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Perioperative Brain Edema in Meningioma Resection Procedures: Case Series and Experience of a Single Center

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Abstract

Meningiomas are the most frequent benign intracranial lesions. They arise from the arachnoidal cap cells and are extra-axially located. Gross total resection in most of the cases is the treatment of choice. Technical aspects such as the presence of perifocal edema renders the resection procedure difficult and are related to postoperative outcome. Edema is not associated with location and size alone. It constitutes actually a phenomenon of the tumor and adjacent brain parenchyma interface and also depends on the secretion of vascular proliferations factors. Herewith, we present our retrospective study concerning 57 patients, who were operated, within the last eighteen months in our tertiary neurosurgical center. In our findings we involved tumor location and histological type. The grade of resection was described according to Simpson's scale and arachoidal plane was evaluated on T2-WI and FLAIR sequences. Furthermore, we have established statistical correlations of neurological outcome utilizing modified Rankin Scale upon the first two months, based on edema index ($p < 0.008$), arachnoidal plane presence ($p < 0.0001$) and the extent of excision ($p < 0.003$), as well. We advocate that surgeon should thoroughly examine the preoperative radiological tools and plan safely the strategy of extirpation beginning from the arachnoidal cleft.

Keywords

Meningioma, Peritumoral brain edema, Arachnoidal plane

Abbreviations

CT: Computer Tomography; **EI:** Edema Index; **FLAIR:** Fluid Attenuated Inversion Recovery; **MRI:** Magnetic Resonance Imaging; **mRS:** Modified Rankin Scale; **PIRE:** Poor Brain Tumor Interface Related Edema; **PTBE:** Peritumoral Brain Edema; **SD:** Standard Deviation; **SIRE:** Strong Brain Tumor Interface Related Edema; **VEGF:** Vascular Endothelial Growth Factor; **WHO:** World Health Organization

Introduction

Meningiomas are the benign intracranial tumor with the highest incidence [1]. They emerge from the arachnoid cap cells and develop as extra-axial lesions and have no specific location predilection [1]. Owing to their benignity surgical resection remains the horseshoe of treatment. The extent of surgical resection is classified according to the Simpson grading system and in less than one third of the cases they recur [2]. The extent of tumor excision remains the most common surgeon-related factor of recurrence; relevant technical aspects such as the arachnoid plane between the tumor and the cerebral cortex and the presence of

preoperative peritumoral brain edema (PTBE) as well, play an important role [1].

PTBE was found to be present in almost 60% of supratentorial meningioma cases. The secretion of vascular endothelial growth factor (VEGF) by the tumor into the adjacent cerebral parenchyma leading to vasogenic brain edema is well related to PTBE. Apart from that, cortical-pial neo-vasculature of the tumor was also found to be well associated with [1].

We conducted our retrospective study to evaluate the occurrence of PTBE and its impact on resection, its relationship with arachnoidal plane and the general effect on the clinical outcome.

Materials and Methods

We have conducted a retrospective study regarding 57 patients operated within the last 18 months in our neurosurgical clinic. Gender distribution concerned 16 male patients and 41 female ones. Their mean age was 58.4 years old (SD 14.33). We initially present a classification of tumor location. Resection grade was characterized based on Simpson's scale [3].

We also evaluated the tumor and parenchyma interface. The cleft between predominantly extra-axial lesions like meningiomas and pial surface, which also shows its intactness, is known as arachnoidal plane [4]. The presence of arachnoidal plane was defined as present or absent in evaluation of T2- and FLAIR- sequences on MRI scan (1.5 Tesla). We considered it sufficient when it circumscribed almost half of the maximum lesion's perimeter.

We calculated brain edema index by using the ratio of the diameter of PTBE at the transverse cut, where maximal tumor diameter was observed, to the maximal tumor diameter. For our evaluation we have also assessed edema on T2- and FLAIR -sequences, respectively on MRI scan (1.5 Tesla). We also examined histology both utilizing WHO-grade classification. Cases where noticeable draining venous and sinus occlusion or obstruction were to be seen were excluded. Immediate postoperative outcome was interpreted according to modified Rankin scale (mRS) at two months after the resection [5].

