Acute haemorrhage into a microcystic meningioma leading to cerebral herniation

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Abstract

Low-grade (WHO level I) meningiomas are slow-growing, benign tumours typically presenting with unspecific symptoms (e.g. headache), seizures, cranial nerve compression and neuropsychological symptoms determined by location and size of the lesion. Haemorrhagic onset and sequelae are rare, and have been described infrequently. This is a case of a 50-year-old male presenting with signs of tentorial herniation secondary to hyperacute intratumoural haemorrhage (ITH) into a previously undiagnosed meningioma. Emergency surgical decompression and exstirpation of the lesion helped to achieve a favourable outcome. ITH has been described in all including benign intracranial neoplasms. Factors associated with a higher risk for haemorrhage in meningiomas are discussed. Though haemorrhages associated with meningiomas have been reported, ITH into low-grade meningiomas leading to herniation remains a rarity. Bearers of known lesions and their treating physicians who opt for conservative or delayed treatment should be aware of this remote complication.

Keywords: herniation, intratumoural haemorrhage, low-grade meningioma

Introduction

Intratumoural haemorrhage (ITH) is a rare complication of meningiomas that can occur spontaneously,^{1,2} after embolization,^{3,4} stereotactic radiation⁵ and perioperatively.⁶ Extratumoural types of haemorrhage, e.g. subdural, subarachnoid, intraparenchymal and intraventricular, have also been described.^{7–9}

We present briefly a case of hyperacute ITH into a previously undiagnosed convexity meningioma leading to symptoms of cerebral herniation. Factors associated with haemorrhage in meningiomas and implications for treatment will also be discussed.

Case report

A 50-year-old previously healthy male presented to the emergency room of the University of Heidelberg neurosurgical department. The patient was found in bed, unresponsive and hypertensive with anisocoria and gaze-deviation to the left. Brief neurological examination revealed a comatose patient with laboured spontaneous respirations. Pupils were fixed and dilated on the right, with sluggish reaction to light on the left. Best motor response was decorticate posturing (Glasgow coma scale score 4). Analgesic sedation (pentobarbital/ fentanyl) and intubation for airway protection was carried out promptly. Cranial computed tomography (CCT) revealed a large, right frontal spaceoccupying lesion with intratumoural haemorrhage. Strong contrast enhancement of the extra-axial, dura-based lesion with hyperostosis of the adjacent calvarium was characteristic of a meningioma. There was obvious midline shift of approximately 2 cm and effacement of basal cisterns with tentorial herniation and impending foraminal herniation (Fig. 1). During imaging the patient developed bilaterally fixed and dilated pupils and prompt transfer to the operating room was arranged for emergency decompression.

A right frontal craniotomy and dural incision was carried out along the non-infiltrated margins of the tumour. This was carefully enlarged along the superior sagittal sinus, where the tumour was partially mobilized in a blunt fashion. After complete microsurgical preparation, the $8 \times 10 \times 10$ cm tumour node was removed without major cortical adhesions. The underlying cortical surface was pulsatile, but remained clearly depressed. After watertight duroplasty with galea-periosteum and removal of reactive hyperostoses, the bone flap was reimplanted and secured with titanium clamps.

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FIG. 1. Unenhanced (left) and enhanced (right) CT demonstrating extra-axial localization, hyperostosis of the adjacent calvarium and intense contrast enhancement of the haemorrhagic right frontal lesion.

Pupils were checked, and found diminished in size and reactive to light.

Postoperatively all sedatives and analgesics were discontinued, the patient regained consciousness promptly without obvious focal-neurological deficits. He was extubated without problems. No tumour residual or haemorrhage were demonstrated on repeat computed tomography (CT) the following day.

Retrospectively the patient recalled occasional headaches, but no circumstances of seizure activity, nausea or vomiting in the past 2-3 months. No history of head trauma or previous exposure to radiation was elicitable. Past medical and surgical history, family history, medications and detailed review of systems were non-contributory. Haematological studies for occult bleeding diastheses was completed without pathological findings. Histopathological examination was confirmative of a microcystic meningioma with haemorrhagic infiltration (WHO level I; Fig. 2).

A pseudomeningocele resolved with repetitive percutaneous drainage. The patient was discharged home in excellent condition on hospital day 9.

