent a craniotomy with total resection of the mass. The postoperative Cranial CT scan reported no residual tumor with a regression of brain edema (**Fig. 2**). The histopathology was AM (WHO grade II) (**Fig. 3**). This case discussed in the multidisciplinary tumor board. Accordingly, the patient was referred for XRT for a total dose of 60-Gy (30 fractions of 2-Gy) over six weeks duration, all delivered with intensity-modulated technique.

The patient reported new-onset of generalized seizures and worsening of left hemiparesis (Grade

3/5 Medical Research Council) three months after completion of XRT. An electroencephalogram revealed epileptic discharges over the right frontal derivations. Cranial MRI reported an iso-signal poorly defined lesion in T1 and T2 sequences compromising the right frontal lobe with extensive central necrosis and peri-lesional edema (**Fig. 4**). Additionally, a ring, cut green-paper enhancement, was seen involving the genu of the corpus callosum (**Fig. 4**). A confirmatory MRS study was used. The metabolites studied were choline (Cho), which appeared at 1.4ppm, N-acetyl aspartate (NAA) at 0.65ppm, creatine (Cr) at 0.6ppm, and lipid at 1.3ppm (**Fig. 5**). Using multi-voxel MRS, the Cho/NAA ratio > 2.15 and Cho/lipid > 1 were favoring a recurrent neoplastic lesion.

Nonetheless, surgery and histopathological description were made and yielded a definitive diagnosis of pure BRN (**Fig. 6**). The lesion was non-vascular and intra-axial involving the right frontal lobe parenchyma and deep, abutting the frontal horn of the lateral ventricle. The patient had improvement of neurologic function after surgical resection.

However, the patient was readmitted due to breakthrough seizures and worsening of left hemiparesis. A high dose of dexamethasone was initiated with concomitant HBO2. The patient showed a further progression of the disease. Thus, he was elected to receive four cycles of 5mg/kg Bevacizumab intravenously every two weeks. However, the patient finally died for refractory brain edema.

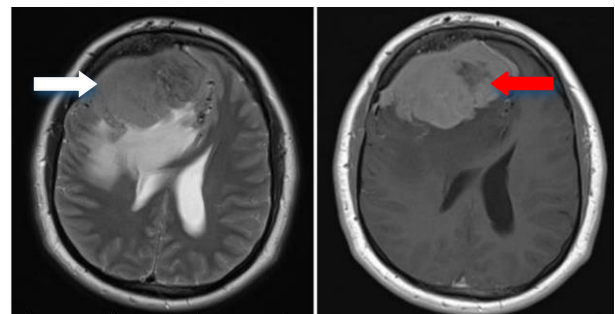


Figure 1. Preoperative, MRI brain of the lesion showing iso-intense signal (White arrow) in the T2-weighted sequence. The tumor homogeneously enhanced with areas of central hypointensity (Red arrow) in post-contrast, T1-weighted images.

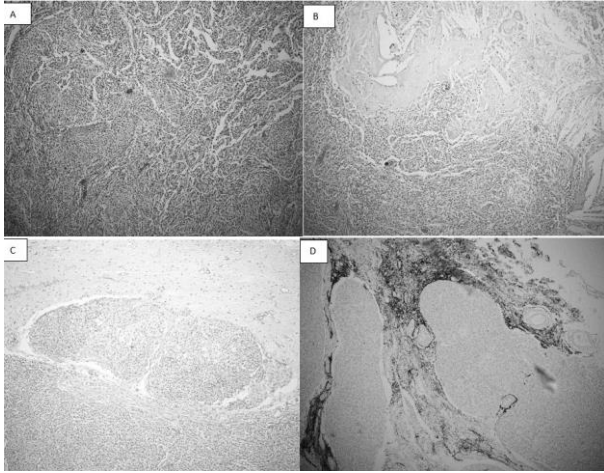


Figure 2. Sections from atypical meningioma show syncytial pattern along with areas of necrosis,10X(A&B). Brain invasion noted in H&E stain and highlighted by GFAP immunostain,10X(C&D).

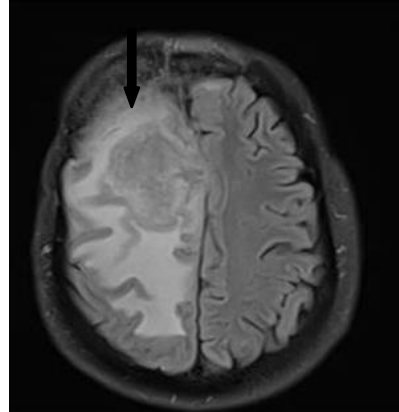


Figure 4. MRI brain of the lesion showing an ill-defined, peripheral enhancing lesion (White arrow) with central necrosis in post-contrast, T1-weighted sequence. The genu of the corpus callosum was also enhanced (Red arrow)—the lesion iso-intense (Black arrow) in the T2-weighted sequence, surrounded by extensive, vasogenic edema.

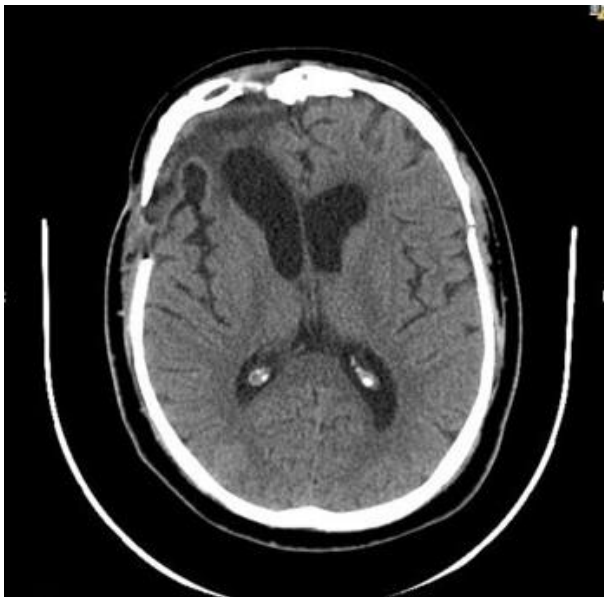


Figure 3. A Postoperative CT scan of the brain showing total excision of the tumor with regression of brain edema.

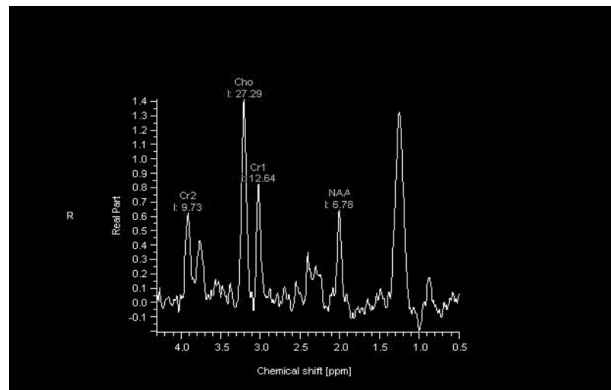


Figure 5. Magnetic resonant spectroscopy showed a high elevation of Cho and depression of NAA.

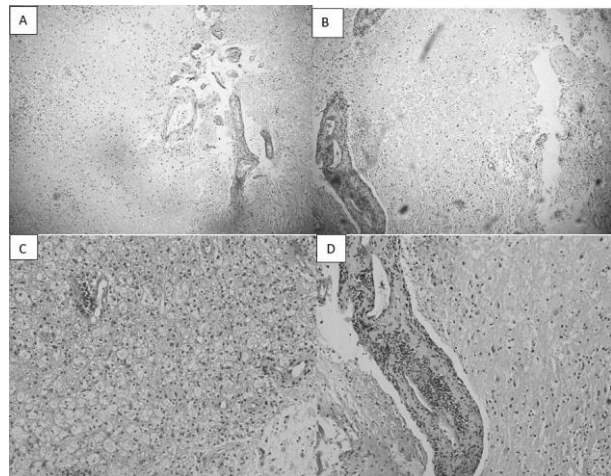
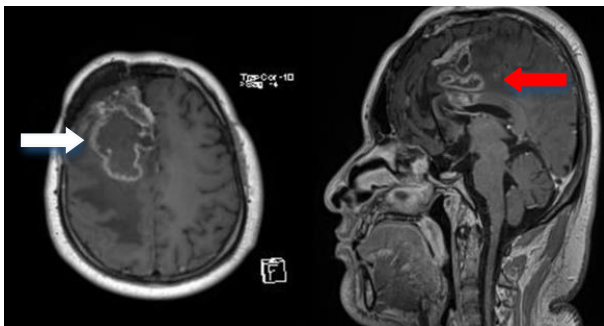


Figure 6. Post RT resection specimen is entirely submitted, and sections show areas of necrosis, mixed inflammation,10x(A&B).

Infiltration by foamy histiocytes, 20x(C) and vasculitis, 20x(D). No neoplastic pathology noted.

DISCUSSION

The incidence of BRN ranged from 3.4% to 16.7% for AM after XRT (1). It peaks at two years after XRT and pursues a regressive course in most cases (5, 6). It regresses 40% at six months and 76% at 18 months from the onset of BRN's radiological changes (6). There is a myriad of reasons for this, including total radiation dose, dose per fraction, treatment duration, irradiated volume, and concurrent use of chemotherapy (4-6). Wang TM et al. implicated a radiation injury susceptibility gene (Cep128) as an underlying mechanism of BRN, as it tightly interacts with multiple radiation-resistant genes (7).

The pathophysiology of BRN is not well understood. However, two main theories suggested. The first theory postulates that irradiation damages endothelial cells by upregulating ceramide. Thus, results in vascular insufficiency and infarction (4, 6, 8, 9). Hypoxia caused by endothelial cell damage leads to the liberation of hypoxia-inducible factor 1 α and vascular endothelial growth factor (VEGF) (4, 6, 8, 9). VEGFs induce new vessel formation, but these tend to be leaky capillaries, resulting in perilesional edema (6, 8, 9). The second theory postulates that necrosis arises due to direct injury of the brain parenchyma, especially glial cells. The glial injury causes demyelination and white matter necrosis (4, 6).

The clinical features of BRN vary depending upon the location and size, including features of increased intracranial pressure. The characteristic findings are seizures, hemiparesis, headache, vomiting, poor concentration, and altered level of consciousness (4-6, 10). The literature also reported neurocognitive impairment (hippocampus), especially in children, which includes poor academic performance, distorted self-image, and psychological distress (6, 11).

MRI of the brain will demonstrate some degree of contrast enhancement surrounded by edema (4-6, 9, 10). Although, the patterns of enhancement described in the literature as swiss cheese, cut green-paper or soup bubble, are believed to favor BRN, these patterns posse a 88% negative predictive value (12). MRS is used to assess the metabolite composition of the lesion (6, 13, 14). On MRS, the peak of Cho and the depression of NAA and Cr

correlated with a neoplastic lesion than BRN. Anbarloui et al. demonstrated that Cho/NAA > 1.8 or Cho/lipid ratio >1 had increased odds of being a pure neoplastic lesion rather than pure necrosis, with sensitivity and specificity of 73% and 75%, respectively, for Cho/NAA ratio, and 87% for Cho/lipid ratio (13).

Our patient's MRS failed to differentiate BRN from tumor recurrence. The study revealed a neoplastic lesion, and the histopathology was purely BRN. Why there was such a non-concordant finding, it is not clear. Hellstrom J et al. found 51/208 cases of clinically indicated MRS to have false-positive MRS findings (14). As demonstrated by this study, MRS findings are not accurate when compared to the histopathology findings.

Positron emission tomography (PET) scan uses 18F-fluorodeoxyglucose (FDG) to assess the tissue activity (4, 6, 10). Necrotic tissue will demonstrate low FDG uptake (4, 6, 10). However, a PET scan may not distinguish BRN when epileptic activity coexists. Sasaki M et al. reported the case of 37 years old female with ependymoma treated by surgery and XRT, complicated later by BRN, presented with seizures, and the PET scan was showing abnormally high FDG uptake (10).

As the viable tumor has an intact vasculature, perfusion MRI can predict tumor recurrence (4, 6, 12, 14). Sugahara et al. suggested that a relative cerebral blood volume (rCBV) >2.1 favors tumor recurrence, while an rCBV value <0.6 favors radiation necrosis (15). However, we could not be able to spare time for this advanced imaging method. We applied surgical intervention to relieve the mass effects and to obtain a histopathology specimen.

BRN responds well to conservative management if diagnosed early (4, 6, 9, 12). Corticotherapy is the first option to treat these cases (6, 9, 12). Other supportive treatments include antiplatelet, anticoagulant, and a high dose of vitamins (6, 9). HBOT utilized to improve tissue oxygenation and neovascularization (4, 6). Several studies found that Bevacizumab, an anti-VEGF monoclonal antibody is effective in treating radiation-induced brain edema (4, 6, 8, 9). However, the safety of Bevacizumab warrants further validation as the only randomized control trial published by Levin VA et al. in 2011 involved a limited number of 14 patients (9). If the conservative management fails or significant mass effects exist, then surgical extirpation is mandatory

(4, 6, 9, 12). Recently, laser interstitial thermal therapy (LITT) has become a treatment option for lesions that are difficult to access or for patients who are not candidates for surgery (16). A review study by Katherine G et al. documented a favorable clinical response after LITT for BRN (16). Unfortunately, none of the mentioned treatment approaches utilized halted the progression of BRN in this patient.

CONCLUSION

This case highlights the fact that BRN is a potential complication of XRT for AM. There is no shadow of a doubt that a diagnosis of BRN is a matter of high importance in all settings since misinterpretation can result in delays in treatment and thus noticeable morbidity and mortality. There is no single modality that can reliably distinguish BRN from tumor recurrence. Thus, multimodality approach is highly recommended.

ABBREVIATIONS

AM: Atypical meningioma; XRT: Radiation therapy; BRN: Brain radionecrosis; MRS: Magnetic resonance spectrometry; HBO2: Hyperbaric oxygen therapy; WHO: World Health Organization; CT: Computed tomography; MRI: Magnetic resonance imaging; Cho: Choline; NAA: N-acetyl aspartate; Cr: Creatine; VEGF: Vascular endothelial growth factor; PET: Positron emission tomography; FDG: 18F-fluoro-deoxyglucose; rCBV: relative cerebral blood volume; LITT: laser interstitial thermal therapy.

REFERENCES

1. Kaur G, Sayegh ET, Larson A, Bloch O, Madden M, Sun MZ, et al. Adjuvant radiotherapy for atypical and malignant meningiomas: a systematic review. *Neuro-Oncology*. 2014;16(5):628-36. PubMed
2. Kumar N, Kumar R, Khosla D, Salunke P, Gupta S, Radotra B. Survival and failure patterns in atypical and anaplastic meningiomas: A single-center experience of surgery and postoperative radiotherapy. *Journal of Cancer Research and Therapeutics*. 2015;11(4):735-9. PubMed
3. Alghamdi M, Li H, Olivotto I, Easaw J, Kelly J, Nordal R, et al. Atypical Meningioma: Referral Patterns, Treatment and Adherence to Guidelines. *Canadian Journal of Neurological Sciences*. 2017;44(3):283-7. PubMed
4. Na A, Haghigi N, Drummond KJ. Cerebral radiation necrosis. *Asia-Pacific Journal of Clinical Oncology*. 2014;10(1):11-21. PubMed
5. Schüttrumpf LH, Niyazi M, Nachbichler SB, Manapov F, Jansen N, Siefert A, et al. Prognostic factors for survival and radiation necrosis after stereotactic radiosurgery alone or in combination with whole brain radiation therapy for 1–3 cerebral metastases. *Radiation Oncology*. 2014;9(1):105. PubMed
6. Ali FS, Arevalo O, Zorofchian S, Patrizz A, Riascos R, Tandon N, et al. Cerebral Radiation Necrosis: Incidence, Pathogenesis, Diagnostic Challenges, and Future Opportunities. *Current Oncology Reports*. 2019;21(8):66. PubMed
7. Wang T-M, Shen G-P, Chen M-Y, Zhang J-B, Sun Y, He J, et al. Genome-wide association study of susceptibility loci for radiation-induced brain injury. *JNCI: Journal of the National Cancer Institute*. 2019;111(6):620-8. PubMed
8. Zhuang H, Shi S, Yuan Z, Chang JY. Bevacizumab treatment for radiation brain necrosis: mechanism, efficacy and issues. *Molecular cancer*. 2019;18(1):21. PubMed
9. Levin VA, Bidaut L, Hou P, Kumar AJ, Wefel JS, Bekele BN, et al. Randomized double-blind placebo-controlled trial of bevacizumab therapy for radiation necrosis of the central nervous system. *International Journal of Radiation Oncology* Biology* Physics*. 2011;79(5):1487-95. PubMed
10. Sasadi M, Ichiya Y, Kuwabara Y, Yoshida T, Inoue T, Morioka T, et al. Hyperperfusion and hypermetabolism in brain radiation necrosis with epileptic activity. *Journal of Nuclear Medicine*. 1996;37(7):1174-6. PubMed
11. Lawrence YR, Li XA, El Naqa I, Hahn CA, Marks LB, Merchant TE, et al. Radiation dose–volume effects in the brain. *International Journal of Radiation Oncology* Biology* Physics*. 2010;76(3):S20-S7. PubMed
12. Dequesada IM, Quisling RG, Yachnis A, Friedman WA. Can standard magnetic resonance imaging reliably distinguish recurrent tumor from radiation necrosis after radiosurgery for brain metastases? A radiographic-pathological study. *Neurosurgery*. 2008;63(5):898-904. Google Scholar
13. Anbarloui MR, Ghodsi SM, Khoshnevisan A, Khadivi M, Abdollahzadeh S, Aoude A, et al. Accuracy of magnetic resonance spectroscopy in distinction between radiation necrosis and recurrence of brain tumors. *Iranian journal of neurology*. 2015;14(1):29. PubMed
14. Hellström J, Zapata RR, Libard S, Wikström J, Ortiz-Nieto F, Alafuzoff I, et al. The value of magnetic resonance spectroscopy as a supplement to MRI of the brain in a clinical setting. *PLoS one*. 2018;13(11). PubMed
15. Sugahara T, Korogi Y, Tomiguchi S, Shigematsu Y, Ikushima I, Kira T, et al. Posttherapeutic intraaxial brain tumor: the value of perfusion-sensitive contrast-enhanced MR imaging for differentiating tumor recurrence from nonneoplastic contrast-enhancing tissue. *American Journal of Neuroradiology*. 2000;21(5):901-9. PubMed
16. Holste KG, Orringer DA. Laser interstitial thermal therapy. *Neuro-Oncology Advances*. 2019. Google Scholar.



Traumatic isolated intracerebellar haematoma without any supratentorial lesion. A rare entity. Management strategy

Jain Sachin Kumar, Gupta Tarun Kumar, Jaiswal Gaurav, Lohar Vishnu Kumar, Prateek Patel

Department of Neurosurgery, RNT Medical College, Udaipur, INDIA

ABSTRACT

Purpose. Pure isolated cerebellar haematoma of traumatic aetiology, without associated posterior fossa sub- or epidural haematomas and without supratentorial bleed is a rare entity. We conducted this retrospective study to analyse the management strategy of isolated traumatic intracerebellar haematoma without supratentorial lesion in our institute.

Methods. We retrospectively reviewed records of more than 15000 head injury patients in our department of neurosurgery between January 2014 and November 2019. In this isolated intracerebellar hematoma patients are 60. Patients were divided into two groups assessed by the GCS score at the time of presentation – Group A (GCS>13) Group B (GCS lesser than or equal to 13). Group A treated conservatively and B surgically. Group A subdivided according to the size of hematoma into 1st (> 3cm) and 2nd (<3 cm). Group B subdivided according to GCS into 1st (<8) and 2nd (8-13).

Results. Most Group B, subgroup 1st (GCS<8) patients found to be associated with poorer outcome (60 %) and subgroup 2nd (GCS 8-13) had only 10 %. Group A subgroup 1st (> 3 cm hematoma) has associated with poor outcome (28.57%) and Subgroup 2nd (< 3 cm) has 4.34%. GCS score at the time of admission, hematoma size, hematoma location, the timing of surgery were important factors for outcome.

Conclusion. We concluded that hematoma size is > 3 cm and GCS > 8 patient should operate within 12 hr. Patient of GCS < 8 results of surgery are poor (60%). If the size of hematoma < 3 cm, lateral hematoma and GCS >13 should be treated conservatively. The factors which may be associated with the poor outcome are Low GCS score at the time of admission (<8), the large size of hematoma (>3cm), median location and delay time of surgery(>12hr).

INTRODUCTION

Haematomas of the posterior fossa are by themselves uncommon and account for only 3.7% of all head injuries. (according to Liau)¹³. Approx 0.6-0.82 % cases have cerebellar hematoma without other posterior fossa lesion^{3,10,14}. But isolated intracerebellar hematoma without supratentorial lesion is very rare (approx 40-50% of isolated cerebellar hematoma). As in 9/21-42.85% in bhardwaj et al⁵ and 8/18 -44.44% in devella et al⁶. In our study it is 60 (50%).

Keywords

traumatic intracerebellar
hematoma,
GCS,
hematoma size



Corresponding author:
Jain Sachin Kumar

Department of Neurosurgery, RNT
Medical College, Udaipur, India

drsachinj6184@gmail.com

Scan to access the online version



The clinical presentation of cerebellar haematoma may be readily apparent with classic signs including ataxia, nystagmus and signs of increased ICP like headache, lethargy and nausea and vomiting. Treatment options for this pathology are still evolving.

These hematomas may be totally asymptomatic, with a sudden increase in size can lead to rapid deterioration of neurological status¹⁸.

Previously tested predictive factors in different studies include are size of hematoma, haematoma location (superficial vs. deep), haematoma volume, GCS of patient, degree of fourth ventricle and cistern deformation and associated hydrocephalus^{9,15,21}.

Previously there was difficulty in diagnose the posterior fossa ICH due to lack of CT but with the increasing use of computed tomography (CT) for screening of all head trauma patients, increasing number of cases have been reported to be diagnosed even before the appearance of symptoms and have thus been treated in a timely manner^{14,22}.

The cerebellum has four functionally important deep cerebellar nuclei (the dentate, emboliform, globose and fastigial nuclei) embedded in the white matter in its centre⁸. The locations of the deep cerebellar nuclei span the vermis and the innermost or medially approximately one third of each hemisphere. So it is divided into medial and lateral group / deep and superficial group.

We conducted this retrospective study to analyze the management strategy of isolated traumatic intracerebellar haematoma in our institute and study the factors which could be associated with the outcome. (like Mode of trauma,GCS,Hematoma size,Timing of surgery,Hematoma location etc).

MATERIALS AND METHODS

We retrospectively screened and (where required) reviewed records of more than 15000 head injury patients who were admitted in our Department of Neurosurgery between January 2014 and november 2019. In this approx 120 patients (0.8%) had intracerebellar hematoma without any other posterior fossa lesion, and in this isolated intracerebellar hematoma without supratentorial lesion are in 60 patients (approx 50 % of Cerebellar ICH without posterior lesion). Only these 60 patients are included.