To assess the normality of the variables we used Kolmogorov-Smirnov test. Comparison between numerical and ordinal variables performed using the non-parametric Mann- Whitney test, when they were two of them and Kruskal-Wallis test when they were three. We used Spearman' s rank correlation coefficient for nonparametric correlation. P-values less than 0.05 in two-tailed tests were considered statistically significant. SPSS v.25.0 software was used for our analysis.

Results

Skull base meningiomas rated 53%, whereas cranial dome ones almost 43%. Convexity and parasagittal locations were the most frequent ones (Table 1). Histology revealed transitional and meningothelial subtypes as the most common ones. Atypical category was noticed in almost 19% of the specimens (Table 2).

Table 1: Location of meningioma.

Location	Frequency	Percent
CPA	3	5.3
Falx	2	3.5
Convexity	13	22.6
Petroclival	2	3.5
Tentorium/petral bone	3	5.4
Posterior fossa/ tentorium	5	8.8
Olfactory groove	4	7
Parasaggital	12	21.1
Lesser wing/sinus cavernosus	11	19.3
Parasellar	2	3.5
Total	57	100

Table 2: Histological results.

Histological type	Frequency	Percent
Metaplastic	1	1.8
Fibroblastic	5	8.8
Transitional	17	29.8
Meningothelial	20	35.1
Psammomatous	3	5.3
Atypical	11	19.3
Total	57	100.0

Degree of resection and the presence of arachnoidal plane are also presented here (Table 3 and 4). We observed good or rather good outcome- mRS equal or less than 3- in 70.2% of our patients within the first postoperative period (Table 5). We have established statistically significant associations among clinical outcome and lesion's excision (Spearman's

Table 3: Degree of resection performed.

Resection classification using simpson scale	Frequency	Percent
I	2	3.5
II	30	52.6
III	14	24.6
IV	11	19.3
Total	57	100.0

Table 4: Presence of arachnoidal plane on T2-weighted MRI.

Arachnoidal plane	Frequency	Percent
Absent	21	36.8
Present	36	63.2
Total	57	100.0

rho = 0.382, p < 0.003), presence of arachnoidal plane (rho = -0.459, p < 0.0001) and edema index (rho = 0.350, p < 0.008). Arachnoidal plane constituted the most significant prognosticator (Table 6).

Table 5: Assessment of outcome within the postoperative period.

Outcome based on modified rankin scale at 2 months	Frequency	Percent
1	8	14.0
2	14	24.6
3	18	31.6
4	9	15.8
5	2	3.5
6	6	10.5
Total	57	100.0

Table 6: Statistical significant associations.

Non-parametric correlations		Modified rankin scale at 2 months
Simpson resection grade	Correlation coefficient	0.382**
	Sig. (2-tailed)	0.003
	N	57
Arachnoidal plane	Correlation coefficient	-0.459**
	Sig. (2-tailed)	0.0001
	N	57
Edema index	Correlation coefficient	0.350**
	Sig. (2-tailed)	0.008
	N	57

Discussion

The etiology of meningioma related cerebral edema is imputed to blood-brain barrier rupture [6]. Additional factors involve histological type, tumor growth, irregular shape and pial cortical blood supply and poor basal venous drainage. VEGF expression portends to an increase in edema with matrix metalloproteinase-9 and interleukin-6 having an important contribution, as well [6].

It is primarily of vasogenic origin and propagates by bulk flow analogous to the pressure gradient between tissues [7]. It also affects predominantly white matter up to ventricular walls with involvement of perivascular spaces [8].

Apart from the aforementioned molecules expression blood supply has an important role. Several authors have stated that the recruitment of cerebral-pial vessels result in edema formation [9]. Edema index (EI), a proportion in other words of edema to the tumor growth per se was introduced as a prognosticator of clinical outcomes [2]. Lee et al. conducted a prospective study utilizing radiological and histological parameters apart from clinical ones and they concluded that tumor growth affects pial-cortical supply which consequently leads to edema and increased perioperative morbidity and mortality [10]. There are also noticeable studies which have demonstrated edema as a prognosticator of poor outcome [11, 12]. Vignes et al. established an association of edema with clinical signs, type of arterial supply, laborious extirpation and post- surgigal morbidity [11]. Markovic et al. drew an association between VEGF expression and PTBE [12].

Arachnoidal plane constitutes also one prognosticator. Villa et al. established the term cleft sign introducing a T2-FLAIR digital subtraction sequence [4]. Edema did not always correlate with the poor cleavage plane. Absent cleft sign in the image subtraction and a minimal intraoperative cleavage plane strongly omens postoperative neurological deficits [4].

