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Tumor recurrence in parasagittal and falicine atypical meningiomas invading the superior sagittal sinus

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Abstract

Objective: Parasagittal and falicine meningiomas are still a challenge in terms of surgical resection. Although maximal safe resection is the main therapeutic approach, numerous postoperative complications can still occur depending on the locations of these tumors. Moreover, previous studies have reported that parasagittal meningiomas have a higher recurrence rate than meningiomas with other locations. **Patients, Materials and Methods:** We retrospectively reviewed 21 patients with parasagittal and falicine atypical meningiomas [World Health Organization (WHO) grade II], nine of whom had their superior sagittal sinus (SSS) invaded by the tumor. We reviewed the demographic information, operative notes, pathological reports, and clinical and imagistic follow-up reports of each patient over a 5-year time span. **Results:** All the patients were surgically treated, and the tumor removal was grade II according to Simpson's grading system in 47.6% and grade III in 19% of the cases. The SSS was invaded in 42.9% of the patients. No immediate mortality or morbidity was revealed by our study. Tumor recurrence/progression documented on postoperative imaging amounted to 14.3% and 19%, 12 and 24 months after surgery, respectively. Furthermore, 36, 48 and 60 months after the surgery, the recurrence rate remained the same, namely in 9.5% of the cases. The recurrence was higher in patients with SSS invasion than in patients with no SSS invasion. The tumor recurrence was slightly more predominant in women, i.e., 6% higher than in the male group. **Conclusions:** In our group of patients with parasagittal and falicine meningiomas, we report a 47.6% Simpson II resection rate and 19% Simpson III resection rate associated with a very low complication rate and no immediately postoperative morbidity and mortality, compared to more aggressive techniques. The recurrence of parasagittal meningiomas predominated after grade III and IV Simpson resection and dural sinus invasion was a negative predictive factor for recurrence. Therefore, the surgery of parasagittal and falicine meningiomas is beneficial, both for tumor control, but also for improving neurological outcome. Aggressive meningioma resection should be balanced with the increased neurosurgical risk.

Keywords: parasagittal meningiomas, superior sagittal sinus, tumor recurrence, microsurgical resection.

Introduction

Meningiomas account for approximately one third of all intracranial tumors, being the most common primary intracranial neoplasm [1] and some of our previous studies have shown an increasing incidence and that these tumors are relative common in the north-eastern region of Romania [2–5].

Atypical meningiomas (AMs) represent about 5–7% of these tumors [6–9], and after the implementation of the World Health Organization (WHO) Classifications of 2000 and 2007, the percentage of these types of tumors increased to 20–30% of all meningiomas [10–12].

Harvey Cushing and Louise Eisenhardt define parasagittal meningiomas as tumors that fill the parasagittal corner, with no cerebral parenchyma between meningioma

and the superior sagittal sinus (SSS) [13], and together with falicine meningiomas, they are the second most common intracranial meningiomas [14–16].

According to previous studies, parasagittal meningiomas recur more frequently than meningiomas with other intracranial locations [17–19], and a thorough understanding of the best surgical approach allowing the maximal safe resection of these tumors is vital for neurosurgeons [20–22].

The most important characteristic of these lesions is their location near the SSS [14, 16, 21, 23] and infiltration of both SSS and large cerebral draining veins, which prevents complete and safe resection of the tumor [24]. Moreover, avoiding neurological impairment is considered crucial as far as these tumors are concerned [8]. Thus, when dealing with these tumors, neurosurgeons are faced with a dilemma: attempting complete resection at the cost of high morbidity

and mortality or choosing a more conservative surgical procedure but exposing the patient to a higher risk of recurrence [25].

Aim

Our research was aimed at assessing the tumor recurrence after surgery of 21 AMs (*WHO* grade II) with parasagittal and falx location.

☒ Patients, Materials and Methods

We retrospectively analyzed 21 patients with the diagnosis of parasagittal and falx AMs (*WHO* grade II meningiomas) who underwent resection procedures at Prof. Dr. Nicolae Oblu Emergency Clinical Hospital, Iași, Romania, between January 1, 2010 and December 31, 2019. We reviewed the demographic information, operative notes, pathological reports, and follow-up clinic and radiographic studies of each patient over a 5-year time span.

The surgical specimens were fixed in 4% formalin, paraffin embedded, sectioned at microtome, and sections of 5- μ m were stained with Hematoxylin–Eosin (HE). In 10 cases, we used other two histological sections of 5- μ m thickness in order to achieve immunohistochemical staining. Two monoclonal antibodies (anti-vimentin and anti-human Ki-67 antigens) were used in these 10 cases. Immunostainings were performed using the EnVision detection system (Dako, Denmark), with 3,3'-Diaminobenzidine as chromogen and Mayer's Hematoxylin for nuclear counterstaining. Antigen retrieval was performed with sodium citrate buffer, in water bath, at 95°C. We considered the positive reaction only when a brown cytoplasmic coloration was obtained with anti-vimentin antibody immunostaining and a nuclear brown staining was visualized in the case of Ki-67 immunostaining. Mean Ki-67 labeling index (LI) was determined by counting using a $\times 40$ objective, both positive and negative nuclei in 10 different fields. The percentage of positive cells in each field was determined and the mean Ki-67 LI was calculated by the arithmetic mean of the 10 previously recorded values. As all the cases analyzed were retrospective, stored slides were taken out and reviewed by two senior neuropathologists (G.F.D and A.S) for grading, according to the *WHO* classification of meningiomas. The histomorphological criteria for grading a meningothelial tumor as an AM were as follows: (a) 4–19 mitoses/10 high-power fields (HPFs) or (b) three or more of the following five characteristics: (i) small cells with a high nuclear/cytoplasmic ratio, (ii) increased cellularity, (iii) prominent nucleoli, (iv) uninterrupted patternless or sheet-like growth, (v) foci of “geographic” or “spontaneous” necrosis [26–29].

