Correlation between the efferent venous drainage of the tumor and peritumoral edema in intracranial meningiomas: superselective angiographic analysis of 25 cases

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Object. The extent of peritumoral brain edema (PTBE) associated with meningiomas can be highly variable. The authors studied the correlation between the development of efferent venous drainage from the tumor and the degree of PTBE that occurs in intracranial meningiomas.

Methods. Twenty-five patients with 27 intracranial supratentorial meningiomas were investigated to identify the correlation between the efferent venous drainage system of the tumor and peritumoral edema. The overall mean age of the patients was 54 years. Seventeen patients (68%) were female and eight (32%) were male. All patients underwent magnetic resonance imaging and digital subtraction angiography. In each meningioma, superselective angiography of the dominant feeding artery was performed, including the late venous phase to evaluate the development of the tumor’s draining vein. An edema index (EI) was introduced to serve as an objective means by which to judge the extent of PTBE. Eleven meningiomas (41%), in which the mean EI was 0.14 ± 0.10, clearly showed dominant draining veins originating from the tumor itself. In the other 16 meningiomas (59%), superselective angiography demonstrated no efferent venous drainage from the tumor, which could account for this group’s mean EI value of 1.49 ± 1.05 (p < 0.001)

Conclusions. The current results suggest that hypoplasia of the efferent draining vein from the meningioma itself contributes to PTBE formation. The development of an efferent venous system mitigates against the formation of PTBE. Intratumoral venous congestion can be considered the main cause of PTBE in meningiomas.

KEY WORDS • meningioma • peritumoral edema • efferent draining vein • superselective angiography

Peritumoral brain edema is one of the most serious complications in the management of intracranial neoplasms. Intracranial pressure is often affected by this phenomenon. The severity and variety of PTBE may limit operative exposure and frequently increase the difficulty and the complexity of surgical extirpation. Therefore, the ability to predict and define PTBE during preoperative evaluation is very important, especially in the management of meningiomas. Nevertheless, its exact pathophysiological mechanism in meningiomas remains unclear. Various causative factors have been discussed in the literature, including tumor size, tumor location, histological differentiation, type of arterial blood supply to the tumor, relationship to hormone receptors, brain ischemia, and compromised physiological venous drainage resulting from tumor mass effects.

Due to the recent advances in microcatheters and the progress in digital subtraction angiography, a certain part of the angioarchitecture of the tumor itself can now be observed. In 25 patients with 27 supratentorial meningiomas representative of extraxial intracranial tumors, the tumors were managed by endovascular treatment and exploration that exploited the capabilities of surgical neuroangiography. The data obtained in these cases were then retrospectively analyzed to determine whether there existed a negative correlation between the development of efferent venous drainage from the meningioma itself and the degree of its PTBE.

Clinical Material and Methods

Patient Population

We consecutively assessed 25 patients with 27 intracranial supratentorial meningiomas who presented between January 2000 and October 2003.

At the time of presentation the mean age of the patients was 54 ± 14 years (± SD; range 30–78 years). The study population was composed of 17 women (68%) and eight...
men (32%). Embolization was performed in relatively large meningiomas that were expected to be supplied mainly from the MMA: 25 patients underwent endovascular embolization in preparation for subsequent extirpation, and two patients underwent palliative embolization to reduce and/or suppress tumor mass growth.

Definition of PTBE by Neuroimaging

Each meningioma and any PTBE that developed were assessed using MR imaging. The tumor volume was estimated on Gd-enhanced T1-weighted images. Evaluation of PTBE was performed using T2-weighted images or fluid-attenuated inversion-recovery sequences. The volumes of tumor and the PTBE were calculated using the application software on the console panel of the MR imaging unit or were approximated from axial, coronal, and sagittal images. The maximal perpendicular diameters (a and b) of the tumor and the PTBE were measured on axial images, and the extent in the coronal direction (c) was measured on coronal or sagittal images. The total volume of the tumor (V{Tumor}) and the volume of the hyperintensity area on T2-weighted images (V{T2-high}) were then estimated using the following formula (assuming that the lesion was a spheroid, in case the volume calculation software is not available on the MR imaging unit’s console panel):

\[
\text{volume} = \frac{4}{3}(a/2)(b/2)(c/2) \text{ mm}^3.
\]