Hematoma volume was assessed by using formula $A*B*C/2$, where A is maximum transverse

diameter of hemorrhage on CT, B is anteroposterior diameter, and C is number of CT slices showing hematoma¹².

Patients were divided in to two groups based on their level of consciousness assessed by the GCS score at the time of presentation – Group A with GCS score greater than 13 and Group B with GCS lesser than or equal to 13. Group A patients were treated conservatively and group B treated surgically.

Data on patient age, gender, GCS score, mechanism of injury, timing of surgery, CT scan findings, management strategy and outcome were gathered and analyzed. These all factors detail given in **Table A**. The mode of injury were broadly categorized as road traffic accident (RTA), fall from height and assault.

Table 1. Demographics and factors associated with isolated traumatic intracerebellar hematoma

S.N	Factor Studied	Details Of Factor	Group A	Group B	Total
1	Number Of Patient		30	30	60
2	Age (Mean Age)		8-60(30)	8-60(36)	
3	Male/Fe male Ratio		3:1	3:1	
4	Mechanism of Injury	RTA	15	22	37
		Fall from height	12	7	19
		Assault	3	1	4
5	GCS	<8		10	10
		8-13		20	20
		>13	30		30
6	Time of Surgery	<12 hr		22	
		12-48 hr		5	
		>48 hr		3	
7	Cerebellar Hematoma Size	>3 cm	7	27	34
		2-3cm	10	3	13
		<2 cm	13	0	13
8	Hematoma Location	Medial or deep 1/3 and vermis	5	10	15
		Lateral or superficial 2/3	25	20	45
9	Status of Fourth Ventricle	Normal	27	6	33
		Compressed	3(mild)	24	27
10	Surgical treatment	Sub Occipital Craniectomy	4(after worsening)	27	31
		VP Shunt	4(after worsening)	3	7

CT scan findings included clot location, size (largest transverse diameter of clot, categorized as > 3 cm or < 3 cm, or clot volume categorized as > 15 ml or < 15 ml), other associated findings and status of the fourth ventricle (normal vs. compressed)

According to all these criteria Group A divided into 2 subgroups according to size of hematoma . 1st has >3 cm and 2nd has < 3 cm size of hematoma. Group B also divided into 2 subgroups according to GCS . 1st has GCS< 8 and 2nd has GCS 8-13.

We also included timing of surgery after injury in surgical group B and from time of worsen in Conservative group A. Timing divided into <12 hr, 12-48 hr and > 48 hr.

We also assess the location of hematoma and divided patients into medial 1/3rd /deep and superficial /lateral 2/3rd location in cerebellum.

Surgical treatment (sub-occipital craniectomy) and insertion of ventriculoperitoneal (VP) shunt was documented. Six month follow-up reports of all patients who turned in for the follow-up were also analyzed. Outcome was documented as favorable or poor based on the Glasgow Outcome Scale at the time of hospital discharge (GOS-HD). GOS 5 was counted as favorable whereas GOS 1-4 counted as poor response.

RESULTS

There are 7 patients in group A subgroup 1st (~ > 3 cm size clot). 5 patients out of 7 (71.4%) , worsened and required surgical treatment (3 sub occipital craniectomy, 2 VP shunt). In these patients 1 expired due to sudden worsening . 1 patient has poor GOS and persist in severe disable stage. Both has delayed surgery and (between 12-48 hr) . Rest 3 patients has good outcome because of early diagnosis and early surgery . So poor outcome is 2/7- 28.57%.

In Group A subgroup 2nd has 23 patients(clot size <3 cm) . In which 3 patient of 2-3 cm clot size (30%) has worsened between 4-6 days , repeat scan suggesting of sudden increase in size in one patient and obstructive hydrocephalus in all 3. Urgent surgical intervention done (with in 12 hr) .VP shunt in 2 patient and suboccipital craniectomy in 1 patient. In this 1 patient expired 1 month after sub occipital craniectomy due to chest infection. Rest 20 patient has good recovery by conservative treatment. So poor outcome is only 1/23- 4.3%.

In group B(surgical group) , subgroup 1st(GCS < 8) has 10 patients , in which 8 patients has hematoma

size more than 3 cm (even 5 patients has hematoma size 4-5cm) and 2 patient has size < 3 cm but in midline .In these 10 patients 3 expired and 3 has severe morbidity. Rest 4 patients survived with favourable results. So 6/10 -60 % has poor outcome inspite of surgery. This result included in **Table B**.

Table 2. Results

S . N	Factor Studied	Detail of factor	Outcome			Mortality
			Poor outcome (GOS 1-4)	Favourable Outcome (GOS 5)	Total	
1	Group A (GCS > 13) (Conservative treatment)	Subgroup 1 st (size >3 cm)(5 /7patient worsens and operated)	2 (28.57%)	5	7	1
		Subgroup 2 nd (size-, < 3 cm) Only 3/23 patient worsens and operated)	1(4.3%)	22	23	1
2	Group B (GCS ~<13) (Surgical Treatment)	Subgroup 1 st (GCS< 8)	6(60%)	4	10	3
		Subgroup 2 nd (GCS-8-13)	2(10%)	18	20	1
3	Timing of surgery	<12 hr	3(12%)	22	25	1
		12-48 hr	5(50%)	5	10	2
		>48 hr	3(100%)	0	3	3
4	Location of hematoma	Deep/medial 1/3 rd	7(46.66%)	8	15	5
		Superficial/lateral 2/3 rd	4(8.88%)	41	45	1

GCS 8-13 included 20 patients , in which 19 patients has hematoma size > 3cm and rest 1 has size 2-3 cm near midline. Only 1 patient expired and 1 has severe morbidity out of 20 patients .One who expired , operated after 12 hr and One patient who has severe morbidity has associated chest infection. So 2/20 – 10% has poor outcome after surgery .

Total 38 patient has undergone surgical procedure from which 8 operated in group A after worsening and all 30 operated in surgical group B.

Out of 3 patients who operated after 48 hr, all 3 patient expired.

(3/3 -100 %). Between 12 -48 hr 10 patient operated In which 2 expired and 3 patient has severe morbidity (5/10-50%). But all 25 patients which are operated before 12 hr had comparable favourable results(1 expired and two has severe morbidity).(3/25-12%). Patient expired in early surgery had chest infection.

VP shunt required only in 3 patients in group B which has hematoma size 2-3 cm, GCS(8-13) and has midline location. VP shunt also done in 2 patient in subgroup 2nd in group A. There is 5 patients in vermis or median ICH in group A and 10 patient in group B. rest all are located laterally.

The poor outcome in our series at the time of hospital discharge in GCS <8 was 6/10- 60%. . Domenico D'Avella⁷ study shows 58.7% poor outcome in GCS<8 .

Poor outcome was higher, 60% (6/10) in GCS < 8 in Group B as against 10 % (2/20) in GCS 8-13 in Group B.

Mortality was 13.33% (4/30) in Group B and only 6.66% (2/30) in Group A. Poor outcome in group A is 3/30-10% and in group B is 8/30- 28.6 % . (in this <8 GCS is 60%, and GCS 8-13 has 10%) So it indicated that GCS is the most important predictor for prognosis in cerebellar ICH , either operate or not and second is size.

We have added pictures of preoperative cerebellar hematoma and postoperatively (after suboccipital craniectomy with hematoma evacuation). **Fig. 1, 2** (1st patient of 40 yr male), **Fig. 3, 4** (2nd patient of 42 yr male).

Figure 1. Pre-operative CT of a 40 yrs. male

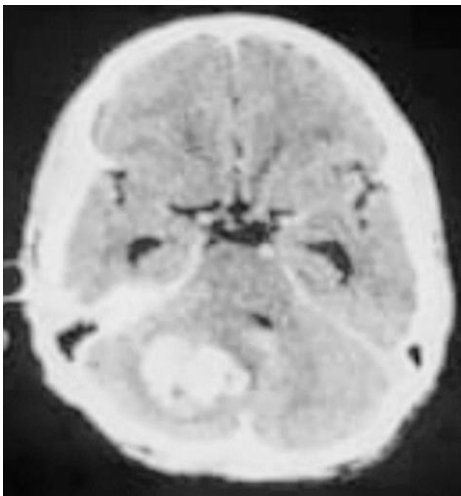


Figure 2. Postoperative CT after sub occipital craniectomy

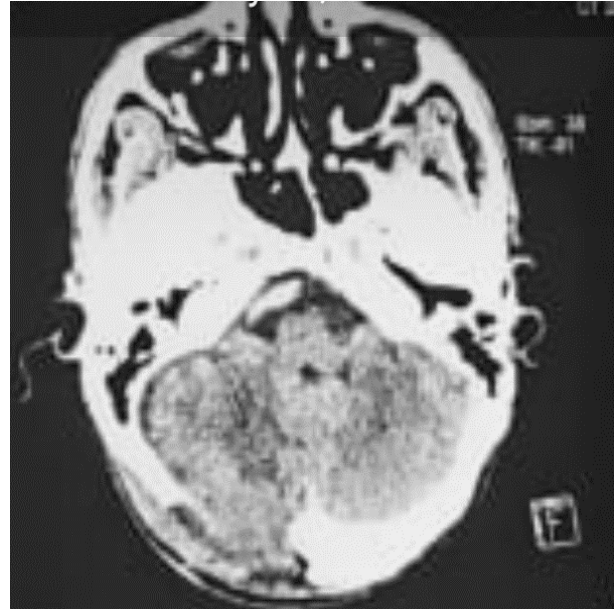


Figure 3. Preoperative CT of a 42 yrs. male

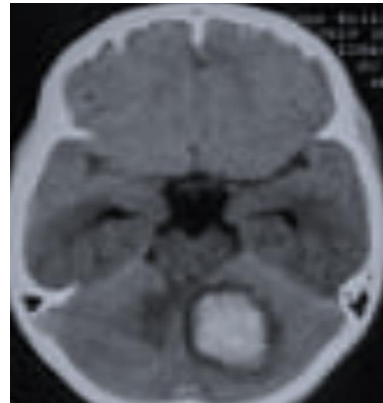
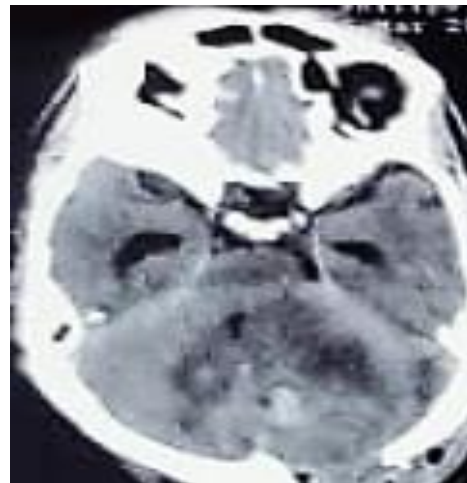


Figure 4. Post-operative scan after suboccipital craniectomy



DISCUSSION

In our study, RTA was the most common 37/60(61.16%) and most damaging mechanism of injury. In this study fall from bike and pillan rider are the most common mechanism of injury. Bhardwaj et al has 15/21(71.14%)⁵, Harsh et al has 15/23 (65.21%)²³.

Second most common is fall from tree in this tribal area which are more (19/60 -31.66%) in comparison to other studies. Bhardwaj et al has 6/21(28.57%), Harsh et al 5/23(21.73%).Last mode of injury are assault.

Fall from height was more common amongst children¹ while assault was more commonly associated with women and the elderly. But in our study , there are history of fall from tree and height in adult also²⁰.

Benign course of intracerebellar hematomas may be more frequent than appreciated so not all traumatic hematomas of the cerebellum require surgery¹⁷. So it is to be decided in which patient we should operate or not to operate.

In accordance with other studies on this topic, CT scan was extremely valuable in predicting patient outcomes²⁰.

Clots greater than or equal to 3 cm in diameter, GCS<8, deep/meadial 1/3rd hematoma location and timing of surgery were all shown by our study to predict a poor outcome.

Outcomes were worse for patients has GCS < 8 in subgroup 1st in Group B^{7,15,25}. Such patients were critically injured and their brain function was already compromised at the time of admission.

In accordance with previous studies on this topic our data showed GCS at initial presentation to be the most predictive clinical tool ^{5,6,7,21,23,25}. Domenico d'Avella et al⁷ suggest that A GCS score of less than 8 was the most powerful adverse prognostic factor (58.78% probability of poor outcome as sole covariate) . In our study poor outcome is 60% in GCS <8. With supratentorial lesion it is 84.61% in harsh et al and 88.78% in d'avella et al.

Mortality was 3/10 (30%) in which 2 patient has median cerebellar hematoma . all 3 had delayed surgery. .Rest 3 patient which has poor outcome in which 2 patient has median hematoma and 1 had delayed surgery.

Outcome is good for GCS 8-13 with surgical treatment. Only 1 patient expired in which hematoma was median and one patient has poor

outcome had delayed surgery (12-48 hr).

Delayed surgery after 48 hr had worst outcome (100%), between 12-48 hr had poor outcome (50%). Early surgery within 12 hr had poor outcome only 12.0%. So Early surgery is good always . it indicated that timing of surgery is one of the most prognostic factor for outcome^{5,7}.

11 patients has poor outcome , in these 7 patient had medial hematoma. so 7/11 (63.63 %) of poor outcome had medial hematoma. Bhardwaj et al has (62.5%) and S. Takeuchi et al²¹ has 9 patient has medial hematoma in 10 poor outcome patient(9/10-90%).So maximum poor outcome occurs in medial and deep hematoma lesion which are also in our study.

Total medial hematoma is 15 patients in which 7 patients had poor outcome (7/15-46.66%) and superficial hematoma in 45 patients in which only 4 patients has poor outcome (4/45-8.88%). It indicates that medial/deep hematoma has poor outcome^{5,15,23}. In group A subgroup 1st 7 patients has hematoma size > 3 cm and 5 worsened (5/7- 71.42%) and then operated .. Subgroup 2nd has size < 3 cm only 3 patient worsened (3/23- 13.04%) , which is also due to midline position. So it is proven that size is important prognostic factor^{4,5,7}. Hematoma of > 3 cm size should operate early whether GCS > 13.So size is important factor to take decision of surgery.

Poor outcome in patient of size> 3 cm in group A is 2/7 -28.57% due to sudden worsening and late surgery . But in < or equal to 3cm poor outcome is only 1/23- 4.3% which is also due to midline hematoma and chest infection. So size is most important factor and equal and less than 3 cm size can treated conservatively^{4,5,7,15,23}.

But in group B , all patient operated , so we can not compare size factor for decision of surgery.

Though trauma is the obvious cause, specific mechanism for this type of injury remains unclear. Takeuchi et al.²¹ created a classification system for the types of trauma causing cerebellar haematomas. Their three classes included coup injuries, countercoup injuries and acceleration-deceleration injuries.

This classification system proved useful in predicting the site of haematoma, with coup injuries thought to be more common^{19,24} causing only superficial bleeds while countercoup injuries resulted in deep cerebellar bleeds.

In all patients undergoing surgical intracerebellar

clot evacuation sub-occipital craniectomy was done, it is best procedure^{2,16} and preferred over sub-occipital craniotomy as posterior fossa has less space for accommodation of any post-operative bleeding or post-operative edema.

Some may note our use of VP shunts over external ventricular drains (EVDs) for certain patients experiencing hydrocephalus resulting from cerebellar haematoma. VP shunt was chosen over EVD placement because in our clinical setting EVDs have allegedly been found to more frequently result in infections as ventriculitis and meningitis three to four days post-EVD placement. However, patients developing acute hydrocephalus need drainage of CSF usually for a period of more than two weeks during which the clot resolves and perilesional edema subsides²³.

HCP can be associated with traumatic intracerebellar clots but not always^{17,22}. Karasawa *et al*¹¹ mentioned of acute HCP in 20% of intracerebellar hematomas, while in our series it was 16.6%.

Total poor outcome is in 11 patients so 11/60-18.33% which is very less in comparison of other studies because in this study only isolated intracerebellar hematoma taken without supratentorial lesion and 50 patients had GCS > 8^{5,6,7,15,21,23}. It also indicates that GCS and associated lesion are important prognostic factor.

CONCLUSION

In an attempt to study the factors which may be associated with poor outcome in isolated intracerebellar haematoma cases we found that GCS score at the time of admission (<8), large size of hematoma (> 3cm), Hematoma location (deep/medial 1/3rd) and delay time of surgery (>12hr) has poor prognosis.

We also concluded that if hematoma size is > 3 cm and GCS > 8 patient should operate, and should operate early within 12 hr.

Median hematoma should be operated and operated early (whether size is 2-3 cm with ventricle compression) because chances of worsening more. But overall prognosis for deep hematoma was poor. Patient of GCS < 8 irrespective to size of ICH s results of surgery are poor (60%).

We also concluded that if size of ICH >3 cm and has ataxia and other symptoms and whether the patient is conscious, but should operate, because chance of worsening is present there or had close

observation for 4-5 days and operated immediately after worsening.

If GCS > 13 and ICH < 3 cm size, patient should be treated conservatively and at least 15 days follow up should be needed. After 15 days there is very less chance of worsening.

The overall prognosis is better than other studies because we excluded other supratentorial lesions and 50 patients had GCS > 8. It also concludes that if there is no associated lesion, chances of low GCS are less. But the most important thing is that it is the rare study in which only true intracerebellar hematoma without supratentorial lesions were included.

CONFLICT OF INTEREST

There is no conflict of interest to disclose.

INFORMED CONSENT

Informed consent was obtained from all individual participants included in this study.

REFERENCES

- Adirim TA, Wright JL, Lee E, Lomax TA, Chamberlain JM. Injury surveillance in a pediatric emergency department. *Am J Emerg Med* 1999;17(6):499-503.
- Aghi M, Ogilvy CS, Carter B. Surgical management of intracerebellar haemorrhage. In Roberts DW, Schmeidek HH, eds. *Schmeidek and Sweet's Operative Neurosurgical Techniques, Indications, Methods, Results*. Vol. 2, 5th ed. Philadelphia: Saunders/Elsevier 2005;1061-1074.
- Arseni C, Maretsis M. Traumatic cerebellar haematoma associated with posterior cerebral fossa subdural haematoma. *Psychiatr Neurol Neurochir* 1972;75:113.
- A. Koziarski, E. Frankiewicz. Medical and surgical treatment of intracerebellar haematomas. *Acta Neurochirurgica* 1991;110:24-28-22.
- Sandeep Bhardwaj, Vinod Sharma, Somnath Sharma, Devendra Purohit, Sanjeev Chopra. Traumatic Posterior Fossa Hematoma, A Rare Entity: Study of 21 Cases. *J Neurosci Rural Pract* 2019;10:675-68.
- D'Avella D, Cacciola F, Angileri FF, *et al.* Traumatic intracerebellar hemorrhagic contusions and hematomas. *J Neurosurg Sci* 2001;45(1):29-37.
- d'Avella D, Servadei F, Scerrati M, *et al.* Traumatic intracerebellar hemorrhage: clinicoradiological analysis of 81 patients. *Neurosurgery* 2002;50(1):16-25. discussion 25-27.
- Deoni SC, Catani M. Visualization of the deep cerebellar nuclei using quantitative T1 and rho magnetic resonance imaging at 3 Tesla. *Neuroimage* 2007;37:1260.
- Ehab Ezzat El Gamal, Ashraf Mohamed Farid, Cerebellar hematomas: management dilemmas, *Tanta medical journal* 2013; 41 (4): 358-363.

10. Fisher RG, Kim JK, Sachs E Jr. Complication in posterior fossa due to occipital trauma; their operability. *J Am Med Assoc* 1958;167:176-82.
11. Karasawa H, Furuya H, Naito H, Sugiyama K, Ueno J, Kin H. Acute hydrocephalus in posterior fossa injury. *J Neurosurg* 1997;86(4):629-632.
12. Kothari RU, Brott T, Broderick JP, et al. The ABCs of measuring intracerebral hemorrhage volumes. *Stroke* 1996;27(8):1304-1305.
13. Liu K. Characteristics of diagnosis and treatment of traumatic intracerebellar hemorrhage [in Chinese] *Zhonghua Wai Ke Za Zhi*. 1997;35(03):166-167.
14. Nagata K, Ishikawa T, Shigeno T, et al. Delayed traumatic intracerebellar hematoma: correlation between the location of the hematoma and the pre-existing cerebellar contusion—case report. *Neurol Med Chir (Tokyo)* 1991;31:792-96.
15. Patnaik A, Mahapatra A K. Traumatic cerebellar haematoma: a review. *The Indian J NeuroTrauma*. 2013;10:24-29.
16. Pollak L, Rabey JM, Gur R, Schiffer J. Indication to surgical management of cerebellar hemorrhage. *Clin Neurol Neurosurg* 1998;100(2):99-103
17. Pozzati E, Grossi C, Padovani R. Traumatic intracerebellar hematomas. *J Neurosurg*. 1982;56(05):691-694.
18. Sokol J H, Rowed D W. Traumatic intracerebellar haematoma. *Surg Neurol*. 1978;10(05):340-341.
19. St John JN, French BN. Traumatic hematomas of the posterior fossa. A clinicopathological spectrum. *Surg Neurol* 1986;25:457-66.
20. Takeshi Satow et al, case report Traumatic Cerebellar Hemorrhage Caused by Fall *JOURNAL OF THE JAPANESE ASSOCIATION OF RURAL MEDICINE* 2015 ; 64 (1) ; 45-49.
21. Takeuchi S, Takasato Y, Masaoka H, Hayakawa T. Traumatic intra-cerebellar haematoma: study of 17 cases. *Br. J Neurosurg*. 2011;25(01):62-67.
22. Tsai FY, Teal JS, Itabashi HH, Huprich JE, Hieshima GB, Segall HD. Computed tomography of posterior fossa trauma. *J Comput Assist Tomogr* 1980;4(3):291-305
23. Viraat Harsh, Anand Prakash, James Marcellus Barry & Anil Kumar Traumatic intracerebellar haematoma: To operate or not to operate? *British Journal of Neurosurgery*, 2014-4
24. Vrankovic D, Splavski B, Hecimovic I, Kristek B, Dmitrovic B, Rukovanjski M, Blagus G, Kovacic D: Anatomical cerebellar protection of contrecoup hematoma development: Analysis of the mechanism of 30 posterior fossa coup hematomas. *Neurosurg Rev* 2000;23:156-160.
25. Wright RL. Traumatic hematomas of the posterior cranial fossa. *J Neurosurg* 1966;25(4):402-409.