Discussion

Meningiomas comprise approximately 20% of all primary intracranial neoplasms.¹⁰ The microcystic variant originally termed 'humid' due to its succulent and spongy macroscopic appearance is rare and accounts for 1.6% of all intracranial meningiomas.^{11,12}

According to the literature, the overall rate of haemorrhage in intracranial neoplasms ranges from 1.5 to 5.4%, metastases and gliomas being the most frequently involved.^{13,14} Meningiomas with haemorrhagic onset are rare, with incidences ranging from 0.5 to 2.4% of all meningeal neoplasms.^{1,14-16} Most cases of haemorrhage associated with meningiomas are extratumoural and subarachnoid, whereas subdural, intracerebral and intratumoural haemorrhage are reported less frequently.⁷⁻⁹

To the best of our knowledge (MEDLINEsearch) no other instance of a microcystic meningioma with haemorrhagic onset has been described in the English literature since its inclusion in the WHO classification in 1993.¹⁷ Microscopically, this variant has a stellate appearance through numerous cells with processes due to microcystic dilatation of the intercellular spaces. This pseudo-astrocytic appearance may be mistaken for astrocytoma.¹² The largest series of histologically proven microcystic meningiomas comprises a total of 11 cases, none of them associated with haemorrhage. The preoperative magnetic resonance (MR) signal characteristics (T1 very low and T2 very high) and enhancing pattern (either homogeneous or peripheral rim enhancement) were reviewed and found to be misleading in 4/11 cases (i.e. interpreted as either glioma or metastasis).¹⁸ In accordance with its spongy consistency, the computed tomography (CT) appearance of microcystic meningiomas is hypodense, almost mimicking brain oedema. Contrast enhancement, however, is marked in the majority of cases.¹⁹

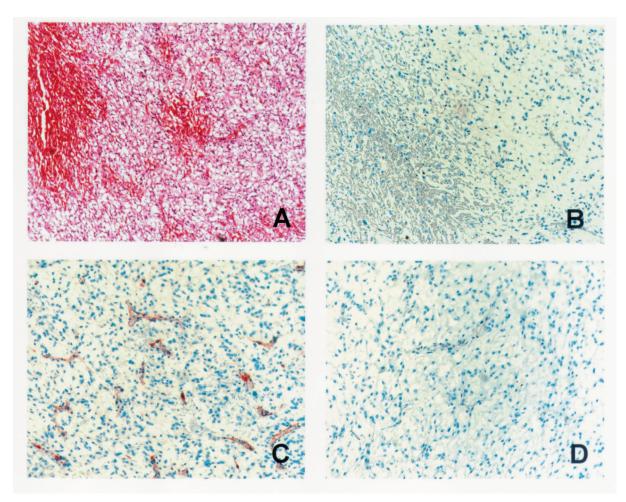


FIG. 2. Histopathological findings. (A) Haematoxylin-eosin stain shows a microcystic meningioma with haemorrhage (\times 100). (B) MIB-1 labelling index is low (< 5%), even in areas adjacent to haemorrhage (\times 100). (C,D) CD31 staining shows a dense capillary network with prominent CD31 expression in areas surrounding haemorrhage (C, \times 100) and a less dense vascularization in other tumour areas with an only slight endothelial expression of CD31 (D, \times 100).

Approximately 50% of all meningiomas grow along the calvarium, half of them parasagittally originating from the falx cerebri. Meningiomas are thought to arise from arachnoidal cells of the leptomeninges. Subtypes are histopathologically described as meningotheliomatous, metaplastic, fibroblastic, transitional, psammomatous, secretory, angiomatous, lymphoplasmacyte-rich and microcystic. According to the WHO-classification¹¹ these are all slow-growing, benign lesions (WHO level I). Nevertheless, aggressive growth into the adjacent bone and brain tissue is occasionally observed. Semibenign (atypical, clear-cell and chordoid) and semi-malignant (papillary, rhabdoid and anaplastic) variants with infiltrative growth, high rates of recurrence and metastasis do exist. Based on larger series of meningiomas with haemorrhagic onset both location and histological subtype are unrelated to the risk of bleeding.^{2,8,9} An increased rate of haemorrhage, however, was reported in 'angioblastic and malignant' meningiomas."