The relationship of the tumor to the PTBE volume was defined as follows:

\[
\text{volume of edema} = \frac{V_{T2-high}}{H11002} \times \text{V{Tumor}}.
\]

Next, a ratio referred to as the EI was introduced as a way to evaluate objectively the extent of PTBE. The edema volume was divided by the tumor volume. An EI value of 0 implies the absence of peritumoral edema, whereas a value of greater than 0 indicates the presence of PTBE.

Endovascular Procedures

All patients underwent selective cerebral angiography in which a modified Seldinger technique was used, including selective internal carotid, external carotid, and/or vertebral artery injections to clarify whether the tumor had a predominantly meningeal or pial supply. After this general four-vessel angiography was completed, microcatheter-based superselective angiography was performed with the aid of high-quality fluoroscopy and roadmapping capabilities. Most superselective angiography examinations were undertaken by navigating the microcatheter tip into the feeding artery, which was usually located in the distal segment of the MMA after passing through the foramen spinosum.

Superselective angiography was conducted while 1 ml contrast medium (Iopamiron; Schering AG, Berlin, Germany) was injected. The angiographic examination included the late venous phase of the digital subtraction angiogram, which lasted up to 14 seconds after contrast injection, to obtain the anatomical and topographical images of the efferent venous drainage system coming from the tumor itself.

If a meningioma presented a significant efferent vein (or veins) within this 14-second period of digital subtraction angiogram acquisition, it was assigned to the well-developed venous drainage system group (Group 1); if an efferent vein (or veins) was not visible within 14 seconds, the tumor was assigned to the poorly developed drainage system group (Group 2). Regardless of the type of supply, great attention was paid to the potential anastomosis between the meningeal artery and the ophthalmic arterial system, as well the intradural parenchymal (pial) supply, based on the knowledge of embryological angiography.

After superselective angiography had been performed and the angioarchitecture of the tumor demonstrated, polyvinyl alcohol particle–based embolization was performed through the same microcatheter. The polyvinyl alcohol particles were 45 to 150 μm and were mixed with the same contrast medium. The end point of the embolic material injection occurred when the terminal segment of the feeding artery started to stagnate.

Statistical Analysis

Values are presented as the means ± SDs. Statistical analysis was performed using either the t-test or the Mann–Whitney U-test.

Results

Location of the Meningiomas and PTBE

Eleven meningiomas were located in the convexity (44%), four in the parasagittal area (16%), three at the sphenoid ridge (12%), one in the middle fossa (4%), two in the tuberculum sellae (8%), and four in the frontobasal area (including the olfactory groove; 16%) (Table 1 and Fig. 1).
There was no significant correlation between tumor location and the extent of PTBE (Fig. 2).

Size of the Meningiomas and PTBE

Overall, the mean volume of the meningiomas was $88.3 \pm 42.5$ cm$^3$. The mean size and distribution of the meningiomas (according to the EI) are summarized in Table 2.

Eight meningiomas had minimal PTBE (an EI $< 0.1$), whereas 17 had relatively marked PTBE (EI $> 0.1$). The mean tumor volume in tumors with minimal PTBE was $108.2 \pm 50.5$ cm$^3$, whereas that in those with marked PTBE was $79.1 \pm 41.1$ cm$^3$ (Table 2). There was no significant difference between these two groups in the mean tumor volume, however, which implies an absent correlation between tumor size and PTBE.