Magnetic resonance imaging (MRI) scanning and MRI angiography were performed in order to determine the tumor origin, its extension and the involvement of the SSS in all 21 patients from our study. From all analyzed cases, only three patients underwent cerebral catheter-based angiography.

The volume of meningiomas was calculated according to the ellipsoidal formula: $volume = \pi/6 \times length \times height \times width$ [30–34] and has been evaluated based on the preoperative images (MRI with contrast agent). Tumor recurrence/progression was defined as any new enhancement

or any increase in size of the tumor remaining in the resection cavity, during serial head MRI [T1 weighed (T1WI) + contrast]. In cases of subtotal resections (Simpson grade III and IV), we named and classified tumor progression as relapse. Peritumoral edema was evaluated as high-intensity extension adjacent to the meningioma on head MRI [T2 weighed (T2WI)] and was evaluated with Hale scale: (0) no peritumoral brain edema: absence of increased T2WI signal surrounding the tumor, (1) mild peritumoral brain edema: ring of increased T2WI signal surrounding the tumor without mass effect, (2) moderate peritumoral brain edema: more extensive, without mass effect, and (3) important peritumoral brain edema with mass effect [2, 35]. The meningioma resection grade was classified according to the grading system suggested by Simpson [36] and relied on the analysis of the pre-operative head MRI scan and intraoperative findings. All the patients had both clinical and MRI postoperative follow-up with head MRI scans with contrast agent 12, 24, 36, 48 and 60 months after surgery to assess the tumor recurrence. Progression free survival for tumor recurrence/progression was evaluated in all patients. This retrospective mono-center study was approved by the local Ethics Committee of Grigore T. Popa University of Medicine and Pharmacy, Iași. The data was statistically processed using Statistical Package for the Social Sciences (SPSS) 25.0 software (SPSS, Inc., Chicago, IL) for Windows. The descriptive statistics parameters were calculated for numerical data and the frequency distributions were calculated for categorical data. In order to compare samples, we used χ^2 (*chi*-squared) and Fisher's tests for categorical data and Student's *t*-test and Mann–Whitney test for numerical data; the significance level was $p < 0.05$.

Operative technique

All the patients underwent craniotomy centered on the meningioma and spanning the SSS. Surgery was performed by A.I.C., M.D.T. and I.P. Craniotomies were performed by a standard method involving an electric cranial drill. The bone was then detached from the subjacent dura mater and removed. The dura was then opened under the microscope, after which the meningioma was exposed and removed using standard microneurosurgical techniques. The tumor was then dissected free from brain tissue around its anterior, posterior, lateral and inferior circumference. In some cases, the tumors had close contact with collateral veins, and the venous sparing approach practiced in our Department aimed both at preserving the SSS and bridging the cortical veins. In all cases, we generally avoided resecting the SSS and falx due to added morbidity. Where possible, the tumors were fully resected.

☒ Results

Patient population and clinical findings

Our group included 15 (71.4%) male and six (28.6%) female patients. The average age at the first operation was 59 years (ranging from 38 to 77 years) and 66.7% ($n=14$) of the patients were younger than 60 years. None of the patients carried stigmata of neurofibromatosis. The most common symptoms encountered were the intracranial hypertension syndrome (71.4%), followed by motor deficit

(52.4%). The ophthalmological examination revealed papilledema in three patients.

Tumor characteristics

There were 15 parasagittal meningiomas and six patients had falxine meningioma. Nine (42.9%) meningiomas were located in the anterior part of the SSS, 10 (47.6%) in the middle part and two in the posterior part of SSS. The tumor volume ranged between 4.54 cm³ and 104.83 cm³ (median, 26.86 cm³), and 52.4% (*n*=11) of the tumors were larger than the median tumor volume. Bone changes including tumoral infiltration or hyperostosis were noted in five (23.8%) patients. 90.5% (*n*=19) of the meningiomas had an irregular aspect of the tumor margins, while 95.2% (*n*=20) showed strong contrast enhancement. Most patients (57.1%) showed important edema and only 23.8% had mild edema. MRI angiography showed SSS infiltration in nine patients. All tumor characteristics can be seen in Table 1.

Table 1 – Characteristics of atypical meningiomas from our study

Characteristics	No. of patients (%)
Location of tumors	<i>Parasagittal</i> 15 (71.4%)
	<i>Falcine</i> 6 (28.6%)
Location of tumors according to the SSS	<i>Anterior</i> 9 (42.9%)
	<i>Middle</i> 10 (47.6%)
	<i>Posterior</i> 2 (9.5%)
Tumor size (volume)	4.544–104.832 cm ³ median, 26.863 cm ³ –
SSS invasion	<i>Invasion</i> 9 (42.9%)
	<i>No invasion</i> 12 (57.1%)
Simpson removal grade	<i>Grade II</i> 10 (47.6%)
	<i>Grade III</i> 4 (19%)
	<i>Grade IV</i> 7 (33.3%)
	<i>No recurrence</i> 8 (38.1%)
Recurrence	<i>After 12 months</i> 3 (14.3%)
	<i>After 24 months</i> 4 (19%)
	<i>After 36 months</i> 2 (9.5%)
	<i>After 48 months</i> 2 (9.5%)
	<i>After 60 months</i> 2 (9.5%)

SSS: Superior sagittal sinus.