Alvernia and Sindou in their prospective study of 100 patients documented a clear correlation between the tumor dimensions on (MRI) and the extent of subpial surgical plane of cleavage. A parallel association was observed with the degree of PTBE seen on preoperative (CT) or T2-weighted MRI sequences and tumor pial vascularization on angiography. Paradoxically, the tumor-brain cortex interface on preoperative T2-weighted MRI sequences had no impact. Eloquent location of lesions in which resection proceeded subpially ended up to poor outcomes [13].

Yin et al. published a study of edema in parasagittal meningiomas focusing on venous compression theory. They implemented a classification of edema taking under consideration the relation of brain-tumor interface (a) and edema-tumor interface (b). When the ratio was b ≤ 1/3 an edema was categorized as poor brain-tumor interface related edema (PIRE). When the ratio was b > 1/3 an edema was annotated as strong brain- tumor interface related edema (SIRE). Measurement was performed in three levels of the greatest surface of the lesion utilizing axial, coronal and sagittal T2-weighted sequences.

Along with that, they evaluated the sinus occlusion and the degree of collaterals development. They concluded that PIRE was highly associated with venous decompensation and worst neurological outcome within the consequent three to six months. Despite the fact that, their topic was the contribution of venous drainage insufficiency to edema formation they stressed the role of brain tumor interface and venous network [14].

Meningeal stratification is an important factor for surgical planning. Arachnoid granulations constitute indentations of arachnoidea matter into dura. Microscopically are comprised of leptomeningeal cells and covered by venous endothelium. The cap of arachnoid cells, wherefrom meningiomas emerge, are placed on top of the of arachnoid granulations core and adjoins the venous endothelium. Thus, meningiomas evolve in the subdural and upper arachnoidal place and are indirectly connected to subarachnoid space [15].

Further anatomical studies showed that, there is a perivascular space around arterioles of cerebrum, which is demarcated by a pial cell stroma. This space is extended on one point from subpial arterioles and ends the perivascular compartment of arteries in the sub-archnoid space. Through this space there is a perivascular channel from parenchymal arteries to the ones of the subarachnoid space. This discrepancy between the two zones, in other words, the subpial/pial-

perivascular and subarachnoid-perivascular is more obvious in the basal cisterns [16].

We consider edema progression, effacement of arachnoidal plane and distortion of cerebral-pial vascularization as different phases of the same process. On the contrary, tumor growth individually is not an element of this phenomenon (Figure 1 and 2).

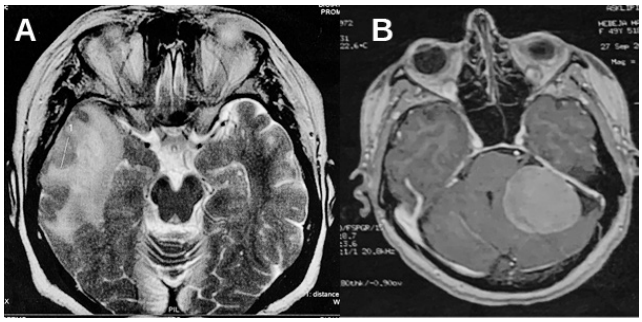

Figure 1: (A)- Atypical small size meningioma eliciting disproportionate edema. It was initially miscalculated as a metastasis and **(B)**- transitional meningioma of posterior fossa with apparent space occupying effect with almost no edema.

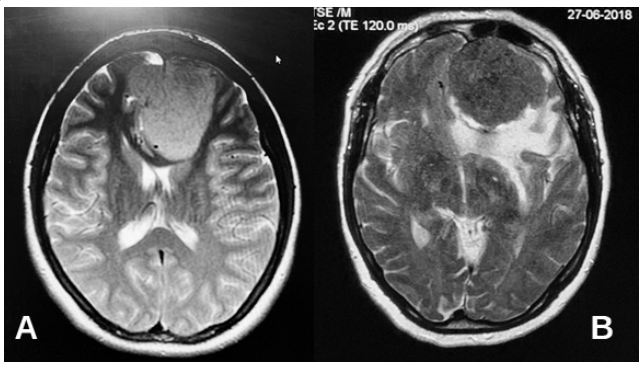

Figure 2: (A)- Frontal parasagittal meningioma and **(B)**- frontal falcine meningioma of meningothelial type resulting in different patterns of edema.