Angiographic Findings and PTBE

Eleven meningiomas were categorized as Group 1 lesions because the efferent venous drainage from the tumor was clearly delineated on superselective angiograms of the feeding artery; 16 meningiomas were categorized as Group 2 lesions because the efferent venous drainage was not clearly observed on superselective angiograms that included the late venous phase. The mean EI in Group 1 was $0.14 \pm 0.10$, whereas that in Group 2 was $1.49 \pm 1.05$ (p $< 0.001$; Table 3).

There were four meningiomas associated with intratumoral arteriovenous shunts that were seen as relatively early venous filling on superselective angiography. One of these drained directly into the inferior sagittal sinus, and the others drained through the MMA. In these meningiomas minimal PTBE was present (mean EI $0.16 \pm 0.14$) (Table 4).

Clinical Outcomes

After endovascular exploration and embolization, all patients fared well, and none suffered new neurological deficits. After embolization, extirpation of the lesion was undertaken in 22 consecutive patients who harbored 23 meningiomas; the histological evaluation of the tissue was then performed to confirm the nature of the tumor.

Neuroimaging After Embolization

Within 48 hours of endovascular exploration and embolization, all patients underwent high-resolution MR imaging. In the group of patients whose 19 meningiomas had an EI of 0.1, significant reduction of the area of PTBE was documented in nine. The majority of the embolized meningiomas on follow-up MR imaging exhibited a decrease in the intratumoral uptake of Gd contrast, which suggests that the tumor was well devascularized.

Relationship Between Histological Type and PTBE

The histological classifications of the 23 tumors included eight meningothelial meningiomas, 11 transitional meningiomas, two fibroblastic meningiomas, and two miscellaneous. There was no significant correlation between histological subtype and EI (Fig. 3).

Illustrative Cases

Case 1

This 56-year-old woman presented with a headache. Mag-
Tumoral venous system and perifocal edema

Magnetic resonance imaging revealed a large 3.5 × 3–cm falx meningioma located in the left internal frontal region. We observed heterogeneous intratumoral hyperintensity on Gd-enhanced T₁-weighted images; no significant hyperintensity was seen in the surrounding tumoral parenchyma on T₂-weighted images. Despite its large size, this meningioma exhibited no peritumoral edema (Fig. 4 left and center).

Superselective angiography was performed from the frontal and parietal branch of the MMA after placement of a 1.5 French semiflow-directed microcatheter. This superselective angiography showed tumor staining with a significant efferent vein originating from the tumor itself and draining into the inferior sagittal sinus (Fig. 4 right).

Case 2

This 66-year-old woman with multiple meningiomas presented after suffering a seizure. An MR imaging study revealed multiple intracranial lesions, one in the left temporal region (Fig. 5A and C) and another in the right paramedian occipital area (Fig. 5B and D). Axial Gd-enhanced T₁-weighted MR imaging (Fig. 5A) and T₂-weighted imaging at the same level (Fig. 5C) demonstrated a left temporal convexity meningioma with a large area of peritumoral edema extending posteriorly. Superselective angiography of this temporal meningioma showed tumor staining but no evidence of a draining vein from the tumor itself (Fig. 5E). The small meningioma that was located in the right paramedian occipital area, however, did not exhibit any significant peritumoral edema (Fig. 5D). Superselective angiography of this right paramedian occipital meningioma revealed tumor staining with a significant drainage system originating from the tumor itself (Fig. 5F arrow). On pathological examination both of the tumors were shown to be meningothelial meningiomas.

Case 3

This 47-year-old man presented with a headache. An MR imaging study showed a large (6.5 × 5.5–cm-diameter) meningioma symmetrically extending from the planum sphenoidale (Fig. 6A–C). At the base of this tumor, there was no peritumoral edema involving the deep white matter of the bilateral inferior frontal gyrus; however, despite the symmetrical extension of the tumor, only the right side of the middle frontal gyrus was affected by significant peritumoral edema (Fig. 6B). Internal carotid artery angiography revealed that the basal part of this tumor was supplied by bilateral transdural ethmoidal branches through the ophthalmic artery and that the superior part of the tumor was supplied mainly from the pial branch through the frontopolar artery (Fig. 6D and E).