Surgical considerations

All patients underwent surgery, and the tumor removal was Simpson grade II in 10 cases, Simpson grade III in four cases and Simpson grade IV in seven cases (Table 1). The correlation between tumor volume and grade of resection revealed that seven of the 10 patients with Simpson grade II resection showed a tumor volume smaller than 26.86 cm³, unlike the Simpson grade III and IV patients, in whom the tumor volume exceeded 26.86 cm³ in over 75% and 70% of the cases, respectively. After surgery, only two of the 21 patients experienced complications consisting of hemorrhage in the remaining tumor cavity, which did not require evacuation. The surgical report on the grade of resection was then MRI confirmed in all cases. There was no postoperative mortality in our series.

Histological findings

All the tumors analyzed were classified as AMs according to WHO criteria [26]. The morphological features of our 21 AMs are depicted in Table 2.

Table 2 – Histological and immunohistochemical features of 21 atypical meningiomas from our study

Morphological features	No. of cases	Percentage
Patternless tumor growth	21/21	100%
Cellularity		
<i>Moderate cellularity</i>	2/21	9.52%
<i>Hypercellularity</i>	19/21	90.47%
Nuclear pleomorphism	21/21	100%
Macronucleoli	7/21	33.33%
Nuclear inclusion	3/21	14.28%
≥4 mitoses/10 HPFs	21/21	100%
Foci of "spontaneous" or geographic necrosis	15/21	71.42%
Vimentin positivity	21/21	100%
Ki-67 LI		
5–7%	2/21	9.52%
7–12%	15/21	71.42%
12–14%	4/21	19.04%

HPFs: High-power fields; LI: Labeling index.

After reviewing the slides, the two senior neuropathologists (G.F.D. and A.S.) identified a patternless tumor growth in all AMs analyzed (21/21 cases; 100%). All the tumors (21/21 cases, 100%) were made up of meningotheial-like cells, but with pleomorphic or atypical nuclei (Figures 1 and 2). Only seven (33.33%) cases presented large and prominent nucleoli (macronucleoli) (Figure 1A), and 3/21 (14.28%) cases presented huge nuclear inclusion (Figure 1B). At high magnitude, an increased number of mitoses (4–6 mitoses/10 HPFs) (Figure 2) was identified in all analyzed cases (21/21 cases; 100%) (Table 2). 15/21 (71.42%) cases exhibited numerous small foci of "spontaneous" or geographic necrosis (Figure 3).

All the tumors analyzed (21/21 cases; 100%) exhibited a positive cytoplasmic immunostaining with anti-vimentin antibody (Figure 4). The Ki-67 LI was evaluated in 10 of the 21 patients. Two of them showed relatively low Ki-67 LI values, not exceeding 7% (2/21 cases; 9.52%), but the mean Ki-67 LI was 9% (a variation between 7% and 14% was identified among the analyzed cases) (Figures 4 and 5; Table 2).

Tumor recurrence

Tumor recurrence was noted in 13 patients over a 5-year follow-up (Table 1). We noticed that the tumor recurrence was present mainly in the men (69.2%), although we did not find statistically significant differences between genders. Furthermore, recurrences are more common in patients under the age of 60 (61.5%), compared to those above this age (38.5%).

Most patients with tumor recurrence had parasagittal meningiomas (76.9%) (Figure 6), most of which were in the middle portion of the SSS (53.8%) (Figure 5). In cases without tumor recurrence, most of the meningiomas were located in the anterior portion of the SSS (62.5%).

Although we did not identify statistically significant differences, we saw that most cases of recurrence had a higher tumor volume than the median volume (69.2%), while in the cases without recurrence, the tumors had a lower volume than the median volume in 75% of cases. All patients with tumor recurrence had irregularly shaped tumor margins (Figure 6). Most patients with relapse had significant edema (61.5%), more than patients without tumor recurrence (50%).

