



Anatomical localization of intracranial grade II meningiomas in North-Eastern Romania. Our 25-years experience

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ABSTRACT

Objective. Our research aims to assess a possible connection between tumour localization and histological subtypes of grade II meningiomas.

Material and methods. 143 patients with grade II WHO meningiomas underwent surgical resection in "Prof. Dr. N. Oblu" Emergency Clinical Hospital Iași between 1990 and 2015. The collected data included: patient age, gender, tumour localization and histopathological diagnosis (atypical, clear cells and chordoid meningioma).

Results. 135 (94.4%) of all 143 patients with grade II meningiomas were atypical meningiomas, 6 (4.2%) were cell clear meningiomas and only 2 (1.4%) were chordoid meningiomas. As concerns their distribution by gender, 79 (55.2%) were female and 64 (44.8%) were male. Grade II meningiomas were most commonly located at convexity 49.7% (n=71), followed by skull base in 30.8% (n=44) of the cases and parasagittal/falcine in 14.7% (n=21) of the patients.

Conclusions. The most common localization of grade II meningiomas was convexity, followed by skull base, parasagittal/falcine and intraventricular areas. We have also noticed that convexity meningiomas are more frequent in women, unlike the other anatomical localizations in which the male-female ratio is almost equal. Therefore, further research is necessary to determine the role of embryological, anatomopathological and genetic factors in underlying the connection between meningioma grade and anatomical localization.

INTRODUCTION

Meningiomas makes up about one third of all primary central nervous system tumours, being the most common brain tumour in adults over the age of 35 (1), with an incidence that has increased in recent years (2, 3). As far as Romania is concerned, an increase in the number of intracranial meningiomas was noted in its North-Eastern region (where this research was conducted) over the 1990-2015 period (4). Although meningiomas are usually benign slow-growing tumours, their

Keywords

atypical meningioma,
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histological aggressiveness may classify them in grade II or III tumours, according to the WHO classification (5, 6). Whereas grade II meningiomas only made up 5-7% of all types of meningiomas before the 2007 WHO classification (7), they currently make up more than 20% of all meningiomas (7, 8, 9). Grade II meningiomas include three histological subtypes: atypical, the most common, and also chordoid and clear cell meningiomas, the occurrence rate of which is considerably lower (10).

Among the multiple prognostic factors that can predict meningioma grade prior to tissue diagnosis (11, 12), several studies also found the anatomical localization (13, 14). Thus, several authors noticed the predisposition of grade II meningiomas for cerebral convexity (13, 15, 16) (Figure 1).

The goal of our research was to analyze grade II meningiomas distribution in North-Eastern Romania over a 25-year period (1990-2015). The patients underwent surgery in "Prof. Dr. N. Oblu" Emergency

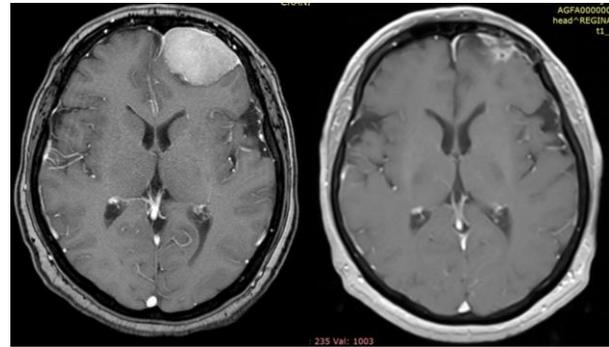


FIGURE 1. Preoperative and postoperative axial T1-weighted images with contrast of an atypical meningioma (Professor Poeata's personal collection)

Clinical Hospital of Iasi, the advantage of this hospital being the fact that it services the whole of North-Eastern Romania, a region with a population of about 4 million inhabitants (17) (Figure 2).