Dorsolumbar angioliipoma. A rare case report and review of literature

Surendra Kumar Gupta¹, Anuj Chhabra²,
Hanuman Kumar Prajapati³, Faran Ahmad⁴

¹ MCh Neurosurgery. Assistant professor. Department of Neurosurgery, AIIMS Raipur, INDIA

² Assistant Professor. Department of Neurosurgery. Kalpana Chawla Government Medical College, Karnal, Haryana, INDIA

³ MCh Neurosurgery. Assistant Professor. Department of Neurosurgery, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, INDIA

⁴ DNB Neurosurgery. Senior Resident. Department of Neurosurgery, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow, INDIA

ABSTRACT

A 55-year-old female was presented with complaints of tingling sensations of the bilateral lower limb with spastic paraplegia for last one year. Her pre-operative contrast MRI study of Dorsolumbar Spine was suggestive of extradural angioliipoma. She underwent D11, D12 and L1 Laminectomy and a mildly vascular yellowish globular extradural mass was found which was excised completely and dural decompression was achieved. Post-operatively, the patient's neurologic symptoms improved.

Conclusion: Spinal angioliipoma is considered a rare benign entity which emulates malignancy. It should be included as a differential diagnosis of the spinal epidural tumour with fat component and a high degree of vascularisation. surgical removal of this epidural tumour through a proper and comprehensive approach provides complete and permanent recovery.

INTRODUCTION

Spinal angioliipoma and angiomyoliipoma are rare tumors, their incidence was noted only 0.14% of all tumors of the spinal axis. It is difficult to distinguish them from spinal lipoma, as they are found mainly in adults. They are localised almost exclusively in the dorsal epidural space of the thoracic spine [4]. They are not associated with any malformation. These lesions usually show no tendency to involve the surrounding tissue although some may show infiltrative process into the bony compartment of the vertebral column [5, 14].

We are reporting a rare case of angioliipoma of the dorsolumbar spine in a 55-year-old female patient that was diagnosed by pathological examination following surgical resection, and discuss the imaging findings of angioliipoma published in literature.

Keywords

spinal extradural tumour,
spinal angioliipoma,
angiomyoliipoma



Corresponding author:
Anuj Chhabra

Assistant Professor. Department of Neurosurgery, Kalpana Chawla Government Medical College, Karnal, Haryana, India

dranujchhabra123@gmail.com

Scan to access the online version



CASE REPORT

A 55-year-old female were admitted in our hospital with complaints of tingling sensation of bilateral lower limb with spastic paraplegia for last one year.

Her neurological examination was showing paraplegia with diminished sensations over B/L lower limbs. Knee and ankle jerks were exaggerated with significant increase in tone. Her MRI (magnetic resonance imaging) dorsolumbar spine was showing signal of the fat and blood vessels. The fatty content was hyperintense on both T1- and T2-weighted images (similar to the signal of subcutaneous adipose tissue) and hypointense on fat-suppressed images. The vascular component was hypointense on T1-weighted and hyperintense on T2-weighted, and showed intense enhancement with Gd-DTPA infusion (Figure 1).



Figure 1. Spindle shaped extradural contrast enhancing on T1W Contrast (1A, D) and hyperintense on T2W (1B,C,E).

She was planned for laminectomy with decompression of cord under general anaesthesia. She underwent D11, D12 and L1 Laminectomy and a mildly vascular yellowish globular extradural mass was found which was excised completely and dural decompression was achieved

On histopathological Examination. Microscopic examination revealed sheets of mature adipocytes

arranged in lobules divided by delicate intervening fibrous septae showing numerous thick-walled blood vessels without elastic lamina. No evidence of malignancy was noted, so histopathology diagnosis of angioliipoma was given (Figure 2).

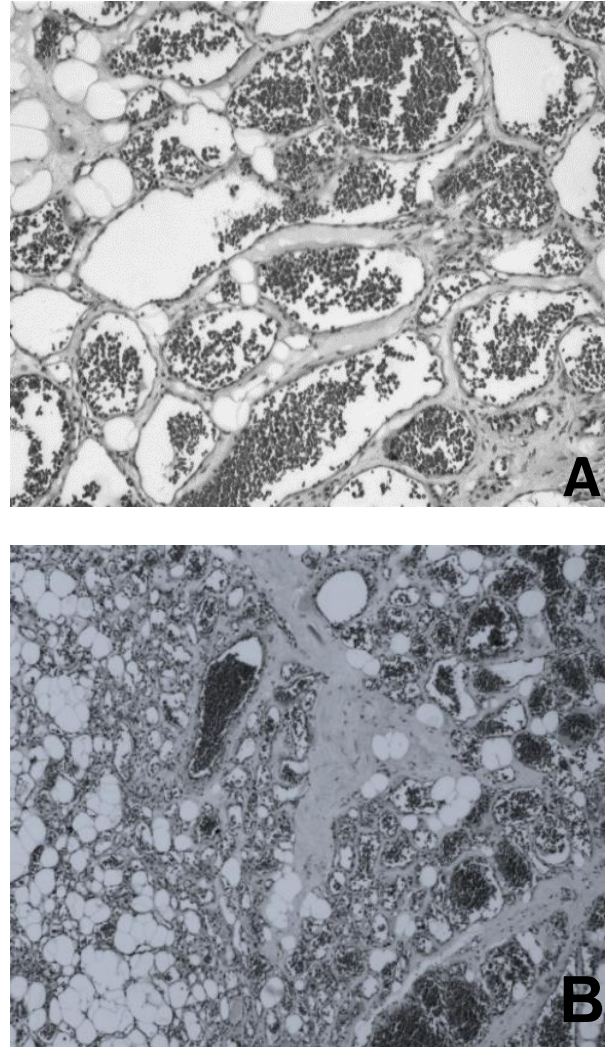


Figure 2. Photomicrographs show mature adipose tissue and proliferated vascular tissue with thin septation and foci of fibrosis (A; H&E, 100X, B; H&E, 400X).

Post-operative Course. The patient's neurologic symptoms improved immediately. On second post-operative day, her power in bilateral lower limb improved to 4/5. She was discharged on fifth post-operative day. On two months follow up, no signs of recurrence and neurological deficits were noted.

DISCUSSION

Howard and Helwig described angioliipoma as one entity in 1960 [7]. They said that the majority of these

tumors are found in subcutaneous vessel, muscle, bone and kidney and it was noted that they have no tendency to recur after excision. More than 50 cases of spinal angioliipoma and angiomyoliipoma have been reported [1-3, 6, 8-11]. After reviewing following clinical and radiologic characteristics were noted:

- 1) These tumors are occurs in middle aged patients usually;
- 2) These are mostly located in the dorsal epidural space;
- 3) They grow in a spindle shape along the spinal canal;
- 4) They lack the associated malformations; and
- 5) They are mostly benign and result in a good postoperative outcome.

Most of spinal angioliipomas are found to be non-filtrating hence complete excision is the rule. In a few reported cases the tumor merges to the extradural fat so that it is difficult to differentiate tumor from the fat [12].

The pathogenesis of Angiomyoliipoma (AML) and Angioliipoma is not clear. Two major theories have been given previously regarding the pathogenesis. One is that primitive pluripotent mesenchyme cells (which provides a common origin to adipose, smooth muscle, and vascular endothelial elements) are developed into tumor by ill-defined stimuli (trauma or other causes). Another theory is that the tumor is a congenital malformation or true hamartoma [7].

It was noted in most patients with spinal AML and angioliipoma that they have complaints of neurological symptoms related to spinal cord compression, such as weakness of the extremities and abnormal sensation below the level of lesion [3]. It was observed that there exists a relationship between pregnancy and accelerated onset of neurologic symptoms in several cases of epidural spinal angioliipoma [13].

For radiological assessment of spinal AML and angioliipoma, previously conventional radiograph, myelography, or CT were used for the purpose of preoperative diagnosis. Recently in such cases MRI were employed. Both spinal AML and angioliipoma appear as elliptical shaped soft tissue mass with heterogeneous marked enhancement at epidural space of thoracic spine. Fat component with high signal intensity on T1-weighted image is often visualized in cases of spinal angioliipoma [8]. However, infiltrative properties such as invasion to

adjacent bone or extension to perilesional space and ventral location have been mentioned as distinctive features of AML compared to major patterns of angioliipoma according to Sakaida et al [14].

Such kind of lesions includes differential diagnosis of fat-containing tumor (such as lipoma, lipomatosis, and liposarcoma), prominently vascular tumor (such as spinal epidural hemangioma), and other T1-high signal intensity lesion (such as epidural hematoma). Epidural lipoma or lipomatosis is an abnormal accumulation of unencapsulated adipose tissue in the extradural space. Because of their fat components, they also display hyper intensity on T1-weighted images and intermediate intensity on T2-weighted images [12]. However, they present with typical Y configuration (with circumferentially compressed dural sac) and show no definite contrast enhancement pattern. Well-differentiated liposarcoma is a rare fat-containing tumor of the spinal canal. It frequently has irregular thick-ended septa. It contains regions of hyperintense signal (compared to fat) on T2-weighted images which are rare in spinal AML [8, 12, 14].

CONCLUSION

Spinal angioliipoma is considered as rare benign entity which emulates malignancy. A sufficient attempt must be made to reach a correct preoperative diagnosis by using reliable imaging techniques such as MRI. It should be included as a differential diagnosis of spinal epidural tumor with fat component and high degree of vascularisation. It can be believed that surgical removal of this epidural tumor through proper and comprehensive approach provides complete and permanent recovery.

REFERENCES

1. Anson JA, Cybulski GR, Reyes M. Spinal extradural angioliipoma, A report of two cases and review of the literature. *Surg Neurol* 1990;34: 173-8.
2. Bender JL, Van Ladinghum JH, Manno NJ. Epidural lipoma producing spinal cord compression: report of two cases. *J Neurosurg* 1974;41:100-3.
3. Geers C, Lecouvet FE, Behets C, Malghem J, Cosnard G, Lengelé BG. Polygonal deformation of the dural sac in lumbar epidural lipomatosis: anatomic explanation by the presence of meningovertbral ligaments. *AJNR Am J Neu-roradiol* 2003;24:1276-1282.
4. Goldblum JR, Weiss SW, Folpe AL. *Enzinger and Weiss's soft tissue tumors*. 6th ed. Philadelphia: Elsevier Saunders, 2013:897-899.

5. Gonzalez-Crussi F, Enneking WF, Arian VM; Infiltrating angioliipoma. *J Bone Joint Surg [Am]* 1966;48:1111-23.
6. Griebel RW, Khan M, Rozdilski B. Spinal extradural angioliipoma: A case report and literature review. *Spine* 1986;11: 47-8.
7. Howard WR, Helwig EB. Angioliipoma. *Arch Derm (Chicago)* 1960; 82:924-33.
8. Hu S, Hu CH, Hu XY, Wang XM, Dai H, Fang XM, et al. MRI features of spinal epidural angioliipomas. *Korean J Radiol* 2013;14:810-817.
9. Kuroda S, Abe H, Akino M, et al. Infiltrating spinal angioliipoma causing myelopathy: Case report. *Neurosurgery* 1990;27:315-8.
10. Padovani R, Tongnetti F, Speranza S, et al. Spinal extrathecal hemangioliipomas: Report of two cases and review of the literature. *Neurosurgery* 1982;11:674-7.
11. Pearson J, Stellar S, Feigin I. Angiomyoliipoma: long term cure following a radical approach to malignant appearing benign intraspinal tumor: Report of three cases. *J Neurosurg* 1970;33: 466-70.
12. Provenzale JM, McLendon RE. Spinal angioliipomas: MR features. *AJNR Am J Neuroradiol* 1996;17:713-719
13. Rubin G, Gornish M, Sandbank J, et al. Spinal Extradural angioliipoma: Case report and review of the literature. *Spine* 1992;17:719-24.
14. Sakaida H, Waga S, Kojima T, Kubo Y, Matsubara T, Yama-moto J. Thoracic spinal angiomyoliipoma with extracanal extension to the thoracic cavity. A case report. *Spine (Phila Pa 1976)* 1998;23:391-39.



Comparative analysis of anterior third ventricle approaches

Deepak Kumar Singh, Kuldeep Yadav, Rakesh Kumar,
Arun Kumar Singh, Vipin Kumar Chand

Department of Neurosurgery, Dr Ram Manohar Lohia Institute of
Medical Sciences, Lucknow, INDIA

ABSTRACT

Background. Third ventricle tumors are uncommon and account for only 0.6 - 0.9% of all the brain tumors⁷. In 1921, Dandy was the first neurosurgeon who successfully removed a colloid cyst from the third ventricle through a posterior transcallosal approach. Despite their unfavourable locations, these tumours can be removed successfully by proper knowledge of anatomical landmarks and by choosing the appropriate approach.

Methods. We performed a retrospective analysis of all patients (17 patients) who underwent surgery for anterior third ventricular masses between March 2018 to March 2020 in the Dr Ram Manohar Lohia Institute of Medical Science Lucknow, Uttar Pradesh.

Results: The most common symptom in our cases was headache, which was present in all (100%) patients, nausea/vomiting in 7 (41%), history of recurrent episodes of drop attacks in 4 (23%), h/o seizure in 2 (11.7%), visual disturbance in 1 (5.4%), memory disturbance in 1 (5.4%) and urinary incontinence in 1 (5.4%) patient. 6 patients were operated with transcallosal-transforaminal approach, 1 patient was operated with transcallosal interforaminal approach, 3 patients were operated with transcortical-transforaminal approach, 1 patient was operated with subfrontal translamina terminalis approach, 1 patient was operated with transcallosal-transchoroidal approach, 5 patients were operated with endoscopically. Gross total excision was achieved in 15 (88%) patients while in 2 (11.7%) patients subtotal resection was done due to their adherence to choroid plexus and optic chiasm. The most common post-operative complication was endocrine dysfunction in the form of diabetes insipidus.

Conclusions. Anterior Third ventricular tumours are mostly benign and best treatment modality is surgical resection. When we analyzed the results of various approaches, we found that despite their unfavourable location, the results were satisfactory for different tumours of different location in the anterior third ventricle, when treated with the carefully planned microsurgical or endoscopic approach with proper knowledge of anatomical landmarks.

INTRODUCTION

Third ventricle tumors are uncommon and account for only 0.6 - 0.9% of all the brain tumors⁷. Third ventricle includes wide variety of lesions ranging from benign to malignant. Majority of intra-ventricular tumors

Keywords
third ventricle,
transcallosal



Corresponding author:
Arun Kumar Singh

Department of Neurosurgery, Dr
Ram Manohar Lohia Institute of
Medical Sciences,
Lucknow, India

aks30041990@gmail.com

Scan to access the online version



are benign, surgery is therefore preferred and is curative. Most common entities for this location are colloid cysts, astrocytomas and craniopharyngiomas. Others lesions for this location are arachnoid cysts, pituitary adenomas, subependymomas, germinomas, central neurocytoma, teratomas, dermoids, meningiomas and choroid plexus papillomas^{12,18}. Third ventricle can be divided into anterior and posterior third ventricle on the basis of an imaginary line connecting foramen Monro to aqueduct Sylvius. Common tumors originating from anterior third ventricle are astrocytomas and craniopharyngiomas; from the posterior third ventricle are meningiomas, choroid plexus papillomas and colloid cysts at the level of foramen Monro⁸. Anterior Third ventricular tumors can be classified as primary and secondary tumors.

Primary tumors: originating purely intraventricular - ependymoma, choroid plexus papilloma, colloid cysts.

Secondary tumors: originating adjacent to third ventricle and secondarily expand within the ventricular cavity - pituitary adenoma, craniopharyngioma, meningioma.

Patients of anterior third ventricular mass usually presents with symptoms secondary to hydrocephalus such as headache, vomiting, blurring or diminution of vision.

In 1921, Dandy was the first neurosurgeon who successfully removed a colloid cyst from the third ventricle through a posterior transcallosal approach, and stated that no treatment short of total removal could have any possible value in the treatment of tumors in this region¹⁰. The anterior transcallosal approach was suggested by Ehni who used this approach for different pathological entities¹¹.

Third ventricular tumors are difficult to treat due to their deep location and proximity to vital neural structures such as thalamus, hypothalamus and vascular structure such as internal cerebral vein and medial posterior choroidal artery. Despite their unfavorable locations, these tumors can be removed successfully by proper knowledge of anatomical landmarks, pre-operative planning and by choosing appropriate approach.

There are various approaches to anterior third ventricle including transcortical-transventricular approach through foramen of Monro²², Interhemispheric - transcallosal - interforaminal approach^{2,5}, Interhemispheric - transcallosal-

transchoroidal - trans-velum - interpositum approach^{9,14}, subfrontal trans - laminar terminalis approach²¹ and Endoscopic approach.

Common surgical complications are seizure following transcortical approach, memory deficit and venous cortical infarct following transcallosal approach. Other postoperative complications are mutism, hematoma, and hemiparesis. Some study suggests that unilateral damage to fornix produces no deficit. The inter-forniceal approach to a lesion of third ventricle carries the potential risk for bilateral damage of fornix, but memory deficit is usually transient by this approach^{4,3}.

METHOD

We performed a retrospective analysis of all patients who underwent surgery for anterior third ventricle mass between March 2018 to March 2020 in the Dr Ram Manohar Lohia Institute of Medical Science Lucknow Uttar Pradesh. 17 patients underwent for surgery of anterior third ventricular mass. We reviewed case sheets, radiological images, pathological reports, surgical reports of all the patients. We also collected data regarding their demographic data, preoperative symptoms and signs, surgical approaches, histopathological reports and postoperative complications.

RESULTS

In our study we reviewed case sheets of 17 patients, who were operated for anterior third ventricle approaches in Dr Ram Manohar Lohia Institute of Medical Sciences Lucknow during a time period from March 2018 to March 2020. In our study there were 12 males and 5 females, age ranged from 9 years to 54 years with mean age of 27 years. Maximum patients (9) were in the age group of 20-30 years.

The most common symptom in our cases was headache, which was present in all (100%) cases, nausea/vomiting in 7(41%), history of recurrent episodes of drop attacks in 4(23%), h/o seizure in 2(11.7%), visual disturbance in 1(5.4%), memory disturbance in 1(5.4%), urinary incontinence in 1(5.4%). One patient presented with altered mental status [Table-1].

Symptoms	No of patients
Headache	17(100%)
Nausea/vomiting	7(41%)
h/o drop attacks	4(23%)

h/o seizure episode	2(11.7%)
Visual disturbance	1(5.4%)
Memory disturbance	1(5.4%)
Urinary incontinence	1(5.4%)

Table 1. Clinical presentation of patients of anterior third ventricle mass.

Surgical approaches	No of patients
Transcortical transforaminal	3
Transcallosal transforaminal	6
Transcallosal interforaminal	1
Transcallosal subchoroidal	1
Subfrontal translaminar	1
Endoscopic excision	5

Table 2. Surgical approaches in patients with anterior third ventricle mass.

Histopathological report	No of patients
Colloid cyst	11
Craniopharyngioma	4
Central neurocytoma	2

Table 3. Histopathological report.

6 patients were operated with transcallosal-transforaminal approach, 1 patient was operated with transcallosal interforaminal approach, 3 patients were operated with transcortical-transforaminal approach, 1 patient was operated with subfrontal translamina terminalis approach, 1 patient was operated with transcallosal-transchoroidal approach, 5 patients were operated endoscopically [Table 2]. Gross total excision was achieved in 15(88%) patients while in 2(11.7%) patients one of craniopharyngioma and one of colloid cyst subtotal resection was done due to their adherence to choroid plexus and optic chiasm.

The most common post-operative complication was endocrine dysfunction in the form of diabetes insipidus in 4 patients and cortisol insufficiency and hypothyroidism in 1 patient due to hypothalamic injury. All four patients of post op endocrine dysfunction were of craniopharyngioma. 3 patients develop post-op seizure in the evening of day of surgery, 2 patients in which post-operative seizure developed were operated by transcortical approach and 1 patient was operated with transcallosal approach.

Histopathological reports of 11 patients were colloid cyst, craniopharyngioma was found in 4

patients and central neurocytoma was seen in 2 patients [Table 3].

DISCUSSION

In current study of anterior third ventricular mass, in maximum patients 11(64%) the diagnosis was colloid cyst and most common symptom was headache seen in 100 % patients, vomiting in 41% patients and history of recurrent drop attacks in 23 % of patients. Similar results were reported by many authors^{13,20}.

The choice of the third ventricular tumors approach basically depends on the location of tumor, differential diagnosis, size, patient's clinical status and anatomical knowledge. It should be underlined that, although several corridors to the third ventricle exist, they all demand the incision of the neural tissue which may be relatively free from the underlying disease. Endoscopic approach remains the commonly used approach for the treatment of colloid cyst with chances of re-operation for residual cyst, but more cost effective and safer than open craniotomy for the resection of colloid cyst.

SURGICAL APPROACHES

Transcallosal approach

Transcallosal approach allow removal of tumor from anterior third ventricle by incising the corpus callosum longitudinally in the direction of corpus callosum less than 2.5 cm (to avoid disconnection syndrome) between the two pericallosal artery at the level of foramen of monro. Genu of internal capsule touches the wall of ventricle in the area lateral to foramen of monro near the anterior pole of thalamus. Retraction should be done at this level minimally to avoid hemiplegia. After incising the corpus callosum we have multiple options to reach the third ventricle. We use trans-foraminal approach in 6 patients, in which 4 patients were of colloid cyst, 1 was of craniopharyngioma and 1 was of central neurocytoma, in all the cases foramen monro was already dilated, there was no need of enlarging the foramen of monro. Gross total excision was achieved in 5 cases; in one patient of craniopharyngioma gross total resection was not achieved due to adherence to choroid plexus and chiasma. Radiotherapy was given later to this patient. We used inter-foraminal approach in 1 patient of craniopharyngioma, located just behind the foramen of monro in midline. The point of entry was approximately 2 cm posterior to

foramen of monro to preserve the hippocampal commissure to avoid temporary or permanent problems with memory function. In this approach the body of the fornix is split in the midline, in the direction of its fibers, to expose the velum interpositum^{3,15,27}. We used transchoroidal approach in 1 patient of craniopharyngioma, the entry was through the tenia fornicis as it has advantage that large veins like a thalamostriate vein which drains the internal capsule and central part of hemisphere and choroidal arteries can be dissected laterally, avoiding injury to these vessels. The transchoroidal and interforniceal approaches have the advantage of giving access to the central portion of the third ventricle behind the foramen of Monro by displacing it, rather than transecting the fibers in the fornix^{19,29}. Transcallosal approach is superior to transcortical approach as it is not dependent on ventricle size, more direct and avoid incision over cortex. **(Figure 1)**

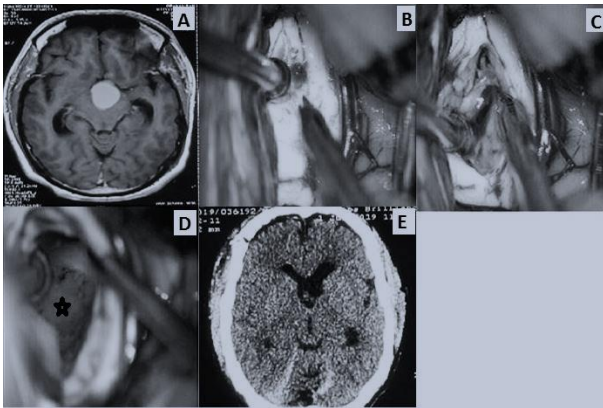


Figure 1. (A) Pre-operative contrast MRI axial scan showing contrast enhancing third ventricular mass (B) Anterior callosotomy between two pericallosal artery (C) Opening the right lateral ventricle (D) Lateral ventricle entered and tumor (marked with star) identified (E) Post-operative CT scan showing complete tumor removal.

