Myxoid meningioma: a rare metaplastic meningioma variant in a patient presenting with intratumoral hemorrhage

Case report

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Myxoid (metaplastic) meningioma is a rare WHO Grade I meningioma subtype arising from the leptomeninges. It has unique Alcian blue stromal staining and distinctive cellular interdigitations, junctional complexes, and nuclear pseudoinclusions on ultrastructural pathology that help to distinguish it from other meningioma variants. The authors describe the case of a rare left middle fossa, extraaxial myxoid meningioma in a 50-year-old woman to emphasize the important histological characteristics and observations essential for making a precise diagnosis. To their knowledge this is the seventh reported case of a myxoid meningioma in the literature and the sixth case in an adult; however, it is the first reported instance of myxoid meningioma in a patient presenting with intratumoral hemorrhage. (http://thejns.org/doi/abs/10.3171/2011.12.JNS111020)

Key Words • myxoid meningioma • metaplasia • laminin • oncology • Type IV collagen • Alcian blue • matrix • nuclear pseudoinclusion

Myxoid (metaplastic) meningioma is a very rare and unusual WHO Grade I variant with unique histological characteristics that may be similar to and confused with higher-grade meningioma subtypes.4,11 We present the case of a myxoid (metaplastic) meningioma in a 50-year-old woman to highlight the important histological features and observations that are critical for making an accurate diagnosis. To our knowledge, there are 5 other reported cases of adult metaplastic (myxoid) meningioma, although none in the neurosurgical literature (Table 1).1,4,6,7 The present case is the first instance of a metaplastic (myxoid) meningioma in an adult presenting with symptomatic intratumoral hemorrhage.

Case Report

History and Examination. This 50-year-old woman presented with a 3-month history of progressive neurological decline, including worsening memory, ataxic gait, and right-sided weakness. Two days prior to her admission, headache and progressive somnolence developed. A CT scan of the head without contrast enhancement revealed a large hypodense mass located in the left middle fossa within the greater sphenoid wing with foci of hyperdensity suggestive of intratumoral hemorrhage. The lesion was exerting mass effect on the left temporal lobe, including the left lateral and third ventricles, with effacement of the suprasellar cistern and evident mass effect on the midbrain, thalamus, and left basal ganglia resulting in approximately 1 cm of midline shift (Fig. 1A). In addition, there was obvious hydrocephalus with dilation of the right ventricular system and transependymal flow due to CSF outflow obstruction. At her initial examination, the patient had a Glasgow Coma Scale score of 9 (V: 2; M: 5; E: 2). She was obtunded but aroused with vigorous stimulation, mumbling incomprehensible words and localizing with both arms.

On MR imaging, the tumor measured 6 × 6 × 4 cm and was located in the left middle fossa compressing the adjacent brain parenchyma. It had low signal intensity on T1-weighted images, with avid contrast enhancement and high signal intensity on T2-weighted images (Fig. 1B and C). The visible CSF vascular clefts and the tumor’s broad-based dural margin along the left anterior petrous surface on the coronal view were most consistent with an extraaxial, dural-based lesion, most likely representing a meningioma.

Abbreviation used in this paper: GTR = gross-total resection.
Operation. A left temporal craniotomy was undertaken, with thorough intradural exposure of the middle fossa floor. The left temporal lobe was gently retracted anterior to the vein of Labbé to gain access to the subtemporal region. The tumor was initially encountered just medial to the inferior temporal gyrus. Using microsurgical technique under an operating microscope, we meticulously dissected the tumor from surrounding brain parenchyma. It had a soft consistency with moderate vascularity, which allowed for an uncomplicated excision. Its main attachment as well as the vascular supply was in the region of the anterior petrous bone, as suggested by MR imaging. We were able to completely peel off the tumor from its tentorial attachment and remove the involved dura, achieving GTR (Fig. 1D). Intraoperative neuromonitoring with somatosensory evoked potentials and motor evoked potentials remained stable throughout the surgery.