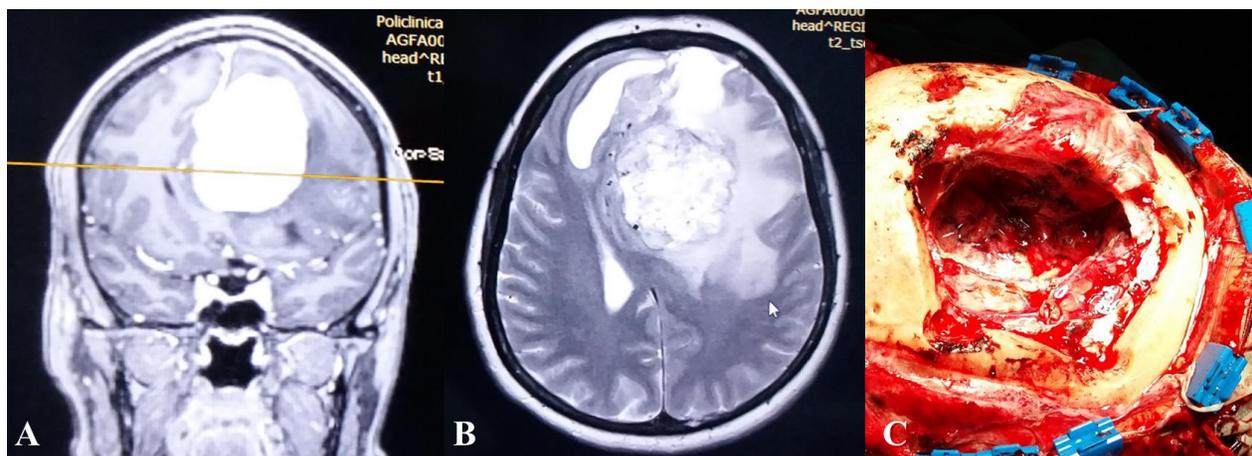


FIGURE 2. Preoperative coronal (A) and axial (B) T1-weighted images with contrast showing a left falx meningioma. Postoperative images showing tumour bed after gross total resection (C) (Assoc. Professor Turliuc's personal collection)

MATERIAL AND METHODS

We have evaluated 143 patients hospitalized in "Prof. Dr. N. Oblu" Emergency Clinical Hospital of Iasi between 1990 and 2015, with histologically proven grade II meningiomas (atypical, clear cells and chordoid). Also, the histological samples have been reviewed according to the current WHO 2016 criteria (18). We have excluded all patients with type 2 neurofibromatosis (2 patients) and those for whom we were unable to collect full information about tumors (16 patients). The collected data included: gender, age, anatomical localization and histopatho-

logical diagnosis (Table I). In order to confirm the anatomical localization of grade II meningiomas, the surgeon's operative notes were taken into consideration. As concerns the intracranial localization of meningiomas, they were divided into four main categories: (1) convexity, (2) parasagittal/falx, (3) skull base and (4) intraventricular.

RESULTS

Of all 143 patients with meningiomas, 79 (55.2%) were female patients and 64 (44.8%) were male

patients. The male: female ratio was 1:1.2. As concerns patients distribution on demographic groups, more than half of them were in the 50-69 year age group (58.1%, n=83). As for the distribution of meningiomas according to anatomical localization, they occurred mostly: 49.7% (n=71) at convex-

ity, 30.8% (n=44) at skull base, 14.7% (n=21) in the parasagittal/falcine area and 4.9% (n=7) intraventricular. Most meningiomas were atypical (94.4%, n=135), followed by clear cell meningiomas (4.2%, n=6) and only 1.4% (n=2) were chordoid. All patient characteristics are shown in Table 1.

Characteristics		Grade II n (%)
No. of patients		143
Gender	female	79 (55.2)
	male	64 (44.8)
Age groups (years)	20-29	3 (2.1)
	30-39	9 (6.3)
	40-49	23 (16.1)
	50-59	42 (29.4)
	60-69	41 (28.7)
	70-79	22 (15.4)
	80-89	3 (2.1)
Tumor localization	Convexity	71 (49.7)
	Skull base	44 (30.8)
	Parasagittal/falcine	21 (14.7)
	Intraventricular	7 (4.9)
Histological subtypes	Atypical meningioma	135 (94.4)
	Clear cell meningioma	6 (4.2)
	Chordoid meningioma	2 (1.4)

TABLE 1. Characteristics of 143 patients with grade II meningioma

DISCUSSION

Our research revealed a predilection of grade II meningiomas for the convexity, as 49.7% (n=71) of them occurred in this area, which is consistent with similar studies (10, 14, 19, 20, 21, 22). Skull base

meningiomas ranked second 30.8% (n=44), followed by the parasagittal/falcine and intraventricular localization (Table 1, Figure 3). The distribution of the anatomical localization of tumors on age groups was similar in both women and men.