Superselective angiography of the left frontopolar artery, which corresponded to the superior part of the tumor, revealed tumor staining and a significant drainage system connected to the superior sagittal sinus (Fig. 6F); however, superselective angiography of the right frontopolar artery, which corresponded to the right superior aspect of the tumor, did not show any significant draining vein in the late venous phase (Fig. 6G).
Overall these angiographic findings suggest that if the tumor or a part of the tumor has a good drainage system, then no edema will be present, whereas if the tumor has no drainage system, then significant PTBE will develop.

**Discussion**

Meningioma is an extraaxial tumor initially supplied by the dural meningeal vessels that originate from the dural attachment points. In the early stage of its growth, a meningioma has no connection with the pial arterial system or the pial venous system, except for intraventricular meningiomas, which are usually supplied predominantly by the choroidal artery.

In the literature, tumor stasis is considered to be one cause of PTBE, and it has been suggested that this stasis occurs because of the compression of an adjacent cortical vein by the tumor. There are some inconsistencies in this proposed mechanism, however, because many meningiomas have been shown to markedly compress the adjacent cortical vein but, nevertheless, are not associated with PTBE. On the other hand, a small tumor can sometimes produce significant amounts of edema. Thus, we postulated that tumor stasis occurs not as a result of the compression of an adjacent cortical vein but from the poor development of the tumor’s drainage system.

Based on this hypothesis, we studied 25 patients in whom meningioma was diagnosed during a 3-year period, and we found that there was a close negative correlation between the extent of PTBE and the development of the efferent vein originating from the tumor.

The authors of recent studies have demonstrated that the pathogenesis of meningiomas, including evidence for tumoral growth and neovascularization, is strongly associated with a wide range of growth factors. Among others, platelet-derived growth factor, epidermal and fibroblast growth factors, sex steroid receptors (including those for progesterone and androgen), endothelin-1, monocyte chemoattractant protein, and VEGF have all been implicated in some aspect of meningioma growth, angiogenesis, or edema-related complications. In particular, the expression of VEGF is considered to play an important role in both meningioma vascularity and peritumoral edema.

It has been reported that the manifestation of VEGF depends on hypoxia of the regional pericyte of the capillary and that it is also regulated by the tonus of the endothelial cells. The effect of VEGF increases in the presence of the vascular permeability that creates PTBE, which is considered to be the main cause of cellular damage due to the creation of cytotoxic edema. Increased expression of VEGF might also be associated with the tumor’s efferent venous drainage system. Should the efferent venous drainage system be poorly developed, resulting stasis and congestion of the intratumoral compartment would directly affect intratumoral pressure. Thus, continuous stasis with increased pressure within the intratumoral vein could be a factor that provokes VEGF expression.
The incidence of PTBE, however, is only approximately 40 to 60%, and there is no clear correlation between the expression of VEGF and the degree of PTBE. If a meningioma has a well-developed efferent draining vein, even with the regional production of VEGF, such a tumor might not induce PTBE, because the transit time of the blood passing through the channel in the tumor is short, resulting in a relatively rapid washout of VEGF. This hypothesis would explain the minimal PTBE that is seen despite a high level of VEGF expression (Table 5).

Conclusions

Superselective angiography of meningiomas clearly delineates intra- and peritumoral angioarchitecture. This modality can provide not only therapeutic guidance but also information about the functional microvascular anatomy, including the venous drainage system of the tumor itself. We observed a strong negative correlation between PTBE and the degree of development of efferent venous drainage originating from the tumor. There was no correlation found between PTBE and other factors, such as tumor size and volume, tumor location, pattern of the feeding arterial system, and tumor histological type.

A larger sample of patients and more detailed molecular biological study are required to confirm our preliminary findings, which have established a possible mechanism of PTBE that may facilitate the management of central nervous system neoplasms.

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