Commentary on:
An Underlying Pathological Mechanism of Meningiomas with Intratumoral Hemorrhage: Undifferentiated Microvessels
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Role of Tumor Vessels' Features in Determining Risk of Bleeding in Meningiomas: Which Came First, the Chicken or the Egg?

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Meningiomas are the most common primary tumor of the central nervous system (CNS) and account for 13%–26% of all intracranial tumors.[1] Because they originate in the meninges, more precisely from arachnoid cap cells located within the arachnoid granulations, they are extra-axial tumors. The great majority of meningiomas are benign, slow-growing, and highly vascularized tumors. Treatment is almost always represented by surgical excision followed in some cases by radiotherapy or radiosurgery, depending on histology and/or amount of residual tumor. Outcome and recurrence rate depend on several factors including some biologic features of the tumor and some aspects directly related to the surgical intervention; some of them can be predicted easily before surgery (e.g., size and location), but others are discovered only during surgery or even after it (e.g., histology).

Obviously, histologic type, benign (World Health Organization [WHO] grade 1), atypical (WHO grade 2), or malignant (WHO grade 3), directly correlates with recurrence rate (and usually survival) and is probably the most important factor. Extent of surgical resection, following the Simpson grading scale,[2] plays a pivotal role as well. It is also established that meningiomas location influences surgical resection and consequently complications and outcome, with convexity meningiomas being considered the simplest to resect and petroclival or cavernous the hardest[3]; nerve and vessel encasement is strictly related to location and adds further risk of postoperative deficits. Other factors include size, peritumoral brain edema (PTBE), soft versus tough tumor consistence, violation versus nonviolation of the arachnoid–pia mater barrier, and tumor inclination to bleeding.

As many other tumors, biology of meningiomas is currently under investigation and, despite great advances in this field, many aspects are still not fully understood. For example, chromosome 22 abnormalities are often demonstrated in meningiomas and chromosome 1 abnormalities have been associated with more aggressive tumors.[4,5] Expression of several growth factors and receptors have been reported in meningiomas.[3]

However, when the surgeon is preparing to approach a meningioma, there are other biologic aspects that will make surgery easy or hard: tumor consistence, presence of PTBE, and, likely the most relevant, conservation of the interface between the tumor and arachnoidal–pia mater barrier. Preoperative radiologic workup can be of great help in depicting tumor consistency, like showing wide areas of calcifications on computed tomography, vessel encasement on magnetic resonance imaging, and vessel displacement or stenosis on digital subtraction angiography. On magnetic resonance images it can sometimes be possible to recognize specific atypical and malignant features of meningiomas, too[3]; it might further help in quantifying PTBE and disruption of the arachnoidal plane.[6,7] Nevertheless, there are cases in which the arachnoidal plane appears conserved on preoperative images and during surgery it is found to be disrupted by the tumor. In these cases, even a "simple" meningioma could become difficult to resect and the patient may develop (unexpected) postoperative neurologic deficits. In such a scenario, we neurosurgeons and scientists lack a complete understanding of meningiomas pathophysiology. Current literature rarely focuses on this characteristic.

Key words
- Brain edema
- Brain tumor
- Hemorrhage
- Meningioma
- Micorovascular density

Abbreviations and Acronyms
CNS: Central nervous system
MVD: Microvascular density
PTBE: Peritumoral brain edema
WHO: World Health Organization

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Another important issue that affects outcome in meningioma treatment and reflects the tumor's biologic behavior is the tumor's inclination to spontaneous bleeding. Meningiomas associated with hemorrhage are rare; the reported incidence is around 1.3%–2.4%[8]; when this happens, though, clinical consequences may be severe, with higher mortality and morbidity rates compared with meningiomas that did not bleed. However, in recent times, with imaging and surgical advances, these rates improved remarkably; not surprisingly, patients presenting with hyperacute onset of symptoms and comatose status are more prone to have a worse outcome.[8] Meningiomas may bleed only intratumorally or both intratumorally and extratumorally. Reviewing our surgical database, since 2008, we found only 2 cases of spontaneous bleeding from intracranial meningiomas, both recurrent atypical WHO grade 2 and both with intratumor and extratumor bleeding (Figure 1). The reason for the low rate of hemorrhage in meningiomas is poorly understood, as are the pathophysiologic mechanisms underlying this phenomenon. Some authors indicated that intratumoral vasculature may be