Transcortical approach

We used transcortical-transforaminal approach in 3 patients. Out of 3, the diagnosis in 2 patients was colloid cyst and in one patient it was central neurocytoma. We entered through right middle frontal gyrus, after reaching lateral ventricle we used transforaminal corridor to remove the tumor as it is a natural orifice to enter third ventricle. Enlargement of foramen of monro was not required in any of the case as it was already dilated due to hydrocephalus. Gross total resection was achieved in all cases. Post-

operative complication in the form of seizure developed in two patients. **(Figure 2)**

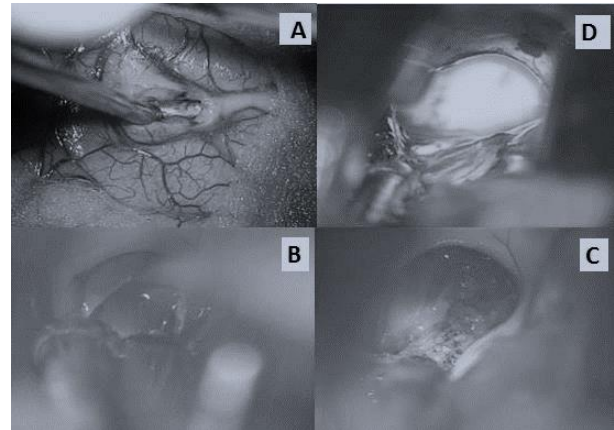


Figure 2. (A) Cortical incision around 1.5 cm in right middle frontal gyrus (B) Entry into right lateral ventricle and identification of cystic mass (C) Excision of cystic mass (D) Complete excision of mass.

Subfrontal translamina terminalis approach

We used subfrontal translamina terminalis approach in one patient of craniopharyngioma which was located in antero-inferior part of anterior third ventricle. After passing the planum sphenoidale, the optic nerves, the chiasm, and both internal carotid arteries are visualized. A1 was identified bilaterally and after incising the lamina terminalis above the chiasm up to the anterior commissure, tumor was seen which was internally decompressed initially and the remaining part of tumor was excised later. **(Figure 3)**

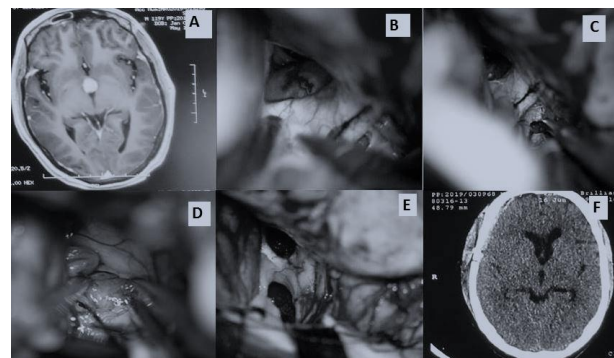


Figure 3. (A) Pre-operative Contrast MRI axial cut showing enhancing mass in third ventricle. (B) Identification and excision of the tumor in pre-chiasmatic and (C) optico-carotid cistern (D) Opening of lamina terminalis and excision of mass (E) complete excision achieved (F) Post-operative scan showing complete excision.

Endoscopic approach

We used endoscopic approach in 6 patients, diagnosis of all patients were colloid cyst. The colloid cyst of the third ventricle is an ideal tumour for endoscopic removal due to its cystic nature. Hydrocephalous was present in all cases which helped us to cannulate the lateral ventricle through planned burr-hole on right side. After reaching the colloid cyst, choroid plexus which was attached to colloid cyst was coagulated. After cauterisation of cyst wall, we opened the cyst wall applying endoscopic micro-scissor and then content was aspirated after that cyst wall was excised with minimal traction. In one patient cyst wall was densely adhered to the choroid plexus which was left in-situ after coagulation to prevent recurrence. (Figure 4)

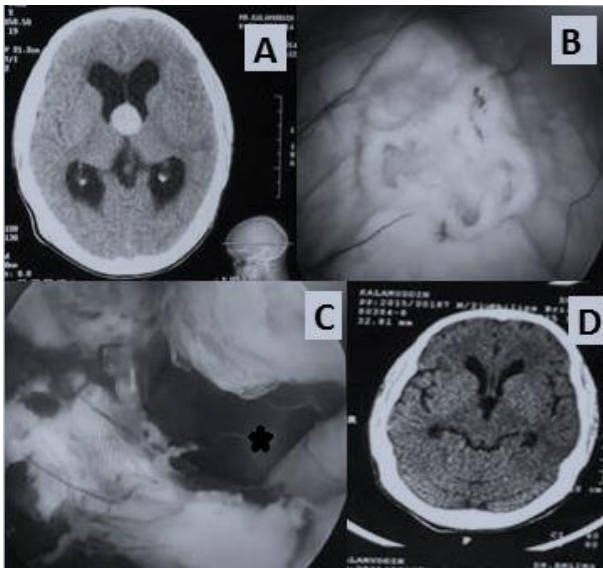


Figure 4. (A) Pre-operative CT scan showing hyperdense mass in third ventricle (B) Endoscopic view of mass filling the third ventricle, wall of the tumor cauterized at foramen of monro (C) Endoscopic view of the third ventricle after complete excision of mass and third ventriculostomy. Basilar artery seen in prepontine cistern () (D) Postoperative scan showing complete excision.

Post-operative complications

In our retrospective study of anterior third ventricular mass patients we encountered with two complication. First complication was post op seizure which was seen in three patients of which two were operated with transcortical approach, one patient was intubated due to seizure and was extubated next morning and one was operated with transcallosal approach, concluded that there are less

chances of post-operative seizure in transcallosal approach. In our study in 66% of patient of transcortical approach post op seizure developed which is very high, may be due to a smaller number of cases operated with transcortical approach. The incidence of postoperative seizures in the transcortical-transventricular approach in some series ranges from 11 to 13%^{6,1,16,17}. Another complication was endocrine dysfunction in the form of diabetes insipidus in 4 patients which was transient and cortisol insufficiency and hypothyroidism in 1 patient due to hypothalamic injury, in these patients hormone replacement was given. All four patients of post op endocrine dysfunction were of craniopharyngioma. In multiple studies hormonal replacement therapy was required in approximately 80% of the children.^{28,23,25,26,24}.

CONCLUSION

Anterior Third ventricular tumors are mostly benign and best treatment modality is surgical resection. When we analyzed the results of various approaches, we found that despite their unfavorable location, in all techniques the results were satisfactory for different tumors of different location in anterior third ventricle, when treated with carefully planned microsurgical or endoscopic approach and with proper knowledge of anatomical landmarks with minimal complication. Transcallosal approach is a safer route, superior to transcortical approach as it is not dependent on ventricle size, direct and avoids incision over cortex. Transcortical approach had more chances of post-operative seizure. Endoscopic approach is good if done by an experienced hand but have limitation of wide visualization. Tumors originating from the antero-superior part of the third ventricle can be easily approached through a transcallosal transforaminal route, whereas lesions arising from the anteroinferior portion of the third ventricle might be safely and effectively approached through subfrontal translamina terminalis approach. In most of the craniopharyngioma patients, post-operative hormone replacement therapy usually needed.

REFERENCES

1. Antunes JL, Louis KM, Ganti SR. Colloid cysts of the third ventricle. *Neurosurgery* 1980;7:450-55.
2. Apuzzo MLJ, AmarA: Thetranscallosalinterforaminal approach, in Apuzzo MLJ (ed) :Surgery of the third

- ventricle. Baltimore, Williams & Wilkins, 1998,ed 2, pp 421-452.
3. Apuzzo MLJ, Chikovani OK, Gott PS, Teng EL, Zee CS, Giannotta SL, Weiss MH: Transcallosal, interforaminal approaches for lesions affecting the third ventricle: Surgical considerations and consequences. *Neurosurgery* 1982;10:547-554.
 4. Apuzzo MLJ, Giannotta SL: Transcallosalinterforaminal approach, in Apuzzo MLJ (ed): *Surgery of the Third Ventricle*. Baltimore, Williams &Wilkins, 1987, pp 354-379.
 5. Apuzzo MLJ, Zee C-S, Breeze RE, DayJD: Anterior and mid-third ventricular lesions: A surgical overview, in Apuzzo MLJ (ed): *Surgery of third ventricular*. Baltimore, Williams & Wilkins, 1998, ed 2, pp 63-68.
 6. Camacho A, Abernathey CD, Kelly PJ, Laws ER Jr. Colloid cyst: Experience with the management of 84 cases since the introduction of computed tomography. *Neurosurgery* 1989;24:693-700.
 7. Chibbaro S, Di Rocco F, Makiese O, et al.: Neuroendoscopic management of posterior third ventricle and pineal region tumors: technique, limitation, and possible complication avoidance. *Neurosurg Rev*. 2012; 35: 331-40.
 8. Citow JS, Macdonald RL, Refai D: Comprehensive neurosurgery board review. New York, Thieme,2020,ed 3,pp 167-185.
 9. Cossu M, Lubinu F, Orunesu G, Pau A, SehrbuntViale E, Sini G, Turtas S: Subchoroidal approach to the third ventricle: Microsurgicalanatomy. *SurgNeurol* 1984; 21:325-331.
 10. Dandy WE. Benign tumours of the third ventricle of the brain: Diagnosis and treatment. Springfield, IL: Charles C Thomas,1933: pp214-236.
 11. Ehni G. Interhemispheric and pericallosal (transcallosal) approach to the cingulate gyri, intraventricular shunt tubes, and certain deeply placed brain tumours. *Neurosurgery* 1984;14:99-110.
 12. Fries G, Perneczky A. Tumors and cysts of the third ventricle. In: Rengachary SS, Ellenbogen RG, eds. *Principles of Neurosurgery*. Edinburgh: Elsevier Mosby; 2005:647-656.
 13. Kumar V, Behari S, Kumar Singh R, Jain M, Jaiswal AK, Jain VK. Pediatric colloid cysts of the third ventricle: Management considerations. *ActaNeurochir (Wien)* 2010;152:451-61.
 14. Lavyne MH, Patterson RH Jr: Subchoroidal trans-velum interpositum approach, in Apuzzo MLJ (ed): *Surgery of the Third Ventricle*. Baltimore, Williams & Wilkins, 1987, pp 381-397.
 15. Lavyne MH, Patterson RH Jr: Subchoroidal trans-velum interpositum approach to mid-third ventricular tumors. *Neurosurgery* 1983;12:86-94.
 16. Little JR, MacCarty CS. Colloid cysts of the third ventricle. *J Neurosurg* 1974;39:230-5.
 17. McKissock W. The surgical treatment of colloid cyst of the third ventricle. *Brain* 1951;74:1-9.
 18. Morrison G, Sobel DF, Kelley WM, Norman D. Intraventricular mass lesions. *Radiology*. 1984;153:435-442.
 19. Nagata S, Rhoton AL Jr, Barry M: Microsurgical anatomy of the choroidal fissure. *SurgNeuro* 1988; 130:3-59.
 20. Nitta M, Symon L. Colloid cysts of the third ventricle: A review of 36 cases. *ActaNeurochir (Wien)* 1985;86:99104.
 21. Patterson RH Jr: Subfrontaltranssphenoidal and trans-lamina terminalis approach, in Apuzzo MLJ (ed): *Surgery of the ThirdVentricle*. Baltimore, Williams & Wilkins, 1987, pp 398-412.
 22. ShucartW: Anteriotranscallosal and transcortical approach in Apuzzo MLJ(ed):*Surgery of third ventricle*. Baltimore, Williams & Wilkins, 1987,pp303-325
 23. Sklar CA. Craniopharyngioma: endocrine sequelae of treatment. *PediatrNeurosurg*. 1994;21(suppl 1):120-123.
 24. Sorva R, Heiskanen O, Perheentupaj. Craniopharyngioma surgery in children: endocrine and visual outcome. *Childs Nerv Syst*. 1988;4:97-99.
 25. Stahnke N, Grubel G, Lagenstein I, et al. Long-term follow-up of children with craniopharyngioma. *Eur J Pediatr*. 1984;142:179-185.
 26. Thomsett MJ, Conte FA, Kaplan SL, et al. Endocrine and neurologic outcome in childhood craniopharyngioma: review of effect of treatment in 42 patients. *J Pediatr*. 1980;97:728-735.
 27. Viale GL, Turtas S, Pau A: Surgical removal of striate arteriovenous malformations.*SurgNeurol*14:321-324, 1980.
 28. Weiner HL, Wisoff JH, Rosenberg ME, et al. Craniopharyngiomas: clinicopathological analysis of factors predictive of recurrence and functional outcome. *Neurosurgery*. 1994;35:1001-1010.
 29. Wen HT, Rhoton AL Jr, de Oliveira EP: Transchoroidal approach to the third ventricle: An anatomic study of the choroidal fissure and its clinical application.*Neurosurgery* 1988; 42:1205-1219.



Spontaneous spinal hematoma. Experiences from a tertiary care centre in South India

Rajeev Mandaka Parambil, Premkumar Sasi, V.M. Pavithran,
V.J. Byjo, Akhil Mohan

Department of Neurosurgery, Government Medical College,
Kozhikode, Kerala, INDIA

ABSTRACT

Background. Spontaneous spinal hematoma (SSH) is a rare condition that can result in severe functional disability and even death. But early detection and prompt intervention can substantially reduce the morbidity. We present a series of seven operated cases of SSH.

Methods. All operated cases of SSH between 2017 and 2019 were studied. The demographic and clinical features, risk factors and imaging features were analyzed. The functional outcome at discharge and 6 months were assessed.

Results. Seven operated cases of SSH with mean age 35(SD-20.9) were studied. Six cases were spontaneous spinal extradural hematomas (SSEDH) and one case was spontaneous spinal subdural hematoma (SSSDH). The most common site was cervicothoracic. Risk factors associated with SSH were thrombocytopenia, pregnancy, and necrotising pancreatitis. Two patients had preoperative Frankel's grade A-B, three had grade C and two had D. The mean interval between the onset of symptoms and surgery was 4.7days.

The functional outcome was dependent on the pre-operative functional status of the patient. Patients with SSEDH and thrombocytopenia had a poor outcome.

Conclusion. SSH even though spontaneous may be associated with risk factors. The presence of thrombocytopenia and preoperative functional status predicted outcome. This is the only single institution case series to report thrombocytopenia as a factor predicting poor outcome.

INTRODUCTION

Spontaneous spinal hematomas (SSH) are relatively rare and the majority of spinal hematomas are due to trauma. SSH includes both spinal extradural hematoma as well as subdural hematoma. The incidence of spontaneous spinal extradural hematoma (SSEDH) is around 0.1/100000 and that of spontaneous spinal subdural hematoma (SSSDH) is still rarer (1)(2). These conditions usually present as emergencies with rapidly progressive neurological deficits. Prompt recognition and early intervention is very important for a better outcome. Spinal hematoma was defined spontaneous when there was

Keywords

spontaneous spinal
hematoma,
outcome,
thrombocytopenia,
pregnancy



Corresponding author:
Akhil Mohan

Department of Neurosurgery,
Government Medical College,
Kozhikode, Kerala, India

akhilmohan84@gmail.com

Scan to access the online version



no associated trauma, iatrogenic injury (secondary to procedures like lumbar puncture, epidural catheter insertion), or post-operative spinal hematoma.

MATERIALS AND METHODS

Setting: Department of Neurosurgery, Government Medical College, Kozhikode, Kerala which is a 3000 bedded teaching hospital in south India where around 2000 neurosurgical cases are operated annually.

Cases: All operated cases of spontaneous spinal hematomas during 2017-2019

All operated cases of SSH during the study period were studied. History was taken to assess any risk factors like hypertension, coagulopathies or bleeding diathesis. Duration from the onset of symptoms to surgery was noted. A neurological examination was done and the preoperative functional status was assessed by Frankel's grade. All patients were evaluated with 1.5T MRI with contrast and MR angiography. The site of the bleed was assessed from MRI and the number of spinal segments involved was noted. All patients underwent standard decompressive laminectomy and evacuation of bleed. Laminectomy was done at the level of maximal cord compression. A maximum of two-level decompressive laminectomy was done. After surgery, the functional status was reassessed at discharge and 6 months. All patients with improvement in Frankel's functional scores were taken as a good outcome.

REPRESENTATIVE CASES

Case 1

A 75-year-old male who was on treatment for necrotizing pancreatitis developed sudden onset of neck pain followed by weakness of bilateral upper limbs and lower limbs. The patient had numbness of the body up to the neck. There was also associated urinary retention. On examination, there was grade 3 power of upper limbs and grade 2 power of lower limbs and blunting of all sensations below the clavicles (Frankels grade C). His routine blood workup showed elevated prothrombin time with an INR of 2.3, platelet count and activated partial thromboplastin time were normal. His S Amylase was 4300. MRI of the cervical spine showed T1 and T2 hyperintense signal from C2 to C6 with cord compression (Figure 1) suggestive of SDH. After correcting the coagulopathy with fresh frozen

plasma transfusions, we proceeded with C4C5 decompressive laminectomy. Dura was bulging with underlying hematoma and was opened in the midline. Thick SDH was evacuated. Postoperatively the lower limb power improved to grade 3 (Frankels grade C). At 6 months follow up both lower limbs and upper limbs had grade 4 power (Frankels grade D).

Case 2

24-year-old 34 weeks pregnant lady presented with complaints of sudden onset neck pain and rapidly progressive weakness of both lower limbs. On examination, she had grade 2 power of both lower limbs and sensory loss below the nipple level (Frankels grade C). Her routine blood investigations were within normal limits. MR imaging of the spine showed T2 intermediate signal lesion noted involving left posterolateral epidural space at C7-T1 vertebral level suggestive of hematoma (Figure 2). The management difficulty in view of 34 weeks completed pregnancy with regards to positioning as well as chances of intrauterine death were well explained. She was taken for caesarian section and after the procedure, in the same sitting C7T1 laminectomy was done in the prone position and the hematoma was evacuated. Postoperatively patient showed improvement in motor power. The baby was shifted to the neonatal ICU for further care. At 6 months follow up the patient was able to walk with support and do her day-to-day activities (Frankels grade D).

Case 3

A 25-year-old male patient presented with fever for 10 days and sudden onset of back pain for one day. He developed rapidly progressive weakness of lower limbs with urinary retention. On examination, he had grade 0 power of both lower limbs and there was sensory blunting below the nipple (Frankels grade B). His lower limb reflexes were absent and plantar was mute bilaterally. On routine blood profile, his platelet count was 17000 but markers for dengue were negative. MR imaging of his spine showed cervicothoracic C5-T11 region spinal anterior extradural hematoma with spinal canal compromise and cord compression. After correcting the platelet count with platelet transfusion, we proceeded for surgery. T4 T5 two-level decompressive laminectomy was done (at the level of maximum cord compression). Postoperatively patient remained

with the same preoperative motor power. At six months follow up the lower limbs were spastic with

flexor spasms and no spontaneous power (Frankels grade B). He is still on a urinary catheter.

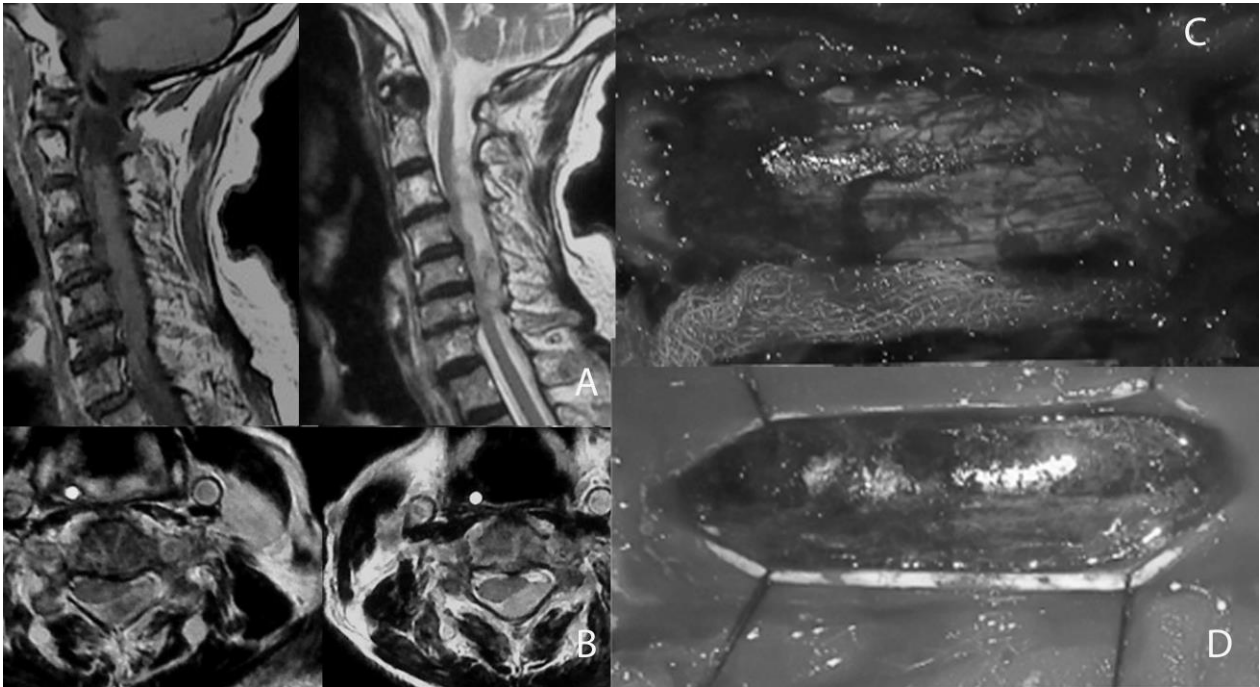


Figure 1. A- T1 T2 sagittal MR section of the cervical spine showing spinal SDH extending from C2-C6 B- T1T2 axial MR sections C- Per operative image showing bluish bulging dura with underlying hematoma D- dura is kept open with thick SDH.