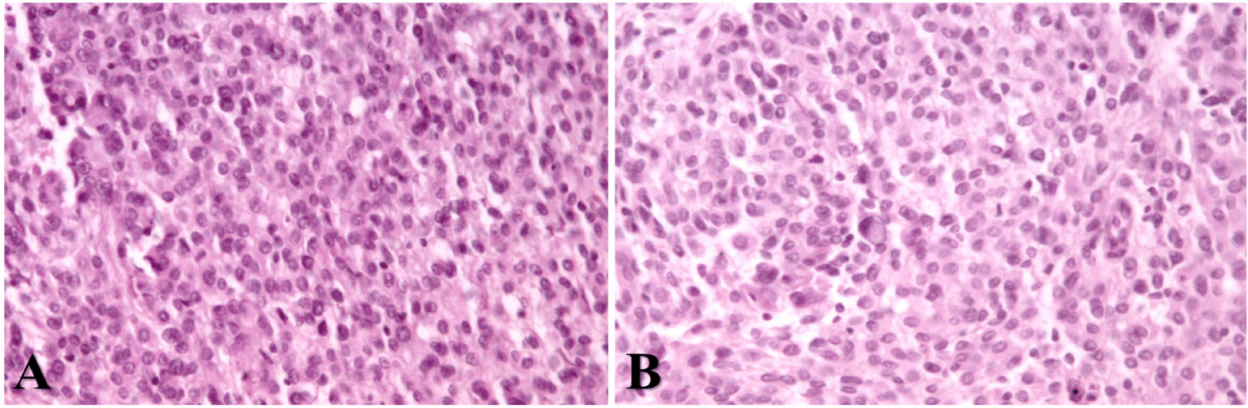


Figure 1 – Male, 57-year-old, parasagittal meningioma invading the middle third of the SSS. Microphotographs show a meningotheial tumor with patternless growth, increased cellularity, and high nuclear/cytoplasmic ratio, and the following supplementary histomorphological criteria: (A) Prominent nucleoli; (B) Moderate nuclear pleomorphism, one mitosis and one huge nuclear inclusion. HE staining: (A and B) $\times 400$. HE: Hematoxylin–Eosin; SSS: Superior sagittal sinus.

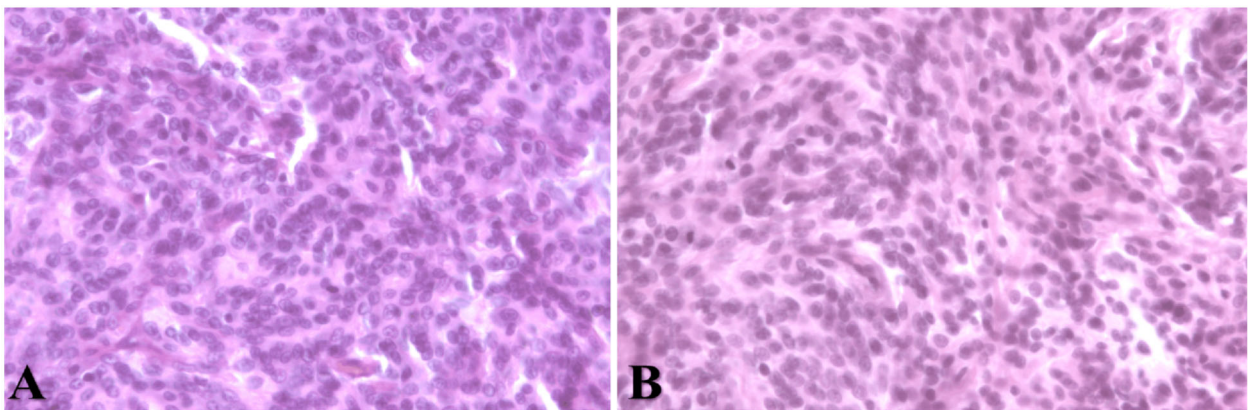


Figure 2 – Male, 63-year-old, parasagittal meningioma invading the posterior third of the SSS. Microphotographs exhibit a meningotheial tumor with patternless growth, very high density of tumor cells, and the following supplementary histomorphological criteria: (A) One mitosis in one HPF; (B) Two mitoses in another HPF. HE staining: (A and B) $\times 400$. HE: Hematoxylin–Eosin; HPF: High-power field; SSS: Superior sagittal sinus.

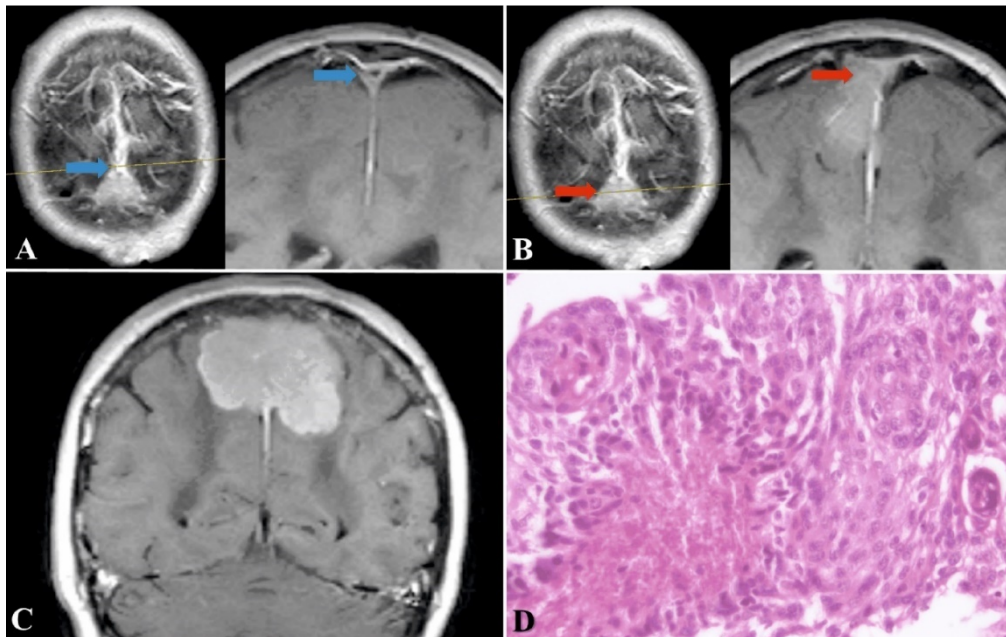


Figure 3 – Male, 62-year-old, parasagittal meningioma invading the posterior third of the SSS: (A) Portion of the SSS that is not invaded by the meningioma (blue arrows) (TIWI + contrast); (B) Portion of the SSS invaded by the meningioma – note that the SSS is no longer patent (red arrows) (TIWI + contrast); (C) Meningioma invading the SSS (TIWI + contrast); (D) Microphotograph demonstrating some concentric structures typical of a meningotheial tumor, but with hypercellularity and focal “spontaneous” necrosis (HE staining, $\times 400$). HE: Hematoxylin–Eosin; HPF: High-power field; SSS: Superior sagittal sinus; TIWI: T1 weighted.