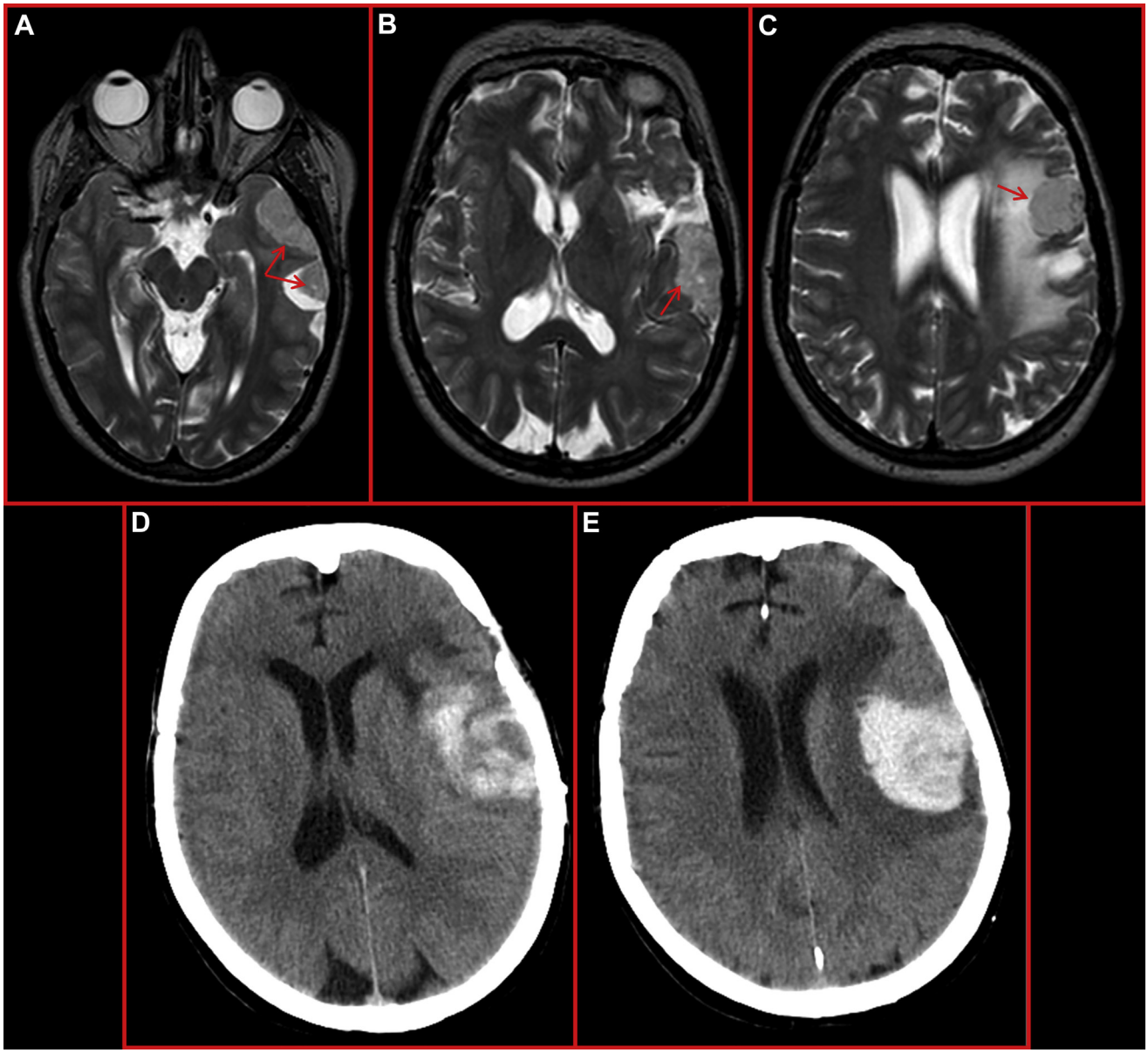

Figure 1. (**A**, **B**, and **C**) T2-weighted axial magnetic resonance images of a 45-year-old female patient affected by multiple atypical recurrent convexity meningiomas on the left side (*red arrows*). While the patient was waiting for a new operation for removal of a new recurrence of her meningiomas, she had an acute headache and onset of right hemiparesis. (**D** and **E**) The axial computed tomography scan revealed acute hemorrhage of the tumors, both within the tumors and extratumorally.