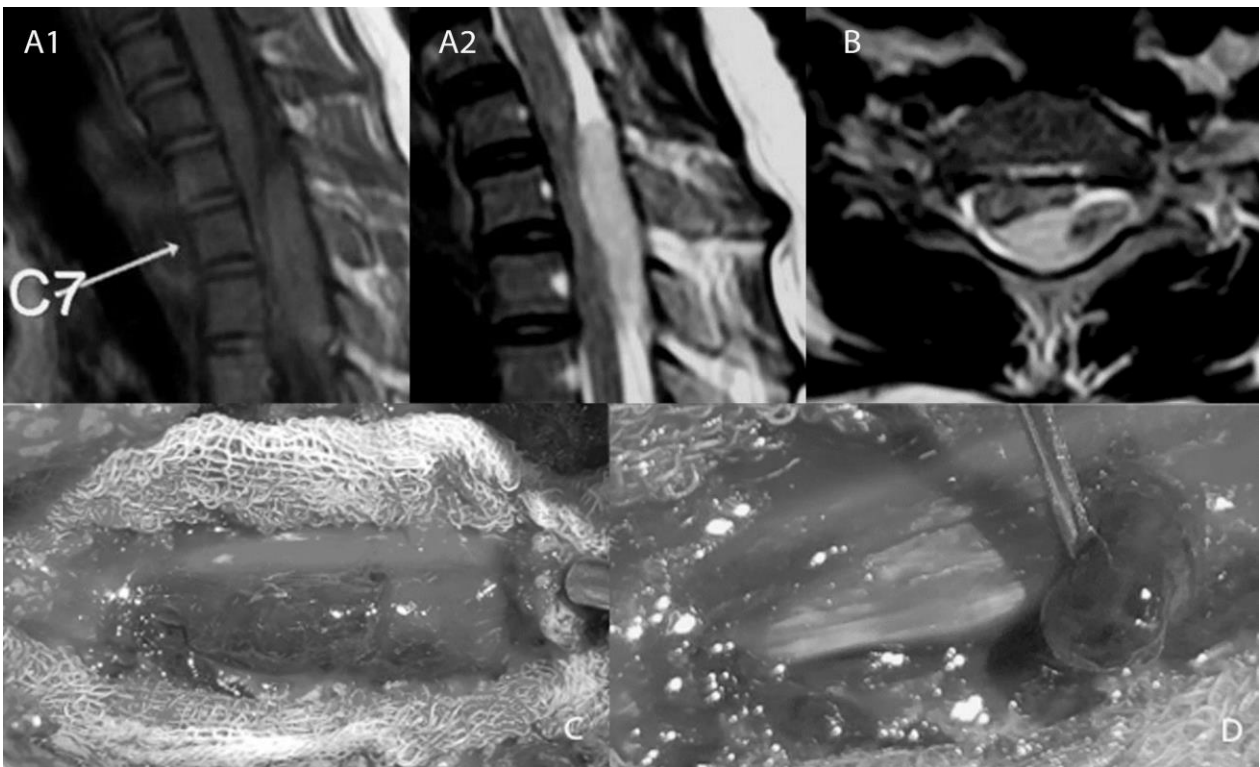


Figure 2. A1, A2- T1 and T2 sagittal MRI of the cervical spine showing SSEDH extending from C6-D2; B- axial MR sections showing SSEDH; C, D - per operative images of decompressive laminectomy and hematoma evacuation.

Cases	Age	Sex	Risk Factor	Platelet count/ μ l	INR	Pre-op Frankel's Grade	Type of SSH	Spinal Level of SSH (segments)	Time from onset to maximal weakness (hours)	Duration till Surgery (Days)	Frankel's Grade at discharge	Frankel's Grade 6 months follow up
1	25	M	Thrombocytopenia	17000	1.1	B	EDH	C7-D11 (13)	6	1	B	B
2	29	M	Nil	4.4 lakhs	1	D	EDH	D1-D2 (2)	72	5	E	E
3	24	F	Pregnancy	4.2 lakhs	0.8	C	EDH	C7-D1(3)	12	2	C	D
4	75	M	Necrotising Pancreatitis	3.3 lakhs	2.3	C	SDH	C2-C6 (5)	24	2	C	D
5	30	M	Thrombocytopenia	15000	1.2	A	EDH	C7-D1(3)	8	2	A	A
6	12	M	Thrombocytopenia	10000	0.9	C	EDH	C7-D3 (5)	10	2	C	C
7	50	F	Nil	2 lakhs	1.1	D	EDH	C5-D4 (8)	12	1	E	E

INR- International normalized ratio

Table 1. Demographic and clinical characteristics of the patients

RESULTS

Of the 7 cases, the mean age was 35 ± 20.9 and 5 (71%) were males (Table 1).

Thrombocytopenia was the most common risk factor and was present in three of our patients. One patient was 34 weeks pregnant and another had necrotising pancreatitis with coagulopathy. Two of them had no known identifiable risk factor. One patient had SSSDH while the rest had SSEDH. The most common level affected for SSEDH was cervicothoracic ($n=5$). The SSSDH was purely cervical. The craniocaudal extension of the hematoma was variable with the longest involvement of 13 spinal segments and the shortest of two segments. Of the SSEDH one patient had anterior spinal EDH and the rest had posterior spinal EDH. All patients had local back pain as the first symptom which heralded the onset of neurological deficits. Five of the patients with Frankel's grade less than 'D' had urinary retention. Five patients had preoperative Frankel's grade A-C and two had 'D'. All patients were operated at the earliest once the general conditions were favourable and the thrombocytopenia/ coagulopathy was corrected. The mean time between the onset of symptoms to maximal weakness was 20.5 hours. But in patients with thrombocytopenia, this was 8 hours. The mean interval between the onset of significant symptoms and surgery in our series was 4.7 days. Of our seven cases, four had improvement in their

Frenkel score and were categorised as a good outcome. At 6 months, all the remaining patients remained in their same preoperative Frenkel score. Those who had thrombocytopenia as risk factor had a poor outcome. Among the patients with thrombocytopenia two patients had fever with thrombocytopenia and for one patient thrombocytopenia was detected on the preoperative blood workup. Also, when the pre-operative functional status was low (Frenkel's A, B, and C) the outcome was poor. The improvement of functional status was significantly dependent on the pre-operative Frenkel's score. We couldn't find any association between the number of segments involved or the time period between the onset of symptoms to surgery with postoperative outcome.

DISCUSSION

SSEDH was first described by Jackson and Bain in the second half of the 19th century while SSSDH was first reported by Schiller (3)(4). SSH is a very rare clinical entity and its presentation can be variable from mild local pain to severe functional impairment in the form of weakness and bowel and bladder involvement. Usually, spinal hematomas are associated with trauma, iatrogenic procedures or spinal surgeries but we studied the patients who had a spontaneous spinal hematoma. The risk factors for SSH include AVMs, coagulation abnormalities,

anticoagulant use, vertebral haemangiomas, hypertension and pregnancy (5). However, in 40-60% of cases demonstrates no identifiable risk factor (6). In two of our patients, we could not identify any risk factors.

Thrombocytopenia was the most common risk factor for SSH in our study which was not reported before. Thrombocytopenia may be associated with a febrile illness which is common in northern Kerala where this study was conducted (7). In our series, two patients with thrombocytopenia had a preceding febrile illness, probably due to viral infection. The most common cause for viral infection with thrombocytopenia is dengue infection which was screened in all patients and was found negative. In a previous study from north Kerala, 26% of cases of thrombocytopenia associated with febrile illness were due to viral infections other than dengue(7). Viral infections causes thrombocytopenia both by decreased production of platelets from bonemarrow, as well as by the increased destruction by antibodies(8).

SSEDH is usually due to bleeding from posterior epidural venous plexus. But Beatty and Winson had postulated an arterial origin for SSEDH particularly in the cervical region since the intrathecal pressure is higher than the venous pressure(9). In all of our cases, we did not find any evidence of vascular malformation with imaging (MR angiography) as well as perioperatively. Bleeding from anterior epidural veins is rarer since they are smaller in caliber and are situated underneath the posterior longitudinal ligament. But anatomical variations are possible where the anterior epidural plexus can have a larger caliber. Among our SSEDHs one was located anterior to the thecal sac. The most common site of SSH in our series was cervicothoracic, probably due to mechanical factors as well as the prominence of epidural veins in the cervical and thoracic regions (6).

The factors associated with poor outcomes were thrombocytopenia and pre-operative functional status. The post-operative recovery depends on the extend of ischemia to the cord which depends on various factors like rate, force, and duration of compression(10). We postulate that in patients with thrombocytopenia as the basic platelet plug formation is not happening to arrest the bleeding there will be a rapid accumulation of blood in the epidural space(11-13). Also, the endothelial supporting function of the platelets is lost which

heralds the bleeding in thrombocytopenia causing endothelial gaps for RBC extravasation(12). Here the rate and force of compression may be very high on the cord and may result in neuronal death. All of our patients with thrombocytopenia had rapid deterioration of their motor power (mean-8hours). This shows the rate and force of compression of the spinal cord are high in these patients which resulted in poor postoperative outcomes. After a thorough literature search, this is the only single-institution case series to report thrombocytopenia as a factor predicting poor outcome. From the literature review, various studies have reported different values of platelet count below which there is a significant risk of major bleeding(14,15). We could not find any association between outcome and time took for surgical intervention from the onset of weakness.

Previous studies have shown that the most important factor determining the long-term outcome is the neurological status of the patient before surgical intervention. Other bad prognostic factors are the onset of severe symptoms in a shorter time frame, the involvement of thoracic cord and lack of sensory sparing. The evacuation of the SSEDH within 12 hours has been reported to predict the outcome(16). We found that the preoperative functional status predicted the outcome in our series.

The presence of SSEDH in pregnancy is even more rare and only 27 cases have been reported^[16,17]. Several theories are attributed to the occurrence of SSEDH during pregnancy. Usually, these hematomas tend to occur during the third trimester as the pressure in the vertebral venous plexus is normally elevated due to the compression by the gravid uterus(20). When there is a sudden change in pressure, as if when the patient sneezes, coughs, or during voiding there can be rupture of these veins resulting in SSEDH.

One of our cases was an SSSDH, which was due to coagulopathy secondary to necrotising pancreatitis of unknown etiology. The pathophysiology of coagulopathy in severe pancreatitis is due to the activation of platelets and various inflammatory cytokines which will result in consumption coagulopathy(21,22). The SSSDH is produced by the bleeding from subarachnoid vessels as the spinal subdural space is devoid of blood vessels unlike the cranial subdural space. The rupture of subarachnoid vessels may be due to trivial

trauma or sudden fluctuations in pressure due to coughing, sneezing, etc. Recently radiculomedullary veins were also postulated to be involved in spinal subdural bleeds (23).

CONCLUSIONS

The most important risk factor which caused SSH in our series was thrombocytopenia. The most common site was cervicothoracic. The outcome was dependent on preoperative functional status. Thrombocytopenia was noted as a bad prognostic factor in our study. The outcome was not dependent on the extent of hematoma or time period between symptom onset and surgery.

REFERENCES

1. Raasck K, Habis AA, Aoude A, Simões L, Barros F, Reindl R, et al. Spontaneous spinal epidural hematoma management: a case series and literature review. *Spinal Cord Ser Cases*. 2017;3(1):1–6.
2. Joubert C, Gazzola S, Sellier A, Dagain A. Acute idiopathic spinal subdural hematoma: What to do in an emergency? *Neurochirurgie* [Internet]. 2019;65(2–3):93–7. <https://doi.org/10.1016/j.neuchi.2018.10.009>.
3. Schiller F, Neligan G, Budtz-Olsen O. Surgery in haemophilia; a case of spinal subdural haematoma producing paraplegia. *Lancet (London, England)* [Internet]. 2(6535):842–5. <http://www.ncbi.nlm.nih.gov/pubmed/18894192>.
4. Jackson R. Case of Spinal Apoplexy. *Lancet* [Internet]. 94(2392):5–6. <https://linkinghub.elsevier.com/retrieve/pii/S014067360267624X>.
5. Groen RJM, Ponssen H. The spontaneous spinal epidural hematoma. A study of the etiology. *J Neurol Sci*. 1990;98(2–3):121–38.
6. Szkup P, Stoneham G. Spontaneous spinal epidural haematoma during pregnancy: Case report and review of the literature. *Br J Radiol*. 2004 Oct;77(922):881–4.
7. Fawas N. M, Beevi B. K, Valliyot B, Balakrishnan S. Study of acute febrile illness with thrombocytopenia in a tertiary care centre. *Int J Res Med Sci*. 2018 Jan 24;6(2):455.
8. Kutty R, Sreemathyamma S, Sivanandapanicker J, Mundhe V, Chhabra K, Peethambaran A. Burden of dengue-related neurosurgical emergencies during an epidemic: A tertiary care experience. *Asian J Neurosurg*. 2019;14(1):211.
9. Kim JK, Kim TH, Park SK, Hwang YS, Shin HS, Shin JJ. Acute Spontaneous Cervical Epidural Hematoma Mimicking Cerebral Stroke: A Case Report and Literature Review. *Korean J Spine*. 2013;10(3):170.
10. Raj R, Seppälä M, Siironen J. Spontaneous Spinal Epidural Hematoma: A Surgical Case Series of Ten Patients. *World Neurosurg*. 2016;93:55–9.
11. George JN. Platelets [Internet]. Vol. 355, *Lancet*. Elsevier Limited; p. 1531–9. <https://linkinghub.elsevier.com/retrieve/pii/S0140673600021759>.
12. Ho-Tin-Noé B, Jadoui S. Spontaneous bleeding in thrombocytopenia: Is it really spontaneous? [Internet]. Vol. 25, *Transfusion Clinique et Biologique*. Elsevier Masson SAS; p. 210–6. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1246782018300624>.
13. Morowski M, Vögtle T, Kraft P, Kleinschnitz C, Stoll G, Nieswandt B. Only severe thrombocytopenia results in bleeding and defective thrombus formation in mice. *Blood*. 2013 Jun 13;121(24):4938–47.
14. Neunert C, Noroozi N, Norman G, Buchanan GR, Goy J, Nazi I, et al. Severe bleeding events in adults and children with primary immune thrombocytopenia: a systematic review. *J Thromb Haemost* [Internet]. 13(3):457–64. <http://doi.wiley.com/10.1111/jth.12813>
15. Nagrebetsky A, Al-Samkari H, Davis NM, Kuter DJ, Wiener-Kronish JP. Perioperative thrombocytopenia: evidence, evaluation, and emerging therapies [Internet]. Vol. 122, *British Journal of Anaesthesia*. Elsevier Ltd; p. 19–31. <http://bjanaesthesia.org/article/S0007091218307530/fulltext>.
16. Bakker NA, Veeger NJGM, Vergeer RA, Groen RJM. Prognosis after spinal cord and cauda compression in spontaneous spinal epidural hematomas. *Neurology*. 2015;84(18):1894–903.
17. Soltani S, Nogaro MC, Jacqueline Kieser SC, Wyatt MC, Kieser DC. Spontaneous Spinal Epidural Hematomas in Pregnancy: A Systematic Review. Vol. 128, *World Neurosurgery*. Elsevier Inc.; 2019. p. 254–8.
18. Maurizio Domenicucci, MD, Cristina Mancarella, MD, Giorgio Santoro, MD, Demo Eugenio Dugoni, MD, Alessandro Ramieri, MD, Maria Felice Arezzo, MS A, Paolo Missori M. Spinal epidural hematomas: personal experience and literature review of more than 1000 cases. *J Neurosurg Spine* [Internet]. 27(2):198–208. <https://thejns.org/spine/view/journals/j-neurosurg-spine/27/2/article-p198.xml>.
19. Samali M, Elkoundi A, Tahri A, Bensghir M, Haimeur C. Anesthetic management of spontaneous cervical epidural hematoma during pregnancy: a case report. *J Med Case Rep* [Internet]. 11(1):171. <http://www.ncbi.nlm.nih.gov/pubmed/28648141>.
20. Kelly MEB, Beavis RC, Hattingh S. Spontaneous spinal epidural hematoma during pregnancy. *Can J Neurol Sci* [Internet]. 32(3):361–5. <http://www.ncbi.nlm.nih.gov/pubmed/16225182>.
21. Kakafika A, Papadopoulos V, Mimidis K, Mikhailidis DP. Coagulation, platelets, and acute pancreatitis [Internet]. Vol. 34, *Pancreas*. p. 15–20. <http://journals.lww.com/00006676-200701000-00002>.
22. Mimidis K, Papadopoulos V, Kotsianidis J, Filippou D, Spanoudakis E, Bourikas G, et al. Alterations of platelet function, number and indexes during acute pancreatitis. *Pancreatology* [Internet]. 4(1):22–7.

<https://linkinghub.elsevier.com/retrieve/pii/S1424390304800048>.

23. Mattei TA, Rehman AA, Dinh DH. Acute Spinal Subdural Hematoma after Vertebroplasty: A Case Report

Emphasizing the Possible Etiologic Role of Venous Congestion. *Glob spine J* [Internet]. 5(5):e52-8. <http://www.ncbi.nlm.nih.gov/pubmed/26430602>.



Cervical extradural metastasis from follicular carcinoma thyroid after 14 years post-thyroidectomy with Elsberg phenomenon

Vijayan Peettakkandy, Shanavas Cholakkal,
Subrat Kumar Soren, Harikrishnan S.

Department of Neurosurgery, Government Medical College,
Kozhikode, Kerala, INDIA

ABSTRACT

Background. Follicular carcinoma thyroid usually metastasises to bone. Common sites of bone metastasis include skull and spine. Spinal metastasis are more common in the cervical region followed by dorsolumbar spine. Cervical extradural lesions present with progressive quadriparesis, sensory loss, dysautonomia, and respiratory distress. Typical Elsberg phenomenon in a cervical extradural lesion is rare. Elsberg phenomenon involves the involvement of ipsilateral upper limb, ipsilateral lower limb followed by contralateral lower limb and contralateral upper limb.

Case presentation. We are reporting a case of 47-year-old lady presented with progressive quadriparesis of 1-month duration. Her weakness started in left upper limb followed by left lower limb, right lower limb and right upper limb weakness. She also had sensory loss below the level of C7. She had undergone near-total thyroidectomy for solitary thyroid nodule 14 years back and was on thyroid supplementation since then. Histopathology at that time was reported as follicular adenoma with Hashimoto thyroiditis. Her right upper limb power was grade 4- Left upper limb grade 1 right lower limb Grade 3, left lower limb grade 2 with hypertonia of both upper and lower limbs. She was evaluated with MRI Spine which showed a dumb bell-shaped extramedullary lesion involving the C5-C6 vertebra with significant cord compression and encasement of the left vertebral artery. USG neck showed left supraclavicular lymph node enlargement and small residual thyroid tissue in the left side of the thyroid. USG guided FNAC from the thyroid tissue and neck nodes were inconclusive. The patient underwent C4 and C5 laminectomy and subtotal excision from the cervical lesion. Histopathology was reported as metastasis from follicular carcinoma thyroid. Postoperatively patient limb power improved to grade 3 left upper and lower limbs and was discharged and later referred for radioiodine ablation

Conclusion. Cervical extradural metastasis from follicular carcinoma thyroid can present with Elsberg syndrome even without any neck swelling even after decades of post thyroidectomy status for a benign aetiology. Laminectomy and decompression may lead to clinical improvement.

INTRODUCTION

Carcinoma thyroid is the fifth common malignancy in women and can be broadly classified in to papillary, follicular, medullary and anaplastic.

Keywords

thyroid,
follicular carcinoma,
cervical extradural,
Elsberg phenomenon



Corresponding author:
Shanavas Cholakkal

Department of Neurosurgery,
Government Medical College,
Kozhikode, Kerala, India

shanavascholakkal@gmail.com

Scan to access the online version



(1) Papillary carcinoma thyroid is the most common variety, which usually metastasise to neck nodes via lymphatic system. Whereas the follicular carcinoma thyroid spreads hematogenously to lungs and bones. More than 80% of bone metastases from all tumors including DTC are located in the axial skeleton red marrow (vertebrae, ribs and hips) owing to high blood flow. (1)Clinically, they present with bone pains, pathological fractures or signs of cord compression. Progressive Quadripareisis with typical Elsberg phenomenon as the presenting manifestation of follicular carcinoma of thyroid in a post near- total thyroidectomy for a benign etiology after several years of thyroidectomy is quite uncommon in medical literature related to this (2).

CASE PRESENTATION

A 47-year-old lady presented with complaints of neck pain of 4 months duration followed by progressive paraparesis of 1 month duration. Weakness initially started as left upper limb weakness 1 month back followed by weakness of left lower limb, right lower limb and right upper limb. At the time of presentation, she was bed ridden. She also complained of numbness over all the four limbs and chest and abdomen and had urinary retention and constipation. She had underwent near total thyroidectomy for Solitary thyroid nodule 14 years back and histopathology was reported as follicular adenoma with Hashimoto thyroiditis. She was under follow up for next 2 years and was on thyroid hormone replacement. On examination, she was conscious, alert, hemodynamically stable. No signs of hyperthyroidism or hypothyroidism. She had a healed thyroidectomy scar in the neck with Left supraclavicular lymphadenopathy and no other palpable swellings. Her right upper limb power was grade 4- Left upperlimb grade 1 right lower limb Grade 3, left lower limb grade 2 with hypertonia of both upper and lower limbs. She had sensory loss below the C7 level. Triceps jerk, knee jerk and ankle jerk were exaggerated bilaterally and plantar was extensor bilaterally.

Her routine blood investigations were normal. ESR was slightly elevated (42 mm/hr). Mantoux test was negative. She was evaluated with MRI C-spine with screening of whole spine which showed an ill-defined lobulated heterogenous enhancing dumbbell shaped probably extradural soft tissue lesion of size 3.5x3.3x3 cm (TxAPxCC) in the C5 and

C6 vertebral level with infiltration in to the body of C6 vertebra. The lesion was extending intraspinally causing severe spinal canal compromise with compression over the spinal cord . The lesion was extending superiorly in to the posterior epidural space from C4 to C7 and was encasing the left vertebral artery at level of C5- C6 vertebra. USG abdomen and chest X ray were normal. Ultrasound neck showed thyroid tissue in the thyroid bed and left supraclavicular lymphadenopathy. FNAC from the left supraclavicular lymphnode and recurrent thyroid were inconclusive.

She underwent C5-C6 laminectomy and subtotal excision of the lesion. The intraoperative findings suggested an extradural lesion at C5-C6 level involving and destroying the C6 vertebra and compressing the spinal cord and encasing left vertebral artery. Histopathology was reported as metastasis from the follicular carcinoma thyroid with TTF-1 positivity. Patient improved clinically postoperatively. At the time of discharge, she had grade 3 power of left upper and lower limbs and grade 4 power of right upper and lower limbs. She underwent radio-iodine scanning followed by radioiodine ablation. She is presently on limb physiotherapy and rehabilitation.



Figure 1. MRI C-spine showing an ill-defined lobulated heterogenous enhancing dumbbell shaped probably extradural soft tissue lesion



Figure 2a. Intraoperative image showing extradural lesion with destruction of C5 and C6 vertebral body with encasement of left vertebral artery.

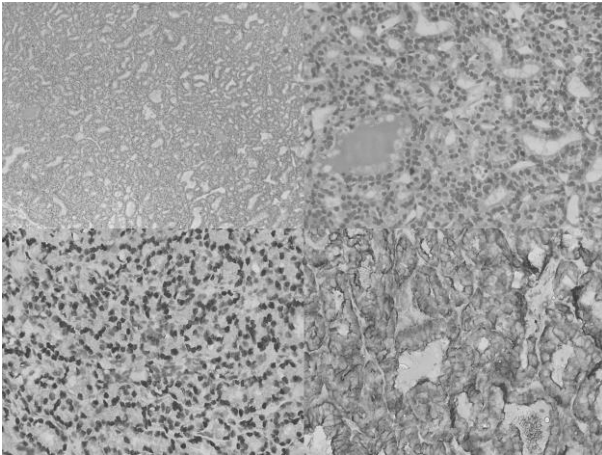


Figure 2b. Histopathology was reported as metastasis from the follicular carcinoma thyroid with TTF-1 positivity.