Besides their invasive properties, vascularization and the propensity to cause oedema are clinically important characteristics of meningiomas. Meningiomas are well vascularized tumours, as demonstrated by the 'tumour blush' on angiography. Increased vascularity of meningiomas as a predisposing risk factor for ITH, however, has been controversial.^{2,15,20}

Vascularity of meningiomas apparently depends on paracrine mechanisms of tumour cells. Both vascular permeability factor/vascular endothelial growth factor (VPF/VEGF) and (putatively) endothelins (ETs) have been shown to correlate with vascularity.²¹ Interestingly, VPF/VEGF is also proposed as a major factor in the formation of peritumoural brain oedema and cystic changes observed in certain meningioma subtypes.²¹ The given subtype of a microcystic meningioma is known to be highly vascularized and has been associated high expression of VPF/VEGF and its respective receptor.²² Others, however, have found VPF/VEGF not to be correlated with vascularity, but with higher malignancy grades.²³

In this case, immunolabelling of the endothelial cell marker CD31 was performed in the operative specimen to assess vascularity of the tumour.¹⁵ A dense capillary network with prominent CD31 expression was demonstrated in areas adjacent to

the haemorrhage, whereas other tumour areas exhibited only slight endothelial expression of CD31.

Immunohistochemistry of proliferation antigens like Ki-67 can be used to determine the 'growth fraction' of a population of cells. MIB-1 is the monoclonal antibody developed against the Ki-67 antigen. The Ki-67 antigen-expressing fraction ('MIB-1 labelling index') is therefore a surrogate of the mitotic rate within tumours. In our case, the MIB-1 labelling index was < 5%, which is considered indicative of benign behaviour.²⁴

Pathophysiological mechanisms underlying ITH are currently not well understood. Yet, several factors associated with haemorrhage in meningiomas have been described:

- The extent of vascularization, as an independent factor involved in haemorrhagic onset meningiomas, is still under debate, as discussed above.
- Atypical vessels, fragility and arachnoidal infiltration, seen in semi-benign or semi-malignant variants, seem to be associated with ITH more often.¹⁵
- Endothelial proliferation and tumour necrosis have been proposed risk factors of haemorrhagic transformation.^{7,20} Macroscopic cysts are thought to result from ischaemic necrosis and/or ITH. They are frequently associated with the microcystic variant found in this case.²¹
- Venous congestion secondary to infiltration and/ or compression of dural sinuses and bridging veins may lead to a higher propensity to bleed.²⁵
- Additionally, association with cerebrovascular malformations has been described and may be an independent factor for ITH in meningiomas.²⁶
- Haemorrhagic diastheses are putative precipitating factors,⁶ as are others (e.g. trauma, stress, hypertension), and are likely to increase the risk for ITH in any of the other circumstances.²

In the case presented above, a benign, microcystic variant meningioma was previously undiagnosed. Intraoperatively, no cerebrovascular abnormality was found nor was a bleeding diasthesis diagnosed subsequently. Therefore, we assume that an intrinsic vessel abnormality or ischaemic portion of the tumour gave rise to ITH. According to imaging characteristics this space-occupying lesion was large enough to critically impair intracranial compliance. Then, even small volumes of ITH could have caused a sudden increase in intracranial pressure with resultant compensatory arterial hypertension. This, in turn, would exacerbate any ongoing haemorrhage, finally leading to cerebral herniation. Despite sustained symptoms of cerebral herniation the patient achieved a good outcome. This could be tentatively explained by adaptation of the cerebral circulation to a slow-growing lesion and tapered loss of intracranial compliance, respectively. Then timing of operative decompression is certainly critical in every spaceoccupying lesion with symptoms of intracranial hypertension.

Conclusion

Haemorrhagic onset meningiomas remain rare and pathophysiology is still incompletely understood. Prevention and outcome of ITH highly depend on early diagnosis and adequate treatment. Even in cases of hyperacute ITH, patients may achieve a good outcome if rapid and radical evacuation is undertaken. Bearers of known lesions and their treating physicians who opt for conservative or delayed treatment should be aware of this remote complication.