That means that extirpation maneuvers should initially take place at this safe zone even in cases, where tumor bulk may be in front of surgeon's visual space (Figure 3 and 4). Therefore, a craniotomy should be tailored taking under consideration the potential changes of visual axis and dissection corridors during the procedure. Further osseous removal in an extended craniotomy reduces the distance to the lesion and prevents from parenchyma traction and edema worsening [17].

Finally, meningiomas with diameter exceeding the 2 cm receive their blood supply from a complex of collateral leptomeningeal arteries in a watershed region. In skull base, though, supply is provided by the dura vasculature following specific distribution. Thus, in these cases dissection, apart from preserving the arachnoidal plane, should advance towards the skull base to control the arterial branches [17].

Our study had its limitations, which was its retrospective design and its sample size, which was not large. Despite that, we intended to show that edema's short-term negative effects may be expected, when it is disproportionately related to the tumor itself and no sufficient demarcation between parenchyma and the lesion exists. Whenever, this demarcation

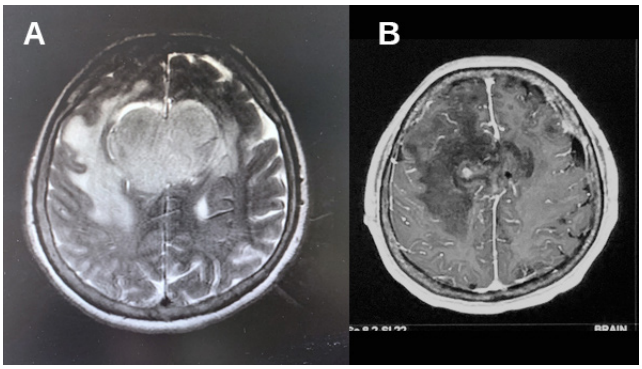

Figure 3: (A)- Falcine meningioma of frontal location with massive perifocal edema as seen on T2-sequences and **(B)**- postoperative resection with residual edema and transient left-sided hemiparesis.

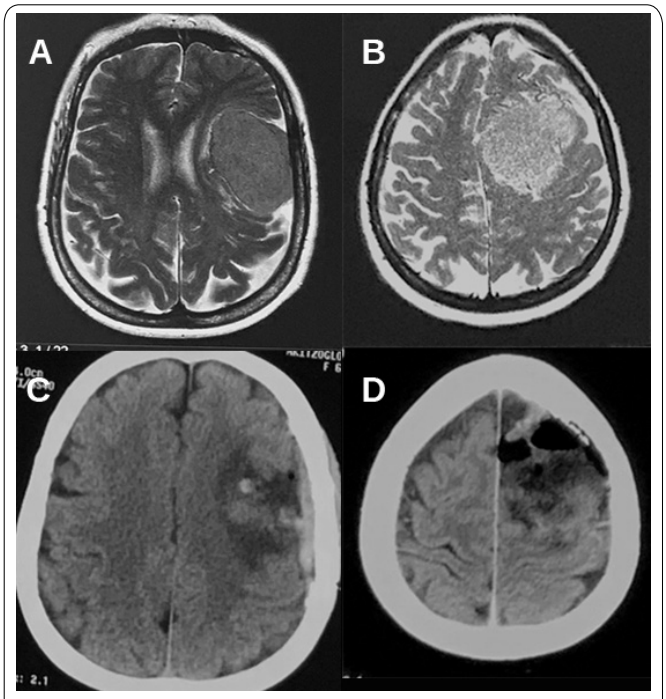

Figure 4: (A)- Fibroblastic, **(B)**- meningothelial meningiomas in eloquent areas with good arachnoidal plane, **(C)** and **(D)**- postoperative control showing gross total resection with excellent postoperative outcomes.

was maintained and the resection proceeded, as radical as possible, outcomes were good. Tumor dimensions alone on the other hand showed no statistically significant association.

Conclusion

PTBE is associated with short-term negative outcomes. Treating neurosurgeons have to be acquainted with its pathogenesis. In additions to that, they should suspect it by evaluating the edema/tumor relationship and effacement of parenchyma/tumor margins, preoperatively, on MRI scans. Respecting arachnoidal plane and achieving the maximal and safest resection, as well, leads to good outcomes.

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