DISCUSSION

Follicular carcinoma usually forms osteolytic metastasis and are common in the skull and spine. Usual site of spinal metastasis in follicular carcinoma is thoracic > lumbar > cervical. (1) Presentation of follicular carcinoma thyroid spinal metastasis may

vary. Patient can present with destruction of the vertebral body, localised tenderness, radiculopathy and with features of myelopathy like quadriparesis or paraparesis, sensory deficits, sphincter disturbances, autonomic dysfunction and respiratory distress. In extradural lesions usually symptoms are progressive as the size of the lesion increases. (3,4)

Elsberg U phenomenon is the progressive quadriparesis with sequential involvement of ipsilateral upper limb, ipsilateral lower limb followed by contralateral lower limb and contralateral upper limb, often described as U-shaped or clockwise involvement of limbs. Elseberg U phenomenon is commonly seen in cervical myelopathy due to cervical extradural lesions or in Foramen magnum pathology and very rarely due to extradural metastasis from follicular carcinoma thyroid. (3,5,6,7)

MRI spine is the investigation of choice for spinal tumours. MRI can help in differentiating the intramedullary tumours from extramedullary and extradural tumours. Bony structure can be properly evaluated by CT spine. (8) Contrast enhanced imaging helps in delineating the relationship of the cervical lesion with vertebral artery as well. If required vertebral artery reconstruction, along with bony reconstruction can help in perioperative planning. Extradural lesions are most commonly tuberculous, myelomatous or metastatic. Hence workup for primary is done routinely. Surgical decompression and biopsy can help in confirmation of diagnosis and clinical improvement

This case is reported in view of the rare clinical presentation of metastatic follicular carcinoma thyroid after 14 years post thyroidectomy without any neck swelling presenting with Elsberg phenomenon. It also suggests the need for more regular followup in cases of follicular adenoma and Hashimoto thyroiditis.

CONCLUSION

Cervical extradural metastasis from follicular carcinoma thyroid can present with Elsberg syndrome even without any neck swelling even after decades of post thyroidectomy status for a benign etiology. Laminectomy and decompression may lead to clinical improvement. Postoperative radioablation may be required in case of incomplete excision.

ABBREVIATIONS

MRI - Magnetic resonance imaging; CT - Computed Tomography; DTC - Differentiated thyroid cancer; FNAC - Fine needle aspiration cytology; ESR - Erythrocyte sedimentation rate.

DECLARATIONS

Ethics approval and consent to participate.

Informed written consent for participation obtained from the Patient and her caretakers.

Institutional Ethics committee approval not obtained as the study did not involve any human trials.

Consent for publication

Informed written Consent for publication obtained from the Patient and her caretakers

Availability of data and material

Data and material available in the Department of Neurosurgery, Govt Medical College, Kozhikode, Kerala, India.

Competing interests

Authors declare that there is no competing interests

Funding

Nil

Authors' contributions

All authors have contributed to the preparation of manuscript. All authors have read and approved the manuscript, and ensure that this is the case.

Acknowledgements

Nil

REFERENCES

1. Parameswaran R, Shulin Hu J, Min En N, Tan WB, Yuan NK. Patterns of metastasis in follicular thyroid carcinoma and the difference between early and delayed presentation. *Ann R Coll Surg Engl.* 2017;99(2):151–4.
2. Ríos A, Manuel Rodríguez J, Balsalobre MD, Febrero B, Tébar J, Parrilla P. [Distant metastases as the initial manifestation of follicular thyroid carcinoma]. *Endocrinol Nutr.* 2009 Apr;56(4):213–4.
3. Upreti V, Sridhar M, Dhull P, Sen A. An unusual cause of progressive quadriparesis. *Indian J Endocrinol Metab.* 2013 Oct 1;17(7):155.
4. Haghpanah V, Abbas SI, Mahmoodzadeh H, Shojaei A, Soleimani A, Larijani B, et al. Paraplegia as initial presentation of follicular thyroid carcinoma. *J Coll Physicians Surg Pak.* 2006 Mar;16(3):233–4.
5. Dong P, Chen N, Li L, Huang R. An upper cervical cord compression secondary to occult follicular thyroid carcinoma metastases successfully treated with multiple radioiodine therapies. *Med (United States).* 2017 Oct 1;96(41).
6. Goldstein SI, Kaufman D, Abati AD. Metastatic thyroid carcinoma presenting as distal spinal cord compression. *Ann Otol Rhinol Laryngol.* 1988;97(4):393–6.
7. Khan MN, Sharfuzzaman A, Mostafa MG. Spinal cord compression as initial presentation of metastatic occult follicular thyroid carcinoma. *J Neurosci Rural Pract.* 2014 Apr;5(2):155–9.
8. Çoban G, Yildirim E, Gemici K, Erinanç H. MRI findings of lumbosacral metastasis from occult follicular thyroid cancer: report of a case. *Surg Today.* 2014 Mar;44(3):553–7.



Surgical options for traumatic fractures of the thoracic and lumbar spine. A series of 20 patients

Elhawary E. Mohamed¹, Aljboor Ghaith S.²,
Buzantian P. Armand²

¹ Benha University Hospital, Neurosurgery Department, Benha, EGYPT

² Emergency Hospital of Saint Pantelimon, Neurosurgery Department, Bucharest, ROMANIA

ABSTRACT

Background context. Thoracolumbar fractures represent a large number of spine injuries in adults. Such fractures are a result of traumatic accidents with high-energy impacts, such as falls from height or following motor vehicle accidents, often resulting in some degree of neurological deficit.

Purpose. To report a total of 20 cases of thoracolumbar fractures in young adults with various neurological manifestations. The majority had indications for transpedicular fixation.

Study Design. Series of 20 cases and review of the literature.

Patient Sample. A series of 20 patients with a history of falling from a height or after motor vehicle accidents (RTA) with complicated fractures at the level of the thoracolumbar vertebrae which present with neurological deficits.

Methods. We report here on a total of 20 patients with a history of falls from height or following RTA. Patients presented to the hospital complaining of back and abdominal pain. Fractures at the thoracolumbar vertebral level were confirmed with imaging studies revealing post-traumatic spinal deformities. All cases were initially considered for conservative medical treatment. However, unstable complicated cases with bone fragment migration as well as spinal canal compression were deemed candidates for surgical intervention via posterior spinal fusion with transpedicular screw fixation.

Written informed consent was gathered from all patients. Detailed history, clinical examination, as well as X-ray, computed tomography and magnetic resonance imaging of the dorsolumbar spine were obtained in all cases. Neurological status was assessed using the Frankel grading for spinal cord injury.

Results. The patients tolerated the operations without complications and remained in stable postoperative condition.

Conclusion. Surgical treatments via transpedicular fixation are extremely efficient for treating unstable and complicated thoracolumbar spinal fractures. Nevertheless, conservative medical treatment is still of high value and should be considered as the first treatment option, especially in stable cases. The patients who underwent surgery showed excellent outcomes and improvement of neurological deficits. The surgical procedure preferred in the present study was the posterior spinal fusion with pedicle screw fixation.

Keywords

spine,
fractures,
surgery,
fixation,
thoracic and lumbar,
screw,
transpedicular,
treatment



Corresponding author:
Aljboor Ghaith S.

Emergency Hospital of Saint
Pantelimon,
Neurosurgery Department,
Bucharest, Romania

ghaith_gtr@yahoo.com

Scan to access the online version



INTRODUCTION

The biomechanical properties of the thoracic spine and thoracolumbar junction directly predispose this anatomically unique region to various types of traumatic injuries. High-energy trauma produced by road traffic accidents (RTA) is the primary cause of injury, followed by falls from a height and sports-related injuries (1). The thoracolumbar vertebrae are associated with a high risk of post-traumatic compression fractures due to the effects of axial loading, which under normal conditions contribute to the natural kyphotic curvature of the thoracic spine (2) (3).

The management of traumatic fractures of the thoracolumbar (T1-L5) spinal column remains controversial. There are a number of publications outlining various treatment strategies aimed at obtaining normal mobilization and stability of spinal fractures. Despite the variety of treatment options presented in medical literature, there has as yet been no definitive consensus with regards to a gold-standard management protocol (4)(5). Nor have there been any reported advantages with respect to patient outcome, despite several operative strategies being currently employed to achieve fracture reduction and fixation. Furthermore, there is a scarcity of supporting evidence in the available literature for choosing conservative versus surgical management or vice versa (6) (7).

While patients with limited vertebral body compression, for example, can benefit from non-operative treatment such as thoracolumbar orthosis, restriction of activities and administration of analgesics (8), surgical management is generally considered of utmost necessity in patients presenting with severe biomechanical spinal instability or acute or chronic neurologic deficit (9). Indications for surgical treatment include unstable injuries associated with neurological deficits, complicated fractures with dislocation or progressive deformations associated with compression of neural structures (10) (11) (12) (13). The primary objectives of surgical treatment of unstable thoracolumbar fractures are optimizing neural decompression, early stabilization, pain relief and adequate nursing care (6) (14).

A number of classification systems have been devised to categorize thoracolumbar fractures. One of the most commonly used classification systems in clinical practice today is the scheme proposed by

Francis Denis in 1983, which has aided in the communication and description of thoracolumbar fractures and their respective treatment strategies among medical practitioners [Figure 1] (15). Denis maintained that complete rupture of the posterior ligamentous complex alone would be insufficient to create spinal instability in flexion, extension, rotation and shear, and that spinal instability at least in flexion would develop only in the presence of additional disruption of the posterior longitudinal ligament and posterior annulus fibrosus (15) (16).

In the Denis classification system, the spine is subdivided into three columns as follows: anterior column (anterior longitudinal ligament [ALL] and anterior two-thirds of the vertebral body and annulus), middle column (posterior one-third of the vertebral body and annulus, posterior vertebral wall and posterior longitudinal ligament [PLL]), and posterior column (all posterior structures of the PLL which include: posterior bony arch and posterior ligamentous complex (supraspinous and interspinous ligaments, capsule, and ligamentum flavum)).

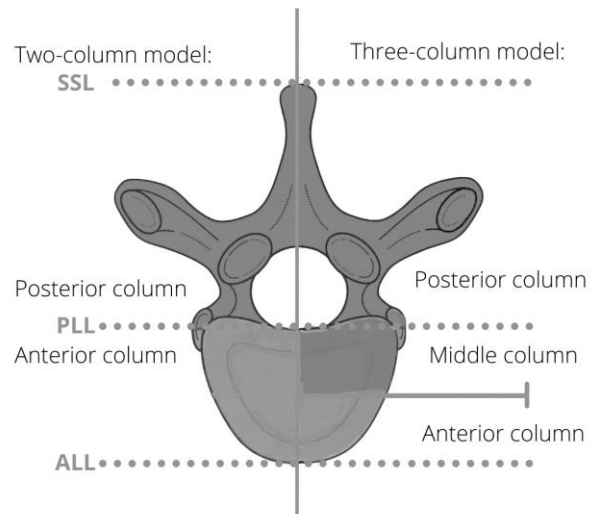


Figure 1. Two-column model compared with three-column model (Denis). In addition to the positions of SSL, PLL and ALL.

The Denis "3-column model" relied on anatomic divisions to guide surgical planning, whereas more modern classification systems such as the Thoracolumbar Injury Classification System (TLICS) emphasize the initial neurologic status and structural integrity of the posterior ligamentous complex as a

guide for surgical decision-making and have demonstrated a high intra- and inter-observer reliability. Other systems, such as the Load-Sharing Classification, also aid as useful tools in planning the extent of instrumentation and fusion (15) (17) (18) (12) (19).

This case study is aimed at presenting our experiences in adult traumatic spinal injury. Radiological findings, treatment strategies, and clinical outcomes were evaluated retrospectively and compared with the available literature.

CASES AND METHODS

Study design

This is a retrospective study conducted at Benha University Hospital, Benha, Egypt, between 2016 and 2020.

We report here a total of 20 patients with thoracolumbar injuries sustained by falling from a height or following RTA, of which 16 had presented with indications for surgical management via transpedicular fixation, i.e., with unstable and complicated fractures associated with neurological deficits. Four cases had no indication for surgical treatment and were treated conservatively.

As per standard procedure for all patients admitted to our clinic, detailed patient histories were gathered, comprehensive physical examinations were performed, and all relevant laboratory investigations were completed for each case. Pre- and postoperative neurological status was assessed using the Frankel Grade classification for spinal cord injury, a functional grading of impairment in activities of daily living, and analysis of gait disturbances (20) (21).

After performing an initial clinical and neurological examination, the diagnosis was confirmed radiologically, i.e., bony structure injury of the thoracolumbar spine was confirmed with computerized tomography (CT), while neural and ligamentous involvement was confirmed with additional magnetic resonance imaging (MRI).

The length of time, from the day of patient admission to the operation, ranged from 3-7 days, depending on the clinical and neurological status of the patient, as well as on trauma severity.

All patients were fully informed with regard to treatment options to manage their injuries, including the aim and scope of the treatment, possible operative and perioperative risks, as well as potential

short- and long-term complications. Informed written consent forms were signed and submitted by all patients upon hospital admission.

CASE REPORTS

Surgical procedures

All patients in the present study with surgical indications were treated with pedicle screw fixation, which is generally considered a safe procedure through which adequate reduction and stability can be achieved, and provides patients with early pain relief and mobility (22). Although either anterior or posterior approaches can be used in spinal fusion surgery, posterior approaches are associated with lower postoperative morbidity rates. Less aggressive than the anterior approach, posterior fixation is associated with several advantages, including less intraoperative bleeding and fewer postoperative complications, while still achieving excellent spinal stabilization (23) (24). Preoperative intravenous antibiotic prophylaxis was administered to each patient.

The posterior approach was utilized for each case in the present study. Each patient was placed in a prone position. A midline posterior incision centered over the affected area was performed with the aid of preoperative X-Ray imaging planning. An initial laminotomy was performed on each patient. Using anatomical landmarks such as the facet joints and transverse processes, it was possible to establish insertion points on the pedicles [Figure 2]. For example, an entry point can be identified by drawing a horizontal line through the middle of the transverse processes, or from the intersection of the upper one-third of the transverse process and a vertical line drawn through the prominent ridge on the superior articular facet.

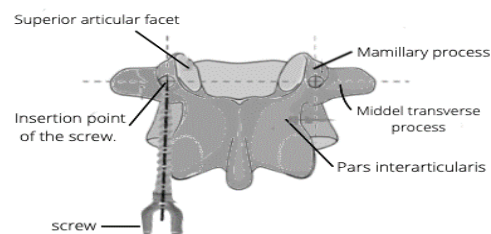


Figure 2. The transpedicular insertion; insertion point of the screw.

Cortical bone was nibbled off at the point of the intersection of these two lines, pilot holes were created using a burr, and a ball handle probe was passed through the cancellous channel in the pedicle and into the vertebral body. Screw angulation and placement were performed using C-arm-guided fluoroscopy.

A transpedicular screw fixation and fusion approach was then employed, with bilateral, two-level pedicle screw placement, followed by bilateral rod placement situated on the fracture level and on at least one adjacent level superiorly or inferiorly, based on the location of the intact endplate. For example, in cases where the inferior endplate was intact and the superior endplate was fractured, screws were inserted caudally to the inferior endplate at an angle of approximately 5°. Transpedicular screw fixation was complemented by placement of adjoining rods with cross-connecting rod reinforcement. Distraction was performed and locking nuts were tightened. The surgical wound was thoroughly irrigated and closed over a suction drain.

POSTOPERATIVE MONITORING AND FOLLOW-UP

Postoperative imaging studies were performed in order to ensure the efficacy of the surgical procedure. Following surgery, patients were transferred to the post-anesthesia care unit for 24 hours. Postoperative patient mobilization was initiated on the first day. The average time for suture removal was approximately 12 days. Patients wore a Taylor brace until the 10th–12th postoperative day, or longer in cases with injuries involving all three columns. Regular physiotherapy and assisted mobilization were continued until the patient was discharged from the hospital. A detailed neurological examination was repeated on the day of patient discharge.

All patients with unstable injuries were monitored with regular follow-up visits: at 4–6 weeks post-operation, and bi-monthly afterwards, for an average total period of 24–36 months. Follow-up visits included clinical, neurological and radiological examinations, as well as documentation of any postoperative complications.

RESULTS

The posterior spinal fixation approach was used in the surgical treatment of 16 cases with unstable thoracolumbar burst fractures. Of the patients

treated surgically, 12 had no neurological deficits at the time of hospital presentation. Transient leg numbness, tingling sensation and pain, immediately after the traumatic event, were reported by eight of these 12 patients, with symptoms subsiding by the time of admission into the emergency department. Persistent neurological deficit was reported by four cases in the study.

Six cases presented with a T12-level fracture, three cases with a T10-level fracture, one case with T9-level fracture and one case of T11-level fracture. Three cases presented with a fracture at the L3-level, and two cases presented with a fracture at the L2 level. There were no cases of dural tears in the present study.

Of the four patients with stable injuries who were managed conservatively, two cases presented with T10-level fractures, one case with a T11-level fracture and one case with a fracture at the L2-level. The mean duration of hospitalization was approximately four weeks.

Preoperatively, eight of the patients presented with normal motor function (Frankel grade E). Six patients presented with preserved, functionally useful voluntary motor function (Frankel grade D). Two cases presented with preserved, nonfunctional voluntary motor function (Frankel grade C).

In follow-up visits at 24–36 months postoperatively, the majority of patients had neurological recovery with either Frankel grade of E or D scores, while one patient had a persistent motor deficit, with a Frankel grade of C score.



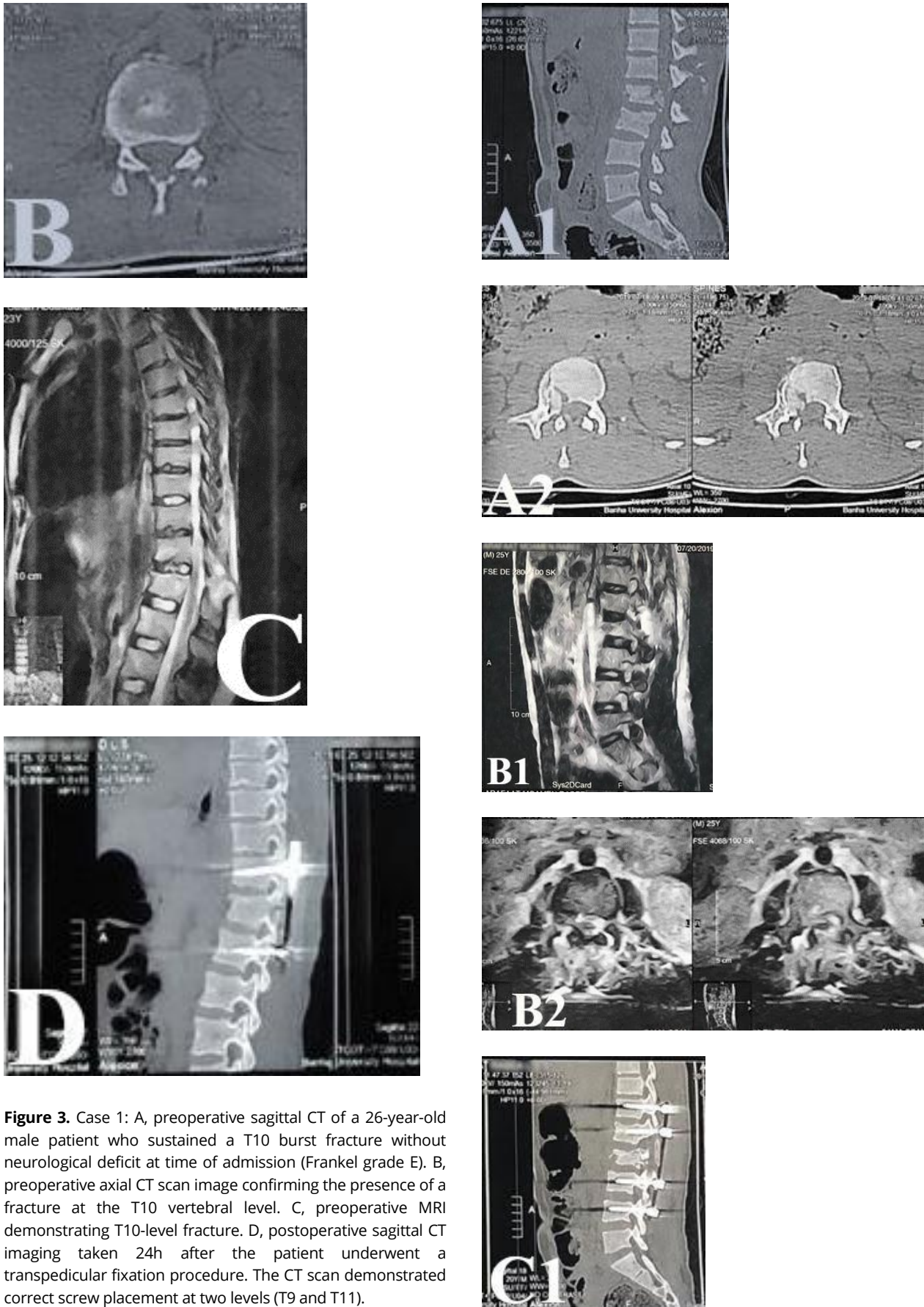


Figure 3. Case 1: A, preoperative sagittal CT of a 26-year-old male patient who sustained a T10 burst fracture without neurological deficit at time of admission (Frankel grade E). B, preoperative axial CT scan image confirming the presence of a fracture at the T10 vertebral level. C, preoperative MRI demonstrating T10-level fracture. D, postoperative sagittal CT imaging taken 24h after the patient underwent a transpedicular fixation procedure. The CT scan demonstrated correct screw placement at two levels (T9 and T11).