References

- Modesti LM, Binet EF, Collins GH. Meningiomas causing spontaneous intracranial hematomas. *J Neurosurg* 1976;45: 437-41.
- 2 Martinez-Lage JF, Poza M, Martinez M, Esteban JA, Antunez MC, Sola J. Meningiomas with haemorrhagic onset. *Acta Neurochir (Wien)* 1991;110:129–32.
- 3 Kallmes DF, Evans AJ, Kaptain GJ, et al. Hemorrhagic complications in embolization of a meningioma: case report and review of the literature. *Neuroradiology* 1997;39:877-80.
- 4 Yu SC, Boet R, Wong GK, Lam WW, Poon WS. Postembolization hemorrhage of a large and necrotic meningioma. *Am J Neurol Res Am J Neuroradiol* 2004;25:506-8.
- 5 Kwon Y, Ahn JS, Jeon SR, et al. Intratumoral bleeding in meningioma after gamma knife radiosurgery. J Neurosurg 2002;97:657-62.
- 6 Gerlach R, Raabe A, Scharrer I, Meixensberger J, Seifert V. Post-operative hematoma after surgery for intracranial meningiomas: causes, avoidable risk factors and clinical outcome. *Neurol Res* 2004;26:61–6.
- 7 Helle TL, Conley FK. Haemorrhage associated with meningioma: a case report and review of the literature. *J Neurol Neurosurg Psychiatry* 1980;43:725-9.
- 8 Kohli CM, Crouch RL. Meningioma with intracerebral hematoma. *Neurosurgery* 1984;15:237-40.
- 9 Lefranc F, Nagy N, Dewitte O, Baleriaux D, Brotchi J. Intracranial meningiomas revealed by non-traumatic subdural haematomas: a series of four cases. *Acta Neurochir (Wien)* 2001;143:977-82.
- Rachlin JR, Rosenblum ML. Etiology and biology of meningiomas. In: Al-Mefty O, ed. *Meningiomas*. New York: Raven Press Ltd; 1991:27-35.
- 11 Kleihues P, Cavenee WK, eds. Pathology and genetics of tumours of the nervous system. WHO classification of tumours. Lyon: IARC Press, 2000.
- 12 Masson P. Les tumeurs humaines, 2nd edn. Paris: Maloine, 1956:977-88.
- 13 Licata B, Turazzi S. Bleeding cerebral neoplasms with symptomatic hematoma. J Neurosurg Sci 2003;47:201-10.
- 14 Kondziolka D, Bernstein M, Resch L, et al. Significance of hemorrhage into brain tumors: clinicopathological study. J Neurosurg 1987;67:852-7.
- 15 Niiro M, Ishimaru K, Hirano H, Yunoue S, Kuratsu J. Clinico-pathological study of meningiomas with haemorrhagic onset. *Acta Neurochir (Wien)* 2003;145:767–72.
- 16 Wakai S, Yamakawa K, Manaka S, Takakura K. Spontaneous intracranial hemorrhage caused by brain tumor: its incidence and clinical significance. *Neurosurgery* 1982;10:437-44.

- 17 Kleihues P, Burger PC, Scheithauer BW. *Histological typing of tumours of the central nervous system*, 2nd edn. Berlin: Springer, 1993.
- 18 Kim SH, Kim DG, Kim CY, Choe G, Chang KH, Jung HW. Microcystic meningioma: the characteristic neuroradiologic findings. *J Kor Neurosurg Soc* 2003;35:401-6.
- 19 Bromley PJ, Grymaloski MR, Zetler PJ. CT appearance of microcystic meningioma. J Comput Assist Tomogr 1996;20: 570-2.
- 20 Kim DG, Park CK, Paek SH, et al. Meningioma manifesting intracerebral haemorrhage: a possible mechanism of haemorrhage. Acta Neurochir (Wien) 2000;142:165-8.
- 21 Sanson M, Cornu P. Biology of meningiomas. Acta Neurochir (Wien) 2000;142:493-505.
- 22 Christov C, Lechapt-Zalcman E, Adle-Biassette H, Nachev S, Gherardi RK. Vascular permeability factor/vascular endothelial growth factor (VPF/VEGF) and its receptor flt-1 in microcystic meningiomas. *Acta Neuropathol (Berl)* 1999;98:414–20.
- 23 Lamszus K, Lengler U, Schmidt NO, Stavrou D, Ergun S, Westphal M. Vascular endothelial growth factor, hepatocyte growth factor/scatter factor, basic fibroblast growth factor, and placenta growth factor in human meningiomas and their relation to angiogenesis and malignancy. *Neurosurgery* 2000; 46:938–47.
- 24 Burger PC, Shibata T, Kleihues P. The use of the monoclonal antibody Ki-67 in the identification of proliferating cells: application to surgical neuropathology. *Am J Surg Pathol* 1986; 10:611–17.
- 25 Barua KK, Tamaki N, Ehara K, Nagashima T, Suzuki H. Spontaneous peritumoral haemorrhage associated with sinus confluence meningioma: case report. *Surg Neurol* 2000; 54:254–9.
- 26 Bitoh S, Hasegawa H, Kato A, Tamura K, Mabuchi E, Kobayashi Y. Meningeal neoplasms associated with cerebral vascular malformations. Surg Neurol 1987;27:469-75.