Histological Evaluation. The frozen histological section showed spindle cells with oval nuclei, along with nuclear pseudoinclusions often seen in a tandem arrangement. There was moderate cellularity with no mitotic figures and no evident necrosis (Fig. 2A–C). The myxoid background stained strongly with Alcian blue (pH 2.5; Fig. 2D). Silver stain for reticulin fibers revealed small amounts of stainable material associated with the neoplastic cells (Fig. 3A). On permanent section, immunohistochemical staining revealed strong immunoreactivity for epithelial membrane antigen (Fig. 3B). There was nonspecific cytoplasmatic staining for S100 protein. The MIB-1 level was consistent with a low proliferation index. The ultrastructural cellular morphology of the neoplastic cells demonstrated extensive cellular interdigitations and desmosomal junctional complexes (Fig. 3C and D). A final diagnosis of myxoid (metaplastic) meningioma, WHO Grade I, was determined.

Postoperative Course. Because GTR was achieved, no adjuvant therapy was instituted. The patient’s postoperative course was uneventful, with rapid and complete resolution of her neurological deficits. Postoperative MR imaging with and without contrast showed complete resection with no evidence of residual tumor. The patient was discharged from the hospital 1 week after surgery, and at a routine follow-up 2 months after surgery she was completely neurologically intact.

Discussion

Metaplastic Meningiomas

Myxoid meningioma is rare type of metaplastic WHO Grade I tumor. The metaplastic tumor type encompasses a broad range of tumor subtypes depending on the mesenchymal differentiation involved. In addition to the myxoid type, osseous, cartilaginous, lipomatous, and xanthomatous subtypes are categorized in this group.9,13 These
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Meningeal tumors are referred to as “metaplastic” because their transformed neoplastic cells demonstrate the full histological characteristics of the cells they mimic. Hence, with lipomatous metaplastic meningioma, the adipocytes resemble true fat cells with their signet-ring appearance. The myxoid appearance in the myxoid type is attributable to the excessive presence of hyaluronic acid and chondroitin sulfate, which impart strong aqua blue staining when stained with Alcian blue at an acidic pH of 2.5. Hyaluronidase reduces the stain and therefore indirectly confirms the presence of hyaluronic acid within the matrix of these cells. There have been several reported cases of metaplastic meningioma in the literature, with the majority being xanthomatous and lipomatous types.

**Myxoid Meningioma: Histopathology and Ultrastructure**

Myxoid meningioma tumor cells are stellate in appearance, with an oval nucleus and scant eosinophilic cytoplasm. They often have a nuclear pseudoinclusion due to invagination of the cytoplasm into the nucleus. Cytoskeletonally, myxoid meningioma tumor cells lack immunoreactivity for laminin, an important structural protein that helps to maintain the integrity of the cells’ basement membrane. In addition, staining for Type IV collagen, a known component of a cell’s basement membrane, is intense within the extracellular myxoid stroma rather than within the cells. Interestingly, Kimura et al. noted the presence of granular pericellular deposits that immunostained for Type IV collagen with a complete lack of reactivity for laminin in a myxoid meningioma specimen from a 25-year-old man. From these findings, the authors concluded that the absence of laminin resulted in disassembly of the basement membrane and its subsequent dispersion in the form of eosinophilic granular bodies within the matrix, carrying the Type IV collagen remnants. It is likely that the problem rests with the lack of expression for laminin receptors affecting the production and assembly of laminin along the basement membrane. Another hypothesis proposes that the release of proteolytic enzymes may be responsible for the breakdown of laminin. However, this theory has little credibility for myxoid meningioma cells, since there is no evidence of antiinflammatory cells and macrophages, which are the source for the lytic enzymes.