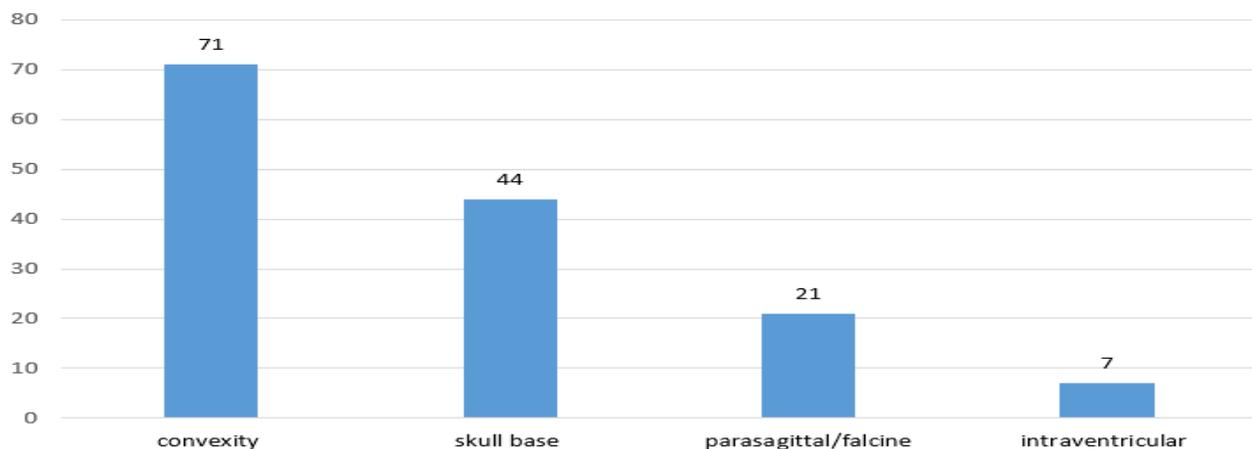


FIGURE 3. Incidence of Grade II meningiomas according to anatomical localization

Although previous studies have demonstrated a predilection of grade II meningiomas for cerebral convexity (13, 15, 16), a clear etiological connection between a particular meningioma grade and its anatomical localization could not be established. However, some authors consider that the histological grade of the tumor may be related to the meninges' complex embryological origin, which has a variable neoplastic potential (23, 24, 25, 26).

Among the first studies that demonstrated the predilection of grade II meningiomas for cerebral convexity were those conducted by Mahmood *et al.* and Maier *et al.* (27, 28). Also, Kane *et al.* later demonstrated that non-skull base tumors would have an increased risk for grade II meningiomas compared to skull base tumors (13). On the other hand, Zhou *et al.* noted that meningiomas located at the median line of the skull base are the least likely to be grade II or III (6), similar to other studies that have revealed that skull base meningiomas are more frequently meningothelial (29, 30) and are also lower grade at initial resection (15). This predilection of meningiomas for various anatomical localizations in the intracranial space could be explained by the distinct embryological origins of non-skull and skull-base dura (14, 15, 30, 31). In this respect, various authors have demonstrated that meninges around the brainstem would arise from cephalic mesoderm, whereas telencephalic meninges arise from neural crest cells (25, 29, 32, 33). This differential meningeal embryogenesis resulted in the predominance of one arachnoid cell type over the other location, which accounts for the aggressive behavior of some meningiomas as compared to others in some anatomical localizations (15). However, genomic studies have shed light on intracranial locations and mutational patterns, as well as on the potential embryonic cancer stem cell-like origin (34).

In a study on 110 patients with incidentally discovered meningiomas, Hashimoto *et al.* also noticed that non-skull base meningiomas have a more aggressive behavior and that skull base meningiomas do not tend to grow when compared to non-skull base meningiomas (35). Moreover, even when these tumors grow, the growth rate was significantly lower in terms of annual growth rate and percentage (35). Also, the same authors demonstrated that 60% of the skull base incidental meningiomas had an exponential pattern of growth, unlike non-skull base incidental meningiomas

characterized by a 33% growth percentage (35). In conclusion, the authors recommend non-skull base meningioma follow-up by magnetic resonance imaging at shorter intervals. The authors mention that the results must be interpreted as most meningiomas fit both exponential and linear patterns statistically (35).

In 2003, the same authors suggested that a loss of 1p was shown to be significantly correlated with malignant progression of meningiomas, analyzing 72 grade II and III meningiomas, with fluorescence in situ hybridization and loss of heterozygosity analyses (35, 36). The authors also pointed out that skull base meningiomas had a significantly lower percentage of cells with 1p loss (20.31%) compared to non-skull base meningiomas (37.87%), suggesting that skull base tumors would have fewer genetic alterations and consequently would have less aggressive biological behavior (35). Similarly, Murphy *et al.* showed in their study that meningiomas originating at the convexity had more chromosomal abnormalities than those arise from skull base (37).

In terms of histopathology, there have been studies that have shown its importance in the prediction of some types of meningiomas for certain intracranial localizations. Thus, McGovern *et al.*, in a study of 216 patients with grade I, II and III meningiomas, claimed that grade I non-skull base meningiomas had a higher MIB-1 labeling index than grade I skull base meningiomas, suggesting that non-skull base tumors may have a more aggressive biology (16). As concerns their recurrence, the same author noted that non-skull base meningiomas, when they recur, have a higher WHO grades than skull base meningiomas (16). Also, in 2018, Turk *et al.* concluded in a study of 40 grade I and II meningiomas that the skull base group had significantly higher CD34 levels than the non-skull base group, suggesting that skull base meningiomas tend to have higher microvascular density and are better vascularized than non-skull base tumors (38).