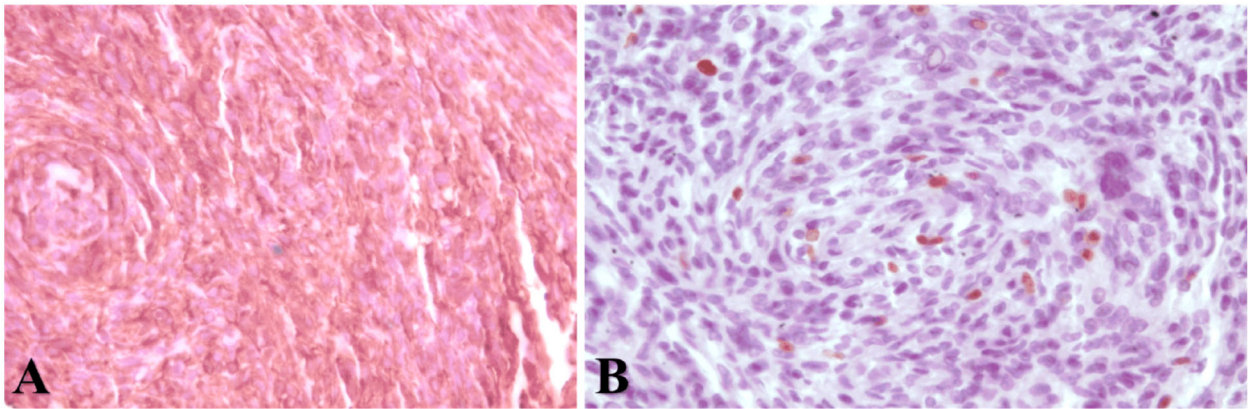


Figure 4 – Female, 59-year-old, falcine meningioma invading the anterior third of the SSS: (A) Microphotography showing strong cytoplasmic positivity for anti-vimentin antibody (IHC, $\times 400$); (B) Microphotograph showing a high Ki-67 LI (11% in this case) (IHC, $\times 400$). IHC: Immunohistochemistry; LI: Labeling index; SSS: Superior sagittal sinus.

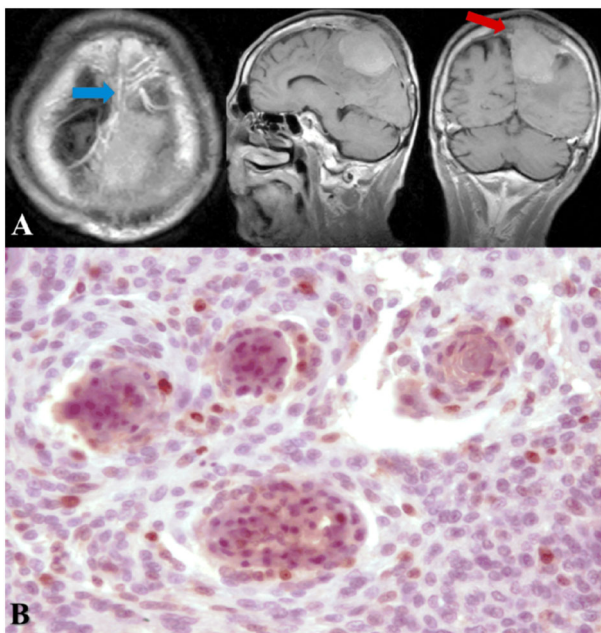


Figure 5 – Male, 58-year-old, parasagittal meningioma invading the middle third of the SSS: (A) SSS (blue arrow) and tumor with invasion of the SSS (red arrow) (T1WI + contrast); (B) Microphotograph demonstrating a high Ki-67 LI (9% in this case) (IHC, $\times 400$). IHC: Immunohistochemistry; LI: Labeling index; SSS: Superior sagittal sinus; T1WI: T1 weighted.

As regards the correlation between tumor recurrence and SSS invasion, 69% of patients with relapse had invaded SSS (Figures 5 and 7), while all patients without invasion

of SSS did not have recurrence. 38.1% ($n=8$) of the 13 meningiomas did not recur over the 5-year follow-up. The statistical differences between the two categories of patients were highly significant ($p=0.002$).

Regarding the relation between the degree of resection and tumor recurrence, we observed that all patients with Simpson grade II resection did not have a recurrence for a period of five years, whereas of the patients who relapsed, most had Simpson grade III (30.8%) or grade IV (53.8%) resection. Moreover, highly significant differences were identified between patients with and without tumor recurrence in terms of the degree of resection ($p=0.002$).

Invasion of the SSS

Regarding the invasion of the SSS, we noticed that 77.8% of the patients with the invaded sinus were men, probably because 71.4% ($n=15$) of the patients in the study group were men. Also, more than half of the tumors that invaded the SSS were located in the middle third of this dural sinus (55.6%, $n=5$) (Figure 5).

We observed statistically significant differences between tumor volume and invasion of the SSS ($p=0.006$). Thus, 88.9% ($n=8$) of the meningiomas that had invaded the SSS had a larger volume than the median volume of 26.86 cm³ (Figure 7). Also, 55.6% ($n=5$) of the meningiomas that had invaded the SSS had significant edema.