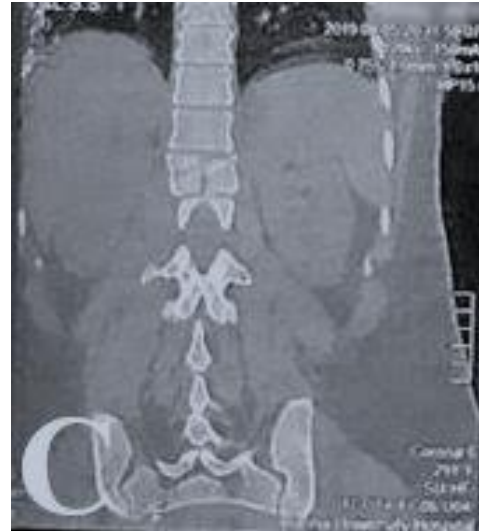
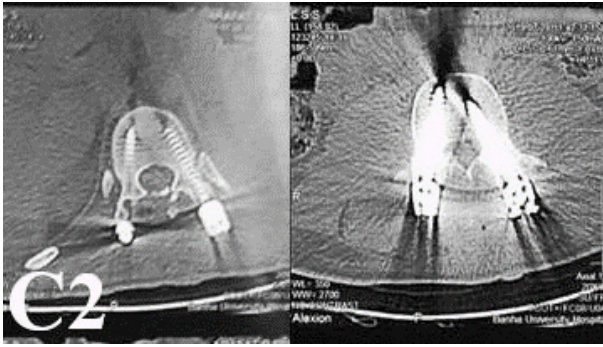


Figure 4. Case 2: A1, preoperative sagittal CT of a 20-year-old male patient who sustained an L2 burst fracture without neurological deficit at time of admission (Frankel grade E). A2, preoperative axial CT image confirming the presence of a fracture at the L2 vertebral level. B1, preoperative sagittal T1-weighted MRI revealing L2 fracture. B2, preoperative axial MRI showing the aspect of the fracture at L2. C1, postoperative sagittal CT scan obtained 24h after the patient underwent a transpedicular fixation procedure. The CT scan demonstrated correct screw placement at two levels superiorly (T12, L1) and two levels inferiorly (L3, L4). There is no significant correction of local post-traumatic kyphosis C2, postoperative axial T1-weighted MRI, 12 months after surgery, at which point the patient had a Frankel grade of E.

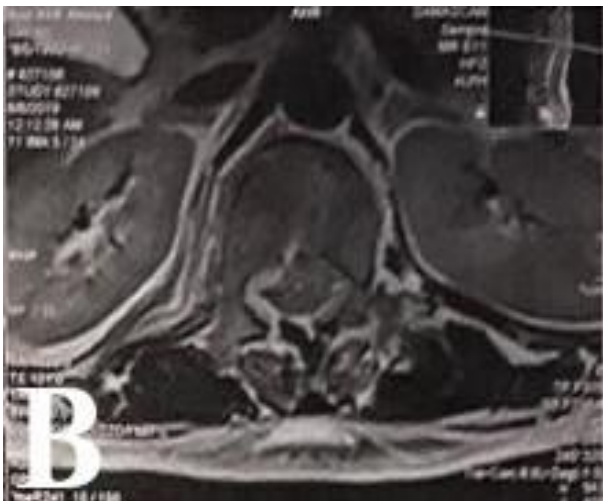
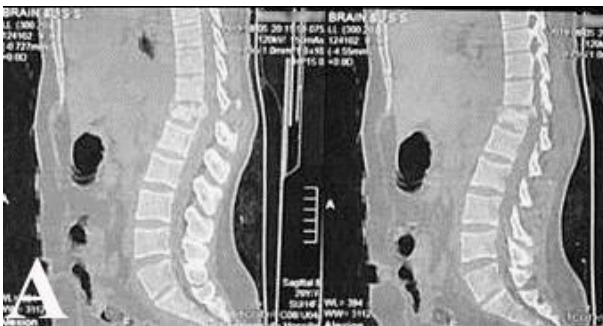




Figure 5. Case 3: A, preoperative sagittal CT of a 29-year-old female patient who suffered a T12 burst fracture without neurological deficit at time of admission (Frankel grade D). B, preoperative axial MRI confirming the presence of a fracture at the T12 vertebral level. C, preoperative coronal CT scan confirming the T12-level fracture. D, preoperative sagittal MRI demonstrating the fracture at T12. E1, postoperative sagittal CT scan acquired 24h after the patient underwent a transpedicular fixation procedure. The CT scan demonstrated correct screw placement at two levels superiorly (T10, T11) and one level inferiorly (L1). E1 and E2, postoperative sagittal and axial T1-weighted MRI revealing correct screw insertion. Serial follow-up CT scans were performed after surgery, with the patient having a Frankel grade of D.

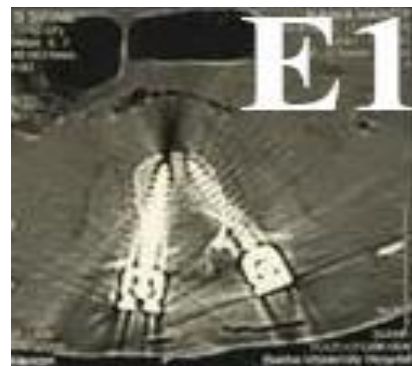


Figure 6. Case 4: A, preoperative sagittal CT of a 17-year-old female patient who was admitted with a burst fracture at the level of L3, with bilateral motor deficit (Frankel grade A). B, preoperative axial MRI confirming spinal cord compression at the L3-level due to the fracture. C, preoperative sagittal MRI demonstrating the presence of the fracture with evidence of spinal cord injury at the L3-level. D, postoperative sagittal CT scan revealing screw insertion at one level superiorly (L2) and at one level inferiorly (L4) relative to lesion. E, postoperative axial T1-weighted MRI revealing correct screw insertion (L2). Serial follow-up CT scans were performed after surgery, with the patient having a Frankel grade of C.

DISCUSSION

The mechanism of injury in the present case series was via fall from a height or road traffic accidents (RTA) (20 cases), resulting in thoracolumbar fractures. Four patients presented with uncomplicated stable fractures, in which conservative management was indicated. The majority of the patients in the study (16 cases) had complicated unstable fractures. The patients were operated using the posterior approach with transpedicular screw fixation within 3-7 days from hospital admission. In our study, the most common site of fracture was located at the T12 vertebral level (6 cases). The surgical interventions proceeded uneventfully with no major intra- or postoperative complications.

All patients who underwent surgery were assessed neurologically pre- and post-operatively at regular intervals. The Frankel Grade classification was used to evaluate neurological function of the patients. Preoperatively, eight cases had Frankel grades of E, six cases had Frankel grades of D and two cases had Frankel grades of C. Following surgical intervention, only one patient had a persistent Frankel grade of C, while the majority of our cases had Frankel grades of D or E, which indicate acceptable results with posterior fixation for unstable thoracolumbar fractures.

CONCLUSION

The main objectives of surgical treatment of thoracolumbar fractures are to improve neurological deficits as classified by the Frankel scale, to prevent spinal cord injuries, and to achieve stability by screw fixation. Our case study demonstrates that posterior transpedicular screw fixation is an effective and safe surgical method to obtain stabilization of the spine. The approach is associated with good surgical outcomes and minimal complications.

REFERENCES

1. Epidemiology of incident spinal fracture in a complete population. C. Burns, R. Hu, C.A. Mustard., 15;21, feb 1996, *Spine*, Vol. 4, pp. 492-9.
2. The contribution of the three columns of the spine to spinal stability. M.F. Lospinuso, et al., T.R. Haheer, J.M. Tozzi., 27, 1989, a biomechanical model., Vol. *Paraplegia*, pp. 432-439. 10.1038/sc.1989.69.
3. Surgical Treatment of Traumatic Fractures of the Thoracic and Lumbar Spine: A Systematic Review of the Literature on Techniques, Complications, and Outcome. E. Buskens, et al, J.J. Verlaan, C.H.,\, Diekerhof., 7, 1 April 2004, Wolters Kluwer Health, Inc., Vol. *Spine*, pp. 803-814. 10.1097/01.BRS.0000116990.31984.A9.
4. Surgical vs. conservative treatment of fractures of the thoracolumbar transition. Klampfer H, et al., Resch H, Rabl M., 103, 2000, Vol. *Unfallchirurg*, pp. 281-288.
5. Thoracolumbar burst fracture. A biomechanical investigation of its multidirectional flexibility. T W McGowen, M M Panjabi T R Oxland., 19, 1994, Vol. *Spine*, pp. 578 -585. 8184353.
6. The three column spine and its significance in the classification of acute thoracolumbar spinal injuries. Denis F. 8, Nov-Dec 1983, Vol. *Spine (Phila Pa 1976)*., pp. 817-31.
7. Spinal instability as defined by the three-column spine concept in acute spinal trauma. F. Denis. 189, Oct 1984, *Clinic Ortho Related Research*, Vol. *Spine*, pp. 65-76. PMID: 6478705.
8. Stability of spinal fractures and fracture dislocations. G. M. Bedbrook. 1, 9 May 1971, Vol. *Paraplegia*, pp. 23-32. doi: 10.1038/sc.1971.3..
9. Pathophysiology and Management of Traumatic Spinal Injuries. Andy Shores, DVM, MS, PhD. 195, 4 July 1992, *Diseases of the spine*, Vol. *Spinal Trauma*, pp. 859-890.
10. Pediatric spinal injury review of 174 hospital admissions. Hamilton MG Myles ST. 5, 1992, *J. Neurosurg*, Vol. 77, pp. 700-704.
11. Spinal fractures and dislocations in children and adolescents. McPhee IB. 6, 1981, Vol. *Spine*, pp. 533-537. 10.1097/00007632-198111000-00001.
12. A prospective multicenter study of cervical spine injury in children. Pressman BD, Shah MN, P Viccellio Simon H., 2, 2001, Vol. *Pediatrics* 108, p. E20.
13. Treatment of unstable thoracolumbar junction burst fractures with short- or long-segment posterior fixation in magerl type fractures. Dogan O, Tabak AY, Altay M, Ozkurt B, Aktekin CN, Ozturk AM., 8, 2007, *Eur Spine J Off Publ*, Vol. 16, pp. 1145-1155.
14. Cortical bone trajectory for lumbosacral fixation: penetrating S-1 endplate screw technique: technical note. Takashi Kato, Keitaro Matsukawa Keitaro Matsukawa 1 , Yoshiyuki Yato., 2, 2014, *J Neurosurg Spine*, Vol. 2014 Aug;21, pp. 203-9. 10.3171/2014.3.SPINE13665.

15. Thoracolumbar spine trauma: review of the evidence. J Jallo, . 2, Jun 2013, *J. Neurosurgery Sci*, Vol. 57, pp. 115-22.
16. Brad J. Chauvin, . Denis Classification. s.l. : StatPearls Publishing, 2020. NBK544310.
17. Incomplete burst fractures of the thoracolumbar spine: a review of literature. C Josten, . 12, 25 May 2017, *Eur Spine J* ., Vol. 26, pp. 3187-319. 10.1007/s00586-017-5126-3.
18. Management of thoracolumbar spine fractures. Weishi Li, . 1, Jan 2014, *Spine J.*, Vol. 14, pp. 145-64. 10.1016/j.spinee.2012.10.041.
19. Does Surgical Intervention or Timing of Surgery Have an Effect on Neurological Recovery in the Setting of a Thoracolumbar Burst Fracture? So Kato. 4, Sep 2017, *J Orthop Trauma*, Vol. Suppl, pp. S38-S43. doi: 10.1097/BOT.0000000000000946..
20. A Comparison of Diagnostic Stability of the ASIA Impairment Scale Versus Frankel Classification Systems for Traumatic Spinal Cord Injury. Amanda Botticello, . 9, Sep 2020, *Multicenter Study*, Vol. *Arch Phys Med Rehabilitation*, pp. 1556-1562. 10.1016/j.apmr.2020.05.016.
21. Posterior short-segment fixation including the fractured vertebra for severe unstable thoracolumbar fractures. Jin Wu, Zhida Chen, Bin Lin. 1, 15 Jan 2018, *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi*, Vol. 32, pp. 59-63. 10.7507/1002-1892.201708082..
22. Surgical outcome of posterior short segment transpedicle screw fixation for thoracolumbar fractures. Vijay Sharma,. 4, Dec 2013, *J Orthop*, Vol. 10, pp. 162-167. 10.1016/j.jor.2013.09.010.
23. Steffee variable screw placement system in the management of unstable thoracolumbar fractures: a Third World experience. R Bahadur,. 10, Dec 1998, Vol. *Injury* 29, pp. 737-42. 10.1016/s0020-1383(98)00173-9.
24. Prognostic factors and optimal management for patients with cervical spinal cord injury without major bone injury. Ippei Kitade, Hideaki Nakajima, Ai Takahashi,. 2, May 2019, *J Orthop Sci*, Vol. 24, pp. 230-236. 10.1016/j.jos.2018.10.001.



Intradural migration of bullet in vertebra corpus after meningitis

Halil İbrahim Gündüz¹, Turan Kandemir²

¹ Eskişehir City Hospital, Department of Neurosurgery, Eskişehir, TURKEY

² Yunus Emre State Hospital, Department of Neurosurgery, Eskişehir, TURKEY

ABSTRACT

In a gunshot injury, the spinal cord of the thoracic region is usually the most affected and damaged part of the body. In most cases, the bullet cannot be removed without causing more damage to the injury. Over time, the bullet tends to travel in different areas of the body. Moreover, cases on bullet movements in the spinal canal were reported in the literature. In this study, we reviewed the diagnosis and treatment of a 27-year-old male patient with a bullet detected in his vertebra corpus, which is caused by a gunshot injury. During the follow-up period, an intradural migration of the bullet from the vertebra corpus was observed. Furthermore, we performed surgery to prevent any future neural damage. In this study, we focused on a case with a gunshot injury, presenting an intradural migration of a bullet from the vertebra corpus after meningitis.

INTRODUCTION

Gunshot injuries (GSI) are the third most common cause of spinal cord injuries after traffic accidents and falls from height. Although the incidence of spinal cord injuries caused by GSI changes according to the countries' level of development, the most common causes of it are suicides, accidents and attacks. Moreover, in developed countries, the approximate percentage of spinal cord injuries caused by GSI among all kinds of spinal cord injuries was reported to be 15% [1,2].

Aside from the aforementioned damages on the spinal cord, secondary injuries, such as the degradation of the spinal cord vascularisation, autoregulation deficiency and hypotension, also worsen the neurological presentation due to systemic effects [3].

In the literature, cases of bullets travelling through the intraspinal canal were reported. In our case, the bullet was first stuck in the vertebra corpus, and removing it through manipulation was not feasible during the surgical operation. But in the follow-up period, it was observed that the bullet had left the corpus and travelled through the spinal canal after meningitis.

Keywords

gunshot injury,
intradural migration,
spinal cord



Corresponding author:
Turan Kandemir

Yunus Emre State Hospital,
Department of Neurosurgery,
Eskişehir, Turkey

turankandemir26@gmail.com

Scan to access the online version



CASE PRESENTATION

A 27-year-old male patient was admitted to the emergency service following the gunshot injury in the chest area. A chest tube was then inserted as the patient had hemopneumothorax. A hole in the patient's body due to the bullet which entered his thorax from right axillary lower region was observed. Based on the neurological examination, the patient had paraplegia in the lower extremity, and anaesthesia was administered below T10; moreover, an anal sphincter reflex was not observed. The steroid protocol treatment from the NASCIS protocol was performed. A bullet was stuck in the T10 corpus was observed using the spinal tomography (Figure 1). Therefore, an urgent surgery was performed. During the surgery, it was observed that the dura and medulla were partially disintegrated. Two-third of the bullet was in the T10 corpus. However, the bullet could not be removed despite further manipulation. The operation was then ended following duraplasty. As no change in the postoperative neurological examination was observed, the patient was required to undergo physical therapy and rehabilitation and was discharged afterwards.



Figure 1. Image of the bullet in the T10 corpus following the gunshot injury.

Due to wound drainage and high fever, the patient was re-admitted a month after the discharge. A meningeal irritation was observed, and the white blood count and C-reactive protein were high. Due to the presence of meningitis, antibiotherapy was started. Moreover, the patient was reoperated since serous wound discharge continued to persist. During the surgery, it was observed that the discharge was coming from an intradural distance. The bullet was stuck in the corpus could not be removed through manipulation. Duraplasty was then performed again, and the wound discharge ended postoperatively. After the antibiotherapy was completed and the wound recovered completely, the patient was discharged and was required to undergo physical therapy and rehabilitation.

Based on the medical imaging performed nearly a year later, it was observed that the bullet in the T10 corpus was dislocated and moved in an intradural distance; it reached the S1 level (Figure 2). Moreover, the neurological deficit of the patient regressed, and the muscle strength of the lower right extremity was evaluated as 4/5 and the lower left extremity 2/5. The patient underwent surgery in order to remove the bullet. During the operation, it was observed that the bullet had reached the L4 level when checked based on the results of the fluoroscopy (Figure 3). L4 total laminectomy was performed after opening the L4 level. When the dura was opened, it was observed that the bullet was in the L3 level. When the patient was in a reverse Trendelenburg position, the bullet moved towards the dural opening and was removed. The dura was closed via primary suturing. Furthermore, no additional deficit was observed in the postoperative neurological examination.



Figure 2. CT image showing the bullet at the S1 level.

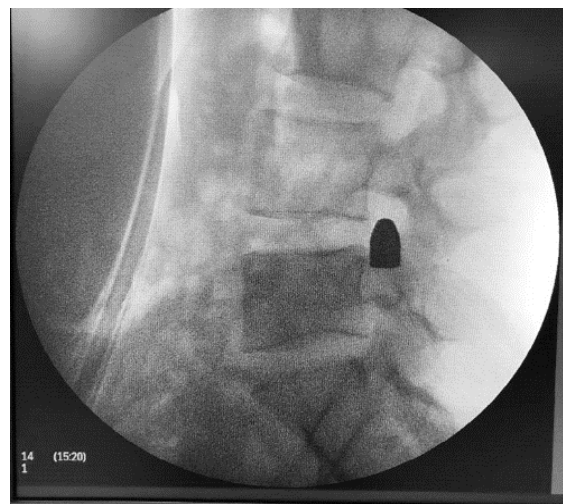


Figure 3. Fluoroscopy image before intraoperative laminectomy

DISCUSSION

Spinal gunshot injuries occur mostly in the thoracic region. Another common place for it to occur is the lumbar region, with the cervical region being the less common ^[4]. Injuries in the cervical region have a more mortal course. In the thoracic region, the spinal canal/cord ratio is lower and the neural damage is higher compared with that in other levels.

In the literature, studies showing a bullet migration in the intervertebral disc level and in the paraspinal mass tissue into the spinal canal were included. Kuijlen et al. presented a case of bullet migration from the paraspinal muscles to the spinal canal at the L3 level ^[5]. Conway et al. presented a case showing a cauda equina development after a bullet migration from the L4 to L5 intervertebral disc level ^[6]. Ceylan et al. presented a case who had back pain caused by a bullet migration anteriorly between the L2 and L3 intervertebral disc levels ^[7]. In our case, the bullet was stuck in the T10 corpus and migrated through the spinal canal in a span of nearly 1 year since the injury. In our case, in contrast to the other cases, two-third of the bullet was stuck in the vertebra corpus which could not be removed by manipulation during the two surgical operations performed, and the bullet spontaneously migrated to the canal following the patient's meningitis treatment.

In a gunshot injury, leaving the bullet inside the body rarely causes infection, neurological deficit and lead poisoning ^[8]. In the case of our patient, the infection occurred followed by a cerebrospinal fluid (CSF) leakage after the first operation. Moreover, gunshot injury treatment is still a disputed and complex subject. Surgery is necessary if CSF leakage, progressive neurological deficit and infection formation co-occur with the infection. Aside from gravity, respiratory movements and CSF fluidity are also factors that affect the bullet movement inside the spinal canal. A neurological deficit may also occur if the bullets move in the spinal canal; in our case, no signs of newly developed neurological deficits were observed. However, a neurological deficit may develop later due to the fibrotic reactions forming in the pia and arachnoid. It was also shown that axon and myelin damage and lead and copper implantation causes induces gliosis in the spinal cord ^[9,10]. Therefore, we decided to remove the bullet piece although our patient lacked any symptom or additional neurological finding.

Computed and direct tomography are usually the first diagnostic options for gunshot injuries. Kafadar et al. reported that a magnetic resonance imaging (MRI) can be performed since the bullet is covered with non-ferromagnetic metals just like copper in low-speed gunshot injuries ^[11]. Although MRI is the appropriate option for the evaluation of neurological tissue damage and causes less artefact compared to computed tomography (CT), its use is limited depending on the patient. Since such cases are required to undergo an urgent operation, a ballistic examination cannot be performed for the bullet as MRI is more commonly used. Moreover, the patient did not have an MRI scan since we did not have the sufficient information about the bullet structure. When our patient was positioned on the operation table, the results of the endoscopy showed that the bullet was moving. The bullet which was at the S1 level based on the preoperative CT scan had reached the L4 level, and we determined our incision accordingly. In the case presented by Genç et al., the bullet moved intraoperatively, and its location was determined via ultrasonography ^[12]. We then performed laminectomy after determining the location of the bullet via endoscopy. However, we did not have to perform a long-level laminectomy and refrained from stabilisation.

Based on the findings of this study, it should be noted that despite being stuck in the bone, most foreign objects can move in later stages. Overall, no neurological deficit following the bullet migration was observed in our patient and necessary measures were taken to prevent any possible neurological deficit. In addition, the individual who caused the injury was also identified by the researchers.

REFERENCES

1. Aarabi B, Alibaii E, Taghipur M, Kamgarpur A. Comparative Study of Functional Recovery for Surgically Explored and Conservatively Managed Spinal Cord Missile Injuries. *Neurosurgery* 1996;39(6):1133-40.
2. Young J. Spinal cord injury statistics: experience of the regional spinal cord injury systems. 1982.
3. Bono CM, Heary RF. Gunshot wounds to the spine. *The Spine Journal* 2004;4(2):230-40.
4. Calik S, Calik M, Esme H. Intraspinal Bullet Migration: A Rare Case Report. *CHEST* 2017;152(4):A44.
5. Kuijlen JM, Herpers MJ, Beuls EA. Neurogenic Claudication, a Delayed Complication of a Retained Bullet. *Spine* 1997;22(8):910-914.

6. Conway JE, Crofford TW, Terry AF, Protzman RR. Cauda equina syndrome occurring nine years after a gunshot injury to the spine. A case report. *JBJS* 1993;75(5):760-763.
7. Ceylan D, Cosar M. Migration of a Bullet in the Lumbar Intervertebral Disc Space Causing Back Pain. *Neurologia medico-chirurgica* 2008;48(4):188-90.
8. Yoshida GM, Garland D, Waters RL. Gunshot wounds to the spine. *Orthop Clin North Am* 1995;26(1):109-16.
9. Bordon G, Burguet Girona S. Gunshot wound in lumbar spine with intradural location of a bullet. *Case Rep Orthop* 2014;2014:698585.
10. Esnal-Baza E, Zaldua-Unanue M, Etxebarria-Foronda I. Neurological Symptoms Secondary to the Intraspinial Migration of a Bullet. *Revista Española de Cirugía Ortopédica y Traumatología (English Edition)* 2007;51(6):351-3.
11. Kafadar AM, Kemerdere R, Isler C, Hanci M. Intradural migration of a bullet following spinal gunshot injury. *Spinal Cord* 2006;44(5):326-9.
12. Genç A, Usseli MI, Pamir MN. When the bullet moves! Surgical caveats from a migrant intraspinal bullet. *Neurologia i Neurochirurgia Polska* 2016;50(5):387-91.