As regards the distribution of meningiomas on genders in the overall number of patients, we revealed a male: female ratio of 1:1.2, with a slight predominance in females, in agreement with other literature studies (14, 19, 39). On the other hand, whereas in the skull base, intraventricular and parasagittal/falcine localizations the male: female ratio was approximately 1:1, location at convexity level was dominated by women, with a male: female

ratio of 1:1.5 (43/28) (Figure 4). In order to justify this predominance of women, research has shown that grade I meningiomas have a high level of progesterone receptor expression relative to grade II and III meningiomas, which seem to have a lower frequency of estrogen and androgen receptors (13, 40, 41, 42), which means close male-female ratios.

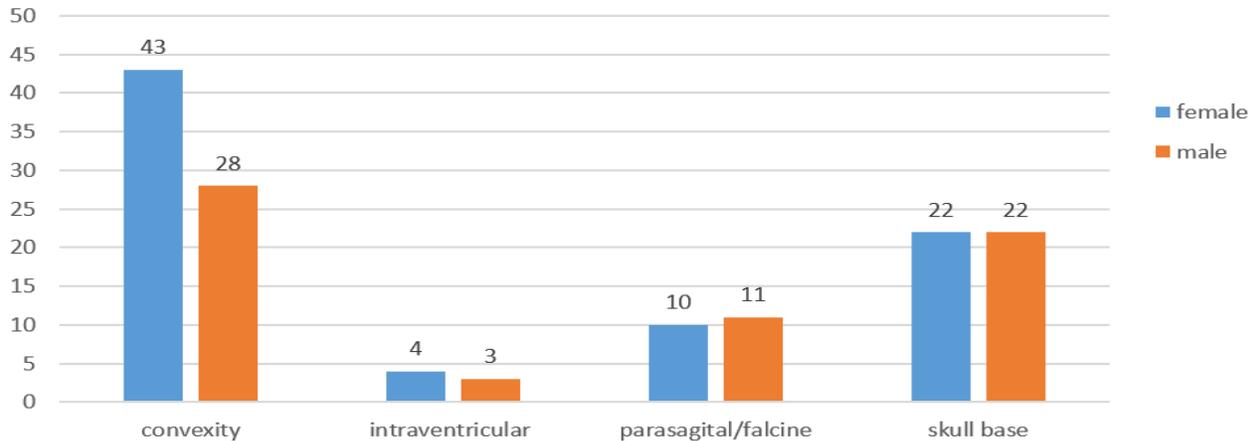


FIGURE 4. Incidence of grade II meningioma according to gender

With regard to the distribution of histological subtypes of grade II meningiomas, atypical meningiomas prevailed in our research (94.4%), followed by clear cell and chordoid meningiomas in a much lower percentage, as there are rare types of tumors (Table 1).

Of all grade II meningiomas, atypical meningiomas are the most common, their percentage increasing to 20-30% of all meningiomas after the introduction of the WHO classification in 2000 and 2007 (2, 8, 9). Like grade I or III meningiomas, atypical meningiomas may develop anywhere in the intracranial space, with some studies reporting a higher frequency of atypical meningiomas at the level of cerebral convexity (8, 27, 44, 45).

Clear cell meningioma is a rare disorder, as it makes up less than 1% of all meningiomas, and English-language literature reports 218 intracranial tumors (46). This percentage is also low in our research, with an incidence rate of this type of meningioma only 4.2% (n=6) over the 25-year period (Table I). Whereas previous studies revealed that the most common localization for clear cell meningioma was the cerebellopontine angle (47, 48, 49), all clear cell meningiomas in our group were located in the

On the other hand, Morokoff *et al.* in a study of 163 convexity meningiomas (grades I, II and III) noted a prevalence of the female sex, with a male: female ratio of 1:2.7 (43). In higher-grade meningiomas, Morokoff *et al.* found a male: female ratio of 1:1, much lower than our ratio of 1:1.5.

parasagittal/falcine area (n = 6). From this point of view, the results of the studies differ from each other: some studies show that the most affected location is convexity (46), whereas others point to skull base (50), particularly cerebellopontine angle, parasagittal tumors having lower occurrence rates (47).

Chordoid meningiomas are also rare types of meningiomas, as only a little more than 100 cases are reported in literature (51, 52, 53, 54, 55, 56). Rare neoplasia with a unique chordoid appearance, chordoid meningioma has a predilection for the supratentorial localization (1, 57), similar to our study in which the two chordoid meningiomas had parasagittal/falcine localization.

CONCLUSIONS

Our study has shown a predominance of grade II meningiomas for cerebral convexity, which is the most common location in the intracranial space, followed by the skull base, parasagittal/falcine and intraventricular locations. We also noticed that convexity meningiomas predominate especially in women. Further research is needed to highlight the role of genetic, embryological and anatomopathological factors in highlighting the

connection between meningioma grade and anatomical localization

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