Statistically significant differences were observed between hyperostosis and invasion of the SSS ($p=0.006$). Thus, 55.6% of meningiomas with invasion of this dural sinus underwent hyperostotic changes (Figure 7).

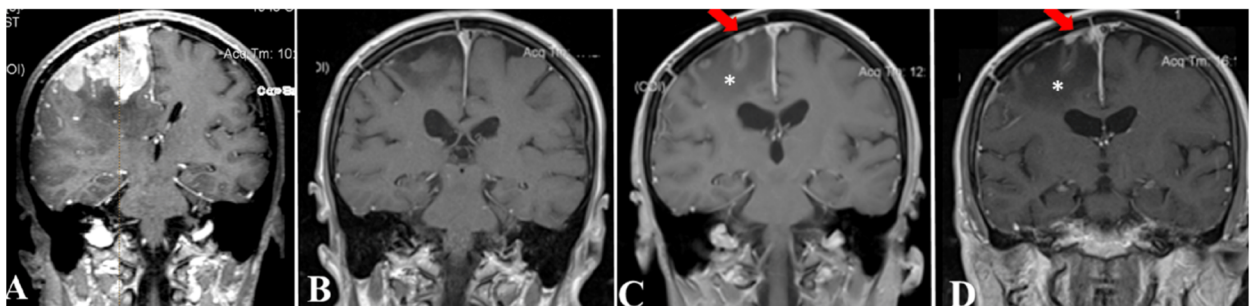


Figure 6 – Female, 65-year-old: (A) Right parasagittal meningioma invading the middle third of the SSS (T1 + contrast); (B) T1WI + contrast MRI at one year showing no recurrence; T1WI + contrast MRI at two years (C) and three years (D) of follow-up showing tumor recurrence (red arrows). MRI: Magnetic resonance imaging; SSS: Superior sagittal sinus; T1WI: T1 weighted.

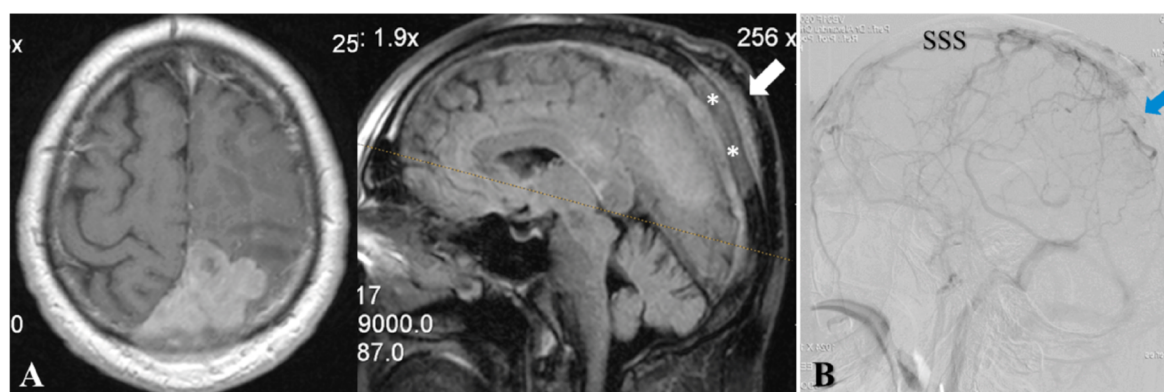


Figure 7 – Male, 63-year-old, parasagittal meningioma invading the posterior third of the SSS with bone infiltration (white asterisk) and extracranial extension (white arrow) (T1WI + contrast); (B) Cerebral catheter-based angiography showing the posterior third occlusion of the SSS by tumor invasion (blue arrow). (Courtesy Dr Nicolae Dobrin). SSS: Superior sagittal sinus; T1WI: T1 weighted.

Discussions

The surgical resection of meningiomas located near dural sinuses has been a challenge due to their proximity or invasion of the dural sinuses or of the large cerebral bridging veins [20, 37–39].

The management approach to these tumors occurring near the dural sinuses has been a matter of debate over the last few years, especially in cases of infiltration and obliteration [40, 41]. In our Department of Neurosurgery, we prefer less aggressive approaches which preserve the venous structures and do not remove tumor invasion from the dural sinus. Although several SSS repair and vein grafting techniques have been proposed in the course of time [42–47], we find that the risks they entail do not surpass the advantages and therefore their use is not justified. The most feared risk of dural sinus reconstruction is thrombosis, which could occur in up to 50% of the cases [48]. Furthermore, as concerns the falx invasion, although some authors recommend the removal of all invaded falx to minimize the risk of recurrence [15], we think that aggressive falx resection puts the draining veins at risk. Furthermore, falx manipulation could cause bradycardia and asystole due to falx trigeminocardiac reflex triggering [49], which is why various authors suggest that falx manipulation should be limited to a minimum and therefore recommend less invasive treatment strategies, such as radiotherapy [22].

Anatomical considerations

In terms of tumor location in relation to the SSS, they occurred as follows: 42.9% ($n=9$) were located in the anterior third, 47.6% ($n=10$) in the middle third and 9.5% ($n=2$) in the posterior portion of the SSS, in line with the literature data. According to them, the distribution of the meningiomas along the SSS in the anterior portion ranges from 14.8% to 33.9%, in the middle portion from 44.8% to 70.4% and in the posterior portion from 9.2% to 29.6% [13, 15, 50, 51].