Ultrastructurally, myxoid meningioma cells are typified by the presence of multiple interdigitating cell processes, junctional complexes, and desmosomes. The nuclear pseudoinclusion resulting from invagination of the cytoplasm into the nucleus is characteristic. The immunohistochemical profile of myxoid meningioma is similar to that of other meningioma types in that it shows reactivity for epithelial membrane antigen and vimentin with little nonspecific S100 reactivity.

The careful histological interpretation and extensive pathological workup, including immunohistochemical staining and evaluation of the ultrastructural morphology under electron microscopy, are essential in making an accurate diagnosis and differentiating “myxoid” metaplastic meningioma from higher-grade meningiomas with similar histological characteristics that may be associated with a worse prognosis. This scenario is well highlighted in the case of chordoid meningioma, a WHO Grade II meningioma.

**Fig. 2.** Photomicrographs (A–C) showing a myxoid, spindle cell neoplasm of moderate cellularity. The neoplastic cells exhibit oval to irregularly shaped nuclei with occasional nuclear pseudoclusions. No significant mitotic figures or tumor necrosis were identified. Photomicrograph (D) showing the myxoid background. H & E (A–C) and Alcian blue, pH 2.5 (D). Original magnification × 400.
gioma that also has a myxoid stroma but differs in cellular appearance and immunohistochemical reactivity. Unlike the myxoid metaplastic meningioma cells, chordoid cells are polygonal in shape with round nucleoli and abundant vacuolated cytoplasm. The cells are often arranged in a cord-like fashion rather than in tandem. Moreover, with myxoid meningioma we almost never see lymphocytic cell involvement. In rare instances, however, and mostly in the pediatric age group in association with Castleman disease, we may come across some lymphocytic cells with the chordoid type. All the aforementioned distinguishing characteristics are important in differentiating low-grade myxoid (metaplastic) meningioma from higher-grade chordoid meningioma. In our case, we resorted to a battery of histological tests to confirm our diagnosis and establish whether there was a need for further surveillance and treatment. Given the benign nature of myxoid (metaplastic) meningioma and the fact that we were able to achieve GTR, no further treatment was proposed.

Intratumoral Hemorrhage

To our knowledge this is the sixth reported case of a myxoid meningioma in an adult. Interestingly, the patient in our case had intratumoral hemorrhage on her presenting head CT scan, which is unusual for a meningioma. The exact pathogenesis of an intratumoral bleed in meningioma is still unclear, but hemorrhage may be caused by endothelial proliferation or vascular occlusion with distal necrosis or may result from the rupture of friable vascular channels. The aforementioned features of endothelial proliferation and the presence of hemorrhage usually signify a more malignant behavior that is atypical for benign meningiomas. According to previous studies, 1.3%-2.4% of meningiomas may bleed. In a large review of 143 previously reported cases of meningiomas in patients presenting with hemorrhage, Bosnjak et al. found 3 main factors associated with an increased propensity for hemorrhage in meningioma: intraventricular and convexity location, fibrous histopathology, and an age < 30 or > 70 years. Interestingly, these authors noted a trend toward an increasing number of anaplastic and anaplastic histopathological subtypes among the reviewed cases that did not reach statistical significance. They surmised that those more malignant histological subtypes might reach significance as more cases accrued. Our case did not exhibit any of the proposed features associated with an increased bleeding tendency. The histologically low-grade tumor was located along the petrous ridge in a 50-year-old woman. Our case illustrates the fact that patients with other benign nonfibrous meningioma subtypes may also present with hemorrhage and that our understanding of the histopathogenesis of intratumoral hemorrhage in meningiomas is still in its infancy.

Natural History

There are no known case series or retrospective cohort studies that help to shed light on the natural course of this disease and its anticipated prognosis. Given its low histological grade, this lesion is believed to carry a good prognosis with little chance for recurrence. Further clinical studies with long-term follow-up are still warranted, however.
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Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Couldwell. Acquisition of data: Krisht, Altay. Analysis and interpretation of data: Krisht, Altay. Drafting the article: Krisht. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Couldwell. Study supervision: Couldwell.

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