Global neurosurgery, Bangladesh and COVID-19 era. A perspective from a low-income country

Robert Ahmed Khan¹, Moshir Rahman²,
Amit Agrawal³, Ezequiel Garcia-Ballestas⁴,
Luis Rafael Moscote-Salazar⁴

¹ Neurosurgery Department, BSMMU, Dhaka, BANGLADESH

² Neurosurgery Department, Holy Family Red Crescent Medical College, Dhaka, BANGLADESH

³ Department of Neurosurgery, All India Institute of Medical Sciences, Bhopal, INDIA

⁴ Center for Biomedical Research (CIB), Faculty of Medicine, University of Cartagena, Cartagena, COLOMBIA

ABSTRACT

Background. COVID-19 has become an alarming pandemic for our earth. It has created panic not only in China but also in developing countries like Bangladesh. Bangladesh has adequate confinements to constrain the spread of the infection and in this circumstance, overall healthcare workers including neurosurgeons are confronting a ton of difficulties. The purpose of this paper is to depict the proficiency of Global neurosurgery in this COVID-19 time.

Method. Global neurosurgery offers the chance of fusing the best proof-based guidelines of care. This paper demonstrated that, in low to middle-income countries, Global medical procedure has been received to address the issues of residents who lack critical surgical care.

Results. Inappropriate and insufficient asset allotment has been a significant obstacle for the health system for decently giving security to the patients. The fundamental training process has been genuinely hampered in the current circumstance. Worldwide health activities have set to an alternate centre and Global neurosurgery as an assurance is slowed down.

Conclusion. This paper recommended that Global neurosurgical activities need to come forward and increase the workforce to emphasize surgical service.

COVID-19 pandemic has brought terrible impacts and vigorously affected medicinal services including the neurosurgical field.^{2,3} This pandemic has represented a challenge for all nations. The entire world is confronting this challenge which requires the engagement of all physicians, including neurosurgeons, to manage COVID-19 outcomes.^{4,5} Although neurosurgery constitutes a small portion of this but still, its impact is significant in those requiring intervention. Thus, the concept

Keywords

global neurosurgery,
COVID-19,
low-income country



Corresponding author:
Moshir Rahman

Neurosurgery Department,
Holy Family Red Crescent Medical
College,
Dhaka, Bangladesh

dr.tutul@yahoo.com

Scan to access the online version



of Global Neurosurgery was conceded to address the difference around the world in neurosurgical caregiving. But at present, the world is facing unprecedented effects of COVID-19. Even though pandemics have a worldwide extension, their impacts on the population are unbalanced.¹ The unequal distribution of health care services amongst different countries is the challenging world facing in the 21st century. Surgery has been identified as a major modifiable factor in saving millions of lives. Global surgery was thus introduced to address the issue of people who lack essential surgical care especially in low to middle-income countries (LMIC).

Global Surgery is defined as an area of study, research, practice, and advocacy that aims to improve health outcomes and achieve health equity for all people in need of surgical and anesthetic treatment, with particular emphasis on underserved populations and populations in crisis.⁷ In this context Global neurosurgery encompass those who suffer from neurosurgical conditions or those who need neurosurgical care.⁸ Global neurosurgery as a new paradigm in care offers the possibility of incorporating the best evidence-based standards of care. Development of research projects and policies. In the Bogota Declaration of Global neurosurgery, 2016 recommendation for amplification of access, alignment of all neurosurgical activity, the advancement of relevant research, assimilation of neurosurgical capacity, and advocacy of universal coverage was made.⁹ It has been estimated that 44% of the world's neurosurgeons reside in high-income countries whereas more than 80% of the disease arises in LMICs.⁶ To mitigate this a global neurosurgical collaboration is required to increase the workforce and strengthen the surgical service.

There has been less consideration coordinated toward the effect of COVID-19 in LMICs. According to a report, nine-in-ten spine cases are in LMICs, and the spine cases make up 39% of the operative cases in LMICs.⁶ Allowing access to surgical procedures to all patients who require them is not a privilege, it is an obligation of the nations. Bangladesh is a country located in Southeast Asia with a population of 164,689,383 people according to UN data. But with around 170 neurosurgeons working in 13 government and few military and private hospitals, it falls way short of providing essential neurosurgical care. Making things worse the current pandemic is making essential neurosurgical care more

inaccessible and backloging of chronic neurosurgical conditions.

During the time of COVID-19 pandemic prioritizing neurosurgical patients has been a major challenge in Bangladesh like many other affected countries of the world. Inappropriate and inadequate resource allocation has been a major obstacle for the health system to function fairly providing safety to the patients. Neurosurgeons are being redeployed to help their colleagues in the hospitals where there was a shortage of personnel. Although this task-sharing and task-shifting are very much necessary in the pandemic situation it resulted in curtailing of neurosurgical service in some instances.¹⁰ There has been an enormous abatement in operative cases which has altogether affected the training of neurosurgical residents as they rely upon elective careful volume to sharpen their clinical and operative skills.¹¹ One of the key elements of providing standard neurosurgical service worldwide is the training of capable and competent neurosurgeons. The country offers post-graduation in neurosurgery in 4 centers. Also, as a part of the commitment for Global neurosurgery, Bangladesh offers post-graduation to neighboring countries. During recent times many neurosurgeons of Nepal have done their post-graduation from Bangladesh. This systemic and rigorous training process has been seriously hampered in the current situation. Although many international conferences and courses were canceled, these were replaced by numerous webinars arranged by different societies where world-renowned neurosurgeons shared their experience and gave their insight. But these opportunities certainly do not make up for the actual training with the first-hand experience. Like most other LMIC countries Bangladesh lack behind in keeping and managing patient data. In any efficient health system, patient data is the key to efficient management. This lack of centralized record-keeping and patient safety disrupts the accountability of service to the patients.¹² Apart from the cessation of certain academic activities, the current pandemic has also taken its toll on the country's research activities. The absence of local research on local needs impedes evidence-based practice.⁷

It is estimated that approximately 13.8 million new operative cases exist worldwide each year. Of these, nearly 5.2 million cases will require additional 23,300 neurosurgeons from LMICs to address them⁶.

As Global health activities have set to a different focus, the Global surgery's niche part Global neurosurgery as a certainty is slowed down. The huge burden on the health care system for the disease as well as the action required to prevent its spread has significantly affected the neurosurgical service of LMIC like Bangladesh. The already loaded of neurosurgical service in an LMIC like Bangladesh is being overburdened by this pandemic. Like any other low-income country Bangladesh is facing difficult challenges in carrying out evidence-based surgical procedures, insufficient research activity as a part of the residency, the economic crisis affecting the country's health sector leading to an indirect impact on neurosurgical patient's budget allocation in health only 5.15% (Tk 292 billion), health insurance not here, lack of health coverage and difficulty in following up the patients. It is during this time of Global crises the need for Global neurosurgical initiatives to come forward and rise to cause of essential and equal neurosurgical care.

Abbreviations

LMIC: Low to middle-income countries

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

The data used in this study are available from the corresponding author on a feasible request.

Competing interests

The authors declare that they have no competing interests.

Funding

No funding.

Author's contributions

RAK, MMR, AA, EGB and LRMS collected data, wrote and reviewed the manuscript. All authors read and approved the final manuscript.

Acknowledgments

The authors would like to thank all the members who were part of this paper.

REFERENCES

1. Quinn SC, Kumar S. Health inequalities and infectious disease epidemics: a challenge for global health security. *Biosecur Bioterror* 2014;12:263-273.
2. Burke JF, Chan AK, Mummaneni V, et al. Letter: The Coronavirus Disease 2019 Global Pandemic: A Neurosurgical Treatment Algorithm. *Neurosurgery* 2020;87:E50-E56.
3. Jean WC, Ironside NT, Sack KD, Felbaum DR, Syed HR. The impact of COVID-19 on neurosurgeons and the strategy for triaging non-emergent operations: a global neurosurgery study. *Acta Neurochirurgica* 2020;162:1229-1240.
4. Kondziolka D, Couldwell WT, Rutka JT. Introduction. On pandemics: the impact of COVID-19 on the practice of neurosurgery. *Journal of neurosurgery* 2020:1-2.
5. Pesce A, Palmieri M, Armocida D, Frati A, Santoro A. Letter: Neurosurgery and Coronavirus (COVID-19) Epidemic: Doing our Part. *Neurosurgery* 2020;87:E48-e49.
6. Dewan MC, Rattani A, Fieggen G, et al. Global neurosurgery: the current capacity and deficit in the provision of essential neurosurgical care. Executive Summary of the Global Neurosurgery Initiative at the Program in Global Surgery and Social Change. *Journal of neurosurgery* 2018:1-10.
7. Meara JG, Leather AJ, Hagander L, et al. Global Surgery 2030: evidence and solutions for achieving health, welfare, and economic development. *Lancet (London, England)* 2015;386:569-624.
8. Haglund MM, Fuller AT. Global neurosurgery: innovators, strategies, and the way forward. 2019;131:993.
9. WFNS. Global Action Framework. Global Neurosurgery Committee 2019.
10. Tsermoulas G, Zisakis A, Flint G, Belli A. Challenges to Neurosurgery During the Coronavirus Disease 2019 (COVID-19) Pandemic. *World Neurosurg* 2020;139:519-525.
11. Weber AC, Henderson F, Santos JM, Spiotta AM. Letter: For Whom the Bell Tolls: Overcoming the Challenges of the COVID Pandemic as a Residency Program. *Neurosurgery* 2020.
12. Agrawal A, Kumar A, Agrawal CS, Pratap A. One year of neurosurgery in the eastern region of Nepal. *Surgical neurology* 2008;69:652-656; discussion 656.



Giant dorsal sacral meningocele in a child

Amit Agrawal

Professor of Neurosurgery. Department of Neurosurgery, Narayana Medical College Hospital, Chinthareddypalem, Nellore, Andhra Pradesh, INDIA

ABSTRACT

Sacral meningoceles are uncommon congenital lesions, usually described in the anterior or lateral position, and they typically are asymptomatic [1,7]. A nine-years male child presented with a progressively increasing swelling over the lumbosacral region since birth.

Sacral meningoceles are uncommon congenital lesions, usually described in anterior or lateral position and are typically asymptomatic.¹⁻⁷ A nine year male child presented with a progressively increasing swelling over lumbo-sacral region since birth. There was no history of any bowel or bladder dysfunctions. Motor and sensory examination was normal. Planters were flexor. Rectal tone was normal. Gait was normal. Results of her sensory, rectal tone and lower limbs motor exams were within normal limits. There were no abnormal skin lesions, skeletal deformities, abnormal sinus or swellings. A physical examination of the patient showed a soft, 4 x 4-cm fluctuant and non-pulsatile mass over sacral region, completely with normal skin without any stigmata. The transillumination test was positive. Routine blood investigations were normal. Magnetic resonance imaging (MRI) of the lumbo-sacral spine showed a large, well-defined cystic over sacrum without any no evidence of internal echoes, solid component or septae (Figure-1 and 2). There was evidence of communication between the cyst and the spinal canal. The patient underwent surgical excision of the swelling and repair of the sac. The large cyst was entered and found to contain clear CSF in a terminal continuation of the spinal subarachnoid space. There was no neural tissue in the sac. And there was no evidence of tethering. Postoperatively, the child had normal neurological and urological function. CT of the brain did not show any evidence of hydrocephalus. He developed CSF leak in post-operative and the defect was repaired with pedicel graft.

A meningocele a developmental defect in the dura resulting in an outpouching of leptomeninges through defect covered with only a layer of skin.⁴ Most of the sacral meningoceles are asymptomatic with a soft tissue mass; they produce clinical symptoms depending on their

Keywords

sacral meningocele,
lipomyelomeningocele,
MRI,
meningocele,
sacral mass



Corresponding author:
Amit Agrawal

Department of Neurosurgery,
Narayana Medical College Hospital,
Chinthareddypalem, Nellore, Andhra
Pradesh, India

dramit_in@yahoo.com

Scan to access the online version



proximity to the spinal cord and nerve roots (e.g. unexplained radiating or low back pain, or sensory or motor deficits, atypical bowel dysfunction^{1-4, 8, 9} The differential diagnosis for the mass lesions in children in sacro-coccygeal area includes meningocele, myelomeningocele, myelocystocele, teratoma, lipoma, hamartoma, lymphangioma, hemangioma, chordoma, and ependymoma.¹⁰⁻¹⁵ MRI is the investigation of choice as it will better delineate the details of the sac and its contents. Also it will help to know the extent of the spinal cord and position of the nerve roots.³ Radiographs may reveal erosion and widening in the sacral bone,⁹ scalloping of the pedicles, laminae and vertebral bodies adjacent to the meningocele resulting in an enlargement of the spinal canal.^{16, 17, 18} Indications for surgical repair include clinically symptomatic patients^{1-3, 8, 19} or if the lesions located in an area where it has greater risk of mechanical trauma or rupture (as in the present case).



Figure 1. MRI of the lumbo-sacral spine T1W, FLAIR and T2W sagittal images showing large, well-defined cystic lesion over sacrum (signal intensity similar to cerebrospinal fluid) without any evidence of internal echoes, solid component or septae.

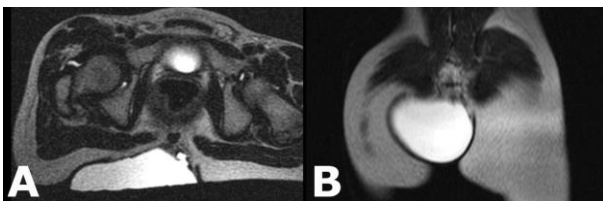


Figure 2. MRI of the lumbo-sacral spine T2W axial images showing large, well-defined cystic lesion over sacrum (signal intensity similar to cerebrospinal fluid).

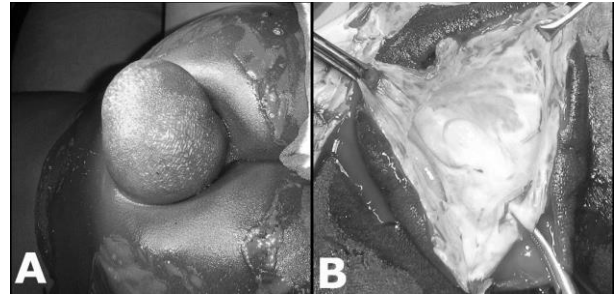


Figure 3. Intraoperative images showing excision and repair of the meningocele.

REFERENCES

1. Nishio Y, Hamada H, Kurimoto M, Hayashi N, Hirashima Y, Endo S. A case of occult intrasacral meningocele presented with atypical bowel symptoms. *Child's nervous system : ChNS : official journal of the International Society for Pediatric Neurosurgery* 2004;20:65-67.
2. Turgut M, Akyüz O, Unsal A. Occult intrasacral meningocele: case report and review of the literature. *Zentralblatt für Neurochirurgie* 2007;68:34-37.
3. Naoumis D, Gkiatas K, Kararizos G, Mitsonis C, Kararizou E. Sacral meningocele in a military pilot, presenting during flight. *Aviation, space, and environmental medicine* 2010;81:141-143.
4. Shetty D, Lakhkar B. Lateral sacral lipomyelomeningocele: a rare anomaly. *Neurology India* 2002;50:204.
5. Lee KS, Gower DJ, McWhorter JM, Albertson DA. The role of MR imaging in the diagnosis and treatment of anterior sacral meningocele. Report of two cases. *Journal of neurosurgery* 1988;69:628-631.
6. Erkulvrawatr S, El Gammal T, Hawkins J, Green JB, Srinivasan G. Intrathoracic meningoceles and neurofibromatosis. *Archives of neurology* 1979;36:557-559.
7. Seddighi A, Seddighi AS. Lateral sacral meningocele presenting as a gluteal mass: a case report. *Journal of medical case reports* 2010;4:81.
8. Shiau JSC, Raden M, Juliano JE. Sacral intraspinal meningocele in a patient presenting with abdominal pain. Case report. *Journal of neurosurgery* 2007;107:53-56.
9. Kiliçkesmez O, Barut Y, Tasdemiroglu E. Expanding occult intrasacral meningocele associated with diastematomyelia and multiple vertebral anomalies. Case report. *Journal of neurosurgery* 2004;101:108-111.
10. Altman RP, Randolph JG, Lilly JR. Sacrococcygeal teratoma: American Academy of Pediatrics Surgical Section Survey-1973. *Journal of pediatric surgery* 1974;9:389-398.

11. Gupta DK, Mahapatra AK. Terminal myelocystoceles: a series of 17 cases. *Journal of neurosurgery* 2005;103:344-352.
12. Yu JA, Sohaey R, Kennedy AM, Selden NR. Terminal myelocystocele and sacrococcygeal teratoma: a comparison of fetal ultrasound presentation and perinatal risk. *AJNR American journal of neuroradiology* 2007;28:1058-1060.
13. Ein SH, Adeyemi SD, Mancor K. Benign sacrococcygeal teratomas in infants and children: a 25 year review. *Annals of surgery* 1980;191:382-384.
14. Güvenç BH, Etus V, Muezzinoglu B. Lumbar teratoma presenting intradural and extramedullary extension in a neonate. *The Spine Journal* 2006;6:90-93.
15. Gross SJ, Benzie RJ, Sermer M, Skidmore MB, Wilson SR. Sacrococcygeal teratoma: prenatal diagnosis and management. *American journal of obstetrics and gynecology* 1987;156:393-396.
16. Dubowitz V, Lorber J, Zachary Rb. Lipoma Of The Cauda Equina. *Archives of disease in childhood* 1965;40:207-213.
17. Heckly A, Carsin-Nicol B, Poulain P, Hamlat A. Diagnosis-related pitfall of a lateral sacral cyst. Case report. *Journal of neurosurgery Spine* 2005;2:72-74.
18. Philip N, Andrac L, Moncla A, et al. Multiple lateral meningoceles, distinctive facies and skeletal anomalies: a new case of Lehman syndrome. *Clinical dysmorphology* 1995;4:347-351.
19. Rengachary SS, O'Boynick P, Karlin CA, Batnitzky S, Price H. Intrasacral extradural communicating arachnoid cyst: cases report. *Neurosurgery* 1981;8:236-240.

Guidelines for authors

1. ETHICS

The publication of an article in Romanian Neurosurgery is a direct reflection of the quality of the work of the authors. The prevention of publication malpractice is first the responsibility of every author and also of our editorial board. Authors must submit accurate information and sufficient details, presenting its objective significance; unethical behaviour is unacceptable.

Plagiarism in all its forms constitutes unethical publishing behaviour and is unacceptable.

For Romanian Neurosurgery the publication ethics and publication malpractice statement are consistent with the recommendations and guidelines of the Committee on Publication Ethics, the World Association of Medical Editors, the International Committee of Medical Journal Editors and Consolidated Standards of Reporting Trials.

Links:

Committee on Publication Ethics

(COPE): <http://www.publicationethics.org>

World Association of Medical Editors

(WAME): <http://www.wame.org>

International Committee of Medical Journal Editors

(ICMJE): <http://www.icmje.org>

2. ENCLOSED LETTER

In addition to the manuscript, the Editorial Board should receive an enclosed letter containing the exclusive reservation of copyright guaranteed by all authors whose manuscripts have already been accepted. If the paper was completely or partially published or exposed previously, a copy or a photocopy of it should be also sent. The technical reports should contain a declaration concerning the financial sources that cover the costs necessary for instruments and methodology acquisition.

In order to illustrate different cases, photos of identifiable patients will not be published without their legal consent or that of their legal representative. The letter containing this consent together with the manuscripts should be sent to the editorial office.

If the author wishes his unpublished manuscripts returned, please note this in the enclosed letter.

3. SENDING OF MANUSCRIPTS

Authors shall ensure that the article has been "spell and grammar checked" prior to the submission.

The manuscript sent for publishing must be submitted in English. The manuscript will be typed without formatting, with a 1-line space. Please enclose 1 copy of the manuscript, tables, graphics and photos. After publishing, the paper and pictures become the property of Romanian Neurosurgery.

There are no article processing charges (NO APCs) and no article submission charges.

4. MANUSCRIPT ELABORATION

Paper sent for publishing should be in accordance with international standards of manuscript submittance. These standards are mentioned in "British Medical Journal" 1988; 296: 404-405 or in "Annals of Internal Medicine" 1988; 108:258-265. The authors are responsible for the accuracy of the information contained in the essay.

4.1. The title page should contain the whole title of the essay and complete names of authors with their academical degrees. If it is necessary, the department, the hospital or the institution where the search has been undertaken, should be also mentioned.

4.2. Please include an additional page containing the title of the essay and the author responsible for correcting of any and of all mistakes and for maintaining correspondence. The address, phone and fax number should be included (e-mail be available).

4.3. A summary, no longer than 300 words, should be written on a separate page. Key-words, no more than 7, should be listed in alphabetical order on the same page. The use of keywords should be approved by the "Index Medicus".

4.4. Text. The introduction should specify the purpose of the paper. The content and the method should give a minute account of the work methodology so that the experiment conclusion could be reproduced and checked up on in other centres. The experiments and medical studies performed on human beings should respect the principles specified in "The Declaration of Helsinki", whereas the experiments done on animals should be in accordance with "The Principles Charta of Animal's Care and Use". The results should not contain references to previous studies. The discussions should reflect the main features of the research.

5. REFERENCES

- typed on 1 line;
- quoted in alphabetical order;
- explanatory footnotes are not accepted;
- unpublished data and personal papers should be quoted inside the text and not in the bibliography;
- entries to the bibliography should appear in the following order: the authors, the title of the essay, the title of the periodical (abbreviated according to the list of abbreviation specified in the "Index Medicus"), the volume number, the page number and the data publication.

6. TABLES AND PICTURES

There should be 1 copy sent. Each table with its own title should be submitted on separate pages. The photos, radiographies, CT scans should be labelled on the back with

the number of each picture, corresponding with the number included inside the text, and the author's name. The label will be placed on the top of the picture. The drawings may be sent on vellum paper, tracing paper or transparent paper. The use of pictures belonging to other publications is accepted, only if mentioning the original source. Further, the partial use of any previously published text is accepted with the approval of its author and editor. All pages should be consecutively numbered, starting with the title page.

7. ABBREVIATIONS

Abbreviations should be consistently used throughout the text and established in a fixed form from the beginning.

8. SUBMISSION

Manuscripts should be sent to the Editor:
Dr St.M. Iencean,
Romanian Neurosurgery

"Gr.T. Popa" University of Medicine and Pharmacy
Universitatii Street, No. 16, 700115, Iasi, Romania
or by e-mail to *mirceasteffan@yahoo.com*.

9. DISCLAIMER

The editors disclaim any responsibility for opinions expressed in the papers.

10. THE REVIEW PROCESS

After the manuscript submission, the peer review process is broken down into the following steps:

1. The Editor assigns Reviewers to the manuscript.
2. The Reviewers review the manuscript.
3. The Editor drafts a decision to be sent to the author/authors.

The review process takes between three weeks and two months.