If in the case of tumors involving the anterior third of the SSS, this sinus can be ligated and divided without complications, this is not possible for tumors involving the middle or posterior portion of the SSS due to the important risk of cortical venous infarction. Moreover, the best surgical management of these meningiomas has not

been established [40, 52]. In a recent systematic review, Giordan *et al.* (2020) argued that neurosurgeons adopt a more aggressive approach regarding meningiomas located in the anterior and posterior third of the SSS, and they prefer a more conservative approach of tumors located in the middle portion of the SSS [53].

Tumor recurrence in relation to SSS invasion and extent of surgical resection

As far as the recurrence rate is concerned, according to some studies, it is as high as 25% for *WHO* grade II meningiomas [54, 55], whereas for parasagittal tumors, recurrence appears in 7.9% to 29% of the cases, regardless of their histopathological grade [36, 56–58]. The recurrence rate for patients with grade II and III meningiomas located in this region is undoubtedly higher than for patients with benign meningiomas [55, 58–64].

Recurrence

Previous studies have reported that parasagittal meningiomas recur more frequently than meningiomas occurring in other intracranial locations [17–19]. In this respect, Ayerbe *et al.* proved that one of the factors more significantly associated with tumor recurrence is parasagittal location, and, furthermore, he reported a higher incidence rate of parasagittal atypical and malignant meningiomas compared to other intracranial locations [65].

In our research, tumors recurred over the 5-year follow-up in 61.9% ($n=13$) of the 21 patients with AMs. We think that this high recurrence rate is due to the fact that our research only included AMs, whereas most reviews include patients with all the three types of meningiomas (*WHO* grade I, II and III) [53, 66], with a tumor recurrence rate ranging from 6.7% to 32.7% [66]. Furthermore, in a recent systematic review of the 26 most important literature studies of meningiomas involving the SSS, Giordan *et al.* concluded that the clear majority of the meningiomas (81%) were benign, whereas AMs amounted to 14% of the histology of the analyzed meningiomas [53]. As concerns the estimated recurrence rate of AMs alone, it is twice the relapse rate of benign meningiomas, *i.e.*, 40% [95% confidence interval (CI): 11–72%]. In our study, most of the patients relapsed within 12 and 24 months, with recurrence rates of 14.3% ($n=3$) and 19% ($n=4$), respectively (Figure 6).

SSS invasion

As far as the influence of SSS invasion on the recurrence rate is concerned, in our opinion, the two factors are connected ($p=0.002$). Thus, 69% of patients with relapse had invaded SSS (Figure 7), while all patients without invasion of SSS did not have recurrence. The statistical differences between the two categories of patients were highly significant ($p=0.002$). When the SSS was invaded, the tumor recurrence rate was significantly higher one and two years after surgery (33.33% in both cases). On the other hand, in the absence of any SSS invasion, no tumor had recurred within 12 months and only 8.33% tumors had recurred within 24 months of the surgery (Table 3).

Table 3 – Tumor recurrence of atypical meningiomas from our study

Recurrence (0–60 months)	No SSS infiltration (%)	SSS infiltration (%)
No recurrence	8 (66.66%)	0
Recurrence after 12 months	0	3 (33.33%)
Recurrence after 24 months	1 (8.33%)	3 (33.33%)
Recurrence after 36 months	0	2 (22.22%)
Recurrence after 48 months	1 (8.33%)	1 (11.11%)
Recurrence after 60 months	2 (16.66%)	0

SSS: Superior sagittal sinus.

Moreover, 66.66% ($n=8$) of all the patients without SSS invasion did not relapse over the 5-year follow-up span. In literature, most studies have reported a close relation between SSS invasion and tumor recurrence, whereas other studies have found no correlation between sinus infiltration and recurrence [20, 39, 67].

Concerning tumor recurrence in relation to tumor location in the SSS, patients with meningiomas located in the anterior SSS relapsed less (44.44%) than patients with meningiomas located in the middle (70%) or posterior portion of the SSS (100%), these findings being in line with literature data [14].

Extent of surgical resection

The grade of resection in meningioma surgery is thought to be one of the most important factors influencing tumor recurrence [67], and in Simpson's first series, the recurrence rate at 10 years was 9%, 19%, 29% and 40% for grades I–IV resections [36]. The recurrence rate is higher in parasagittal and falxine meningiomas [14, 50] and, in the case of meningiomas with these locations, total resection cannot always be achieved.

Regarding the correlation between tumor recurrence and Simpson resection grade, we noted that 80% of all the patients with Simpson II resection ($n=8$) did not relapse over the 5-year follow-up. Also, the tumors of patients with Simpson III resection started to recur after 24 months, and those of patients with Simpson IV resection, after 12 months. Highly statistically significant differences were identified between patients with and without tumor recurrence regarding the degree of resection ($p=0.002$). In this respect, most studies in literature have proven that the recurrence of AMs was closely connected to the resection grade, which was identified as one of the most important

predictive factor for recurrence [68–75]. Thus, various authors have proven that a high grade of complete resection was associated with a low recurrence rate, unlike incomplete resections [68–83].

The most evident cause of recurrence in parasagittal and falxine meningiomas was the failure to achieve complete and radical resection of the meningioma [50]. High recurrence rates were also found in our research in the patients with SSS invasion, which were approximately 33%, 25%, 22% and 3% at 12, 24, 36 and 48 months, respectively, as compared to the cases with non-invasion of SSS (Table 3). On the other hand, literature studies have suggested that a more aggressive approach could be correlated with a higher risk of venous infarction and with the worsening of pre-existing motor deficits, and that it lowers but does not eliminate the risk of tumor relapse. In other words, an "aggressive" surgery is not immune to tumor recurrence [53].

Significance of histological features

There are few studies in the literature that have analyzed the prognosis of meningiomas of the SSS, regardless of their degree of malignancy, focusing more on the neuro-surgical technique [84] or on the gamma-knife treatment [85, 86].

Our study highlights the histopathological and immunohistochemical characteristics of AMs and proves that these tumors have a wide range, without also having a particular pattern of organization, high cell density, nuclear pleomorphism, mitosis, nuclear inclusions, and necrosis microfoci, respecting the *WHO* Classification criteria from 2016. There are, however, cases that deviate from this standard because they have a moderate cellularity and a Ki-67 LI with values less than 7%. In contrast, other AMs developed in the SSS have macronucleoli, intranuclear inclusions and a high Ki-67 LI, around the value of 14%, which signified a risk of rapid recurrence. Moreover, the presence of micro foci of necrosis has not been identified in all cases. It is also significant that the Ki-67 LI had values that ranged between 5% and 14%, which means that samples are needed from as many tumor areas as possible, especially as an AM can evolve by malignant transformation from a previous grade I meningioma, which developed over a fairly long period of time. Nonetheless, as the latest *WHO* Classifications (2000, 2007 and 2016) show, it is fairly difficult to classify a tumor in the group of AMs due to the fact that the neuropathologist must take into account a large number of histological and immunohistochemical variables, which must combine in order to reach a correct diagnosis [29, 87, 88].

Postoperative functional outcome

Another aspect related to meningiomas occurring near the SSS is their morbidity and mortality rates. As concerns postoperative neurological worsening, it is not uncommon in the surgery of parasagittal and falxine meningiomas, immediate mortality in microsurgical experience ranging in previous reports from 3.7 to 12.6% [13, 15, 51, 89]. Recent studies have reported much lower mortality rates, *i.e.*, 2% [39, 50, 53, 86], yet the postoperative complication rates are still high, *i.e.*, 14–20%, even in recent studies [20, 39, 86, 90].

In our series, postoperative complications occurred in only two patients and they consisted of bleeding in the remaining tumor cavity, which did not require surgical evacuation. Both patients had tumors in the middle portion of the SSS and our findings confirm the conclusions of other studies: meningiomas involving the middle portion of the SSS entail a higher risk for complications and increased morbidity [22, 91]. In our research, we may argue that, due to more caution in protecting and preserving the SSS and the large cerebral draining veins, no mortality or morbidity were noted in any patients.

Papilledema is another clinical element specific to the intracranial meningioma pathology. Therefore, literature studies have proven that meningiomas that involve the major dural sinuses can impede on cerebral venous outflow, which results in venous and intracranial hypertension, with subsequent decreased resorption of the cerebrospinal fluid [92, 93]. In our group of patients, papilledema occurred in three patients (one woman and two men), with an intracranial hypertension syndrome on admission. Two of the three patients also had a motor deficit. As concerns tumor location, two of the three meningiomas occurred in the parasagittal region and one was a falcine meningioma. The tumor volume was higher than the median tumor volume in all three cases. Also, in all three patients, the SSS was invaded by the tumor, which confirms the literature correlations between dural sinuses invasion and intracranial hypertension syndrome [93, 94, 95].

Tumoral volume, gender, and recurrence

As concerns the tumor volume and recurrence correlation, we noted that 75% ($n=6$) of the eight meningiomas that did not recur had volumes smaller than the mean tumor volume (26.86 cm³). Moreover, as concerns tumor recurrence within 12, 24 and 36 months of the surgery, respectively, we noted that larger meningiomas, the tumor volume of which is higher than the mean tumor volume, are more prone to recurrence. This is consistent with literature studies, according to which a larger tumor volume is a prognosis factor for recurrence [34, 50, 80, 96–99]. This may be accounted for by the fact that larger tumors pose additional challenges in achieving tumor resection as complete as possible, and consequently, the patient has a higher risk of tumor recurrence.

Literature has shown that there is a correlation between gender and *WHO* grade of meningioma, in the sense that men are more likely to have higher-grade tumors [63, 100]. Women are more prone to benign (*WHO* grade I) meningiomas, whereas AMs are more frequent in men [50]. These data account for the male predominance in our review, as 71.4% ($n=15$) of the cases were men. As concerns the rate recurrence in relation to the patient's gender, the rate was approximately similar, namely 60% in men and 66% in women.

Study limitations

Our study has some limitations, the most important being that fact that it was done retrospectively. Our follow-up period amounted to five years, and this is comparable with other follow-up periods, yet we recommend longer follow-up periods in order to detect delayed recurrence patients.

Conclusions

In our series of parasagittal and falcine meningiomas, we report a 47.6% Simpson grade II resection associated with a very low complication rate and no immediate postoperative morbidity and mortality, compared to more aggressive techniques. Tumor recurrence of parasagittal and falcine meningiomas predominated after Simpson grade III and IV resection. Surgery of parasagittal and falcine meningiomas which preserves the dural sinuses yields good surgical and clinical outcome. Aggressive meningiomas resection should be balanced considering the important surgical risk. Adjuvant therapy for residual tumor could also be considered.

Conflict of interests

The authors declare that they have no conflict of interests.

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