

Case Report

Myxopapillary ependymoma with anaplastic features: A case report with review of the literature

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Abstract

Background: Myxopapillary ependymoma (MPE) with anaplastic features is extremely rare, with only three case reports in the literature.

Case Description: We report the case of a MPE with anaplastic features in a 24-year-old female who presented with a dominant lumbar mass along with intracranial and sacral metastases. Upon gross total resection of the dominant tumor located at L2-L3, it appeared to arise from the filum terminale, and had a solid component in addition to soft or necrotic areas. Histologically, the tumor was composed of the two classic components of MPE: (1) low-grade ependymal cells surrounding blood vessels, producing the papillary appearance and (2) perivascular myxoid material between blood vessels and ependymal cells, creating the myxopapillary appearance. The high-grade anaplastic component showed hypercellularity, brisk mitotic rate, and vascular proliferation, with frequent pleomorphic cells and atypical mitotic figures. It was positive for vimentin and glial fibrillary acidic protein (GFAP); negative for epithelial membrane antigen (EMA), CAM5.2, creatine kinase 7 (CK7), CK20; and the MIB-1 index (Ki-67) was 8–38%. Ten months after initial resection, follow-up magnetic resonance imaging revealed new lesions in (1) the hypothalamus, (2) the left pons, and (3) the left medial temporal lobe, which were treated with radiosurgery. Eight months later (18 months from initial surgery), the patient underwent thoracic laminectomy for a large leptomeningeal metastasis at T6 and T8.

Conclusion: The present case of MPE with anaplastic features is the fourth case on record in the medical literature.

Key Words: Anaplastic ependymoma, myxopapillary ependymoma, myxopapillary ependymoma with anaplastic features

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INTRODUCTION

Ependymomas are primary central nervous system (CNS) tumors that arise from the ependymal cells lining the choroid plexus, the white matter adjacent to the angulated ventricles, and the central canal of the spinal cord. In the 2016 World Health Organization (WHO) classification of CNS tumors, ependymal tumors are divided into five major subtypes: myxopapillary ependymoma (MPE) and sub-ependymoma (grade I), classic ependymoma (grade II), RELA fusion-protein positive ependymoma (grade II or III), and anaplastic ependymoma (grade III).^[15]

MPEs are usually benign, slow growing gliomas that have been primarily described in the conus-cauda equina-filum terminale region, though rare occurrences in the cervico-thoracic spinal cord, lateral ventricle, and brain parenchyma have been reported.^[1,14,19,20,23]

Distant metastases to brain parenchyma and other organs have also been reported.^[8,12,13,16,18,21,22,24-26] They differ from other ependymomas morphologically and biologically, and frequently require immunohistochemical analysis in order to differentiate them from phenotypically similar chordomas or chondrosarcomas.^[20] Average age of presentation is 36 years, with a significant male predilection (2.2:1).^[17]

Anaplasia in ependymomas is usually defined by the presence of anaplastic features, such as hypercellularity, frequent mitotic figures, pseudopalisading necrosis, vascular proliferation, and cellular as well as nuclear pleomorphism.^[15] However, histologic criteria for the classification and grading of anaplasia in ependymomas has historically been and remains a contentious issue, which ultimately makes their diagnosis and prognosis subjective and difficult. These tumors are usually locally invasive, have a higher propensity to spread to other areas of the neuraxis via cerebrospinal fluid pathways, and have higher rates of tumor recurrence and decreased rates of survival.^[6,17]

We report the case of a MPE with anaplastic features in a 24-year-old female. Clinical, histopathological, and immunohistochemical findings are hereby described.

CASE REPORT

History and examination

A 24-year-old female presented with acute on chronic exacerbation of several months of back pain with new right radicular pain in the right thigh and lateral leg.

On physical examination, the patient was a well-developed, well-appearing young female in no acute distress. She did not have any cutaneous lesions, including axillary freckling, café au lait spots, or

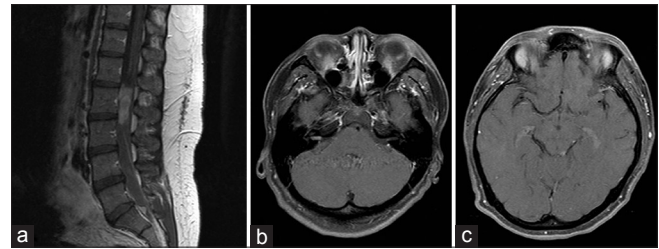


Figure 1: (a) Contrast enhanced sagittal T1-weighted magnetic resonance imaging demonstrates a homogeneously enhancing mass centered on L2-3 as well as a small sacra drop metastasis in the sacrum (arrowhead). Axial T1 contrast enhanced MRI demonstrates bilateral enhancement in the internal auditory canals, and a small enhancing focus was identified in the region of the left tectum (panels b and c, respectively)

cutaneous neurofibromas. Her neurologic examination was unremarkable with intact nerve function; similarly, her motor examination was unremarkable with 5/5 motor strength in all extremities.

Magnetic resonance imaging (MRI) of the lumbar spine with and without contrast demonstrated an enhancing mass occupying the majority of the spinal canal from L2-L3 [Figure 1a]. Because of the clinical impression of ependymoma, preoperative pan-imaging of the neuraxis was obtained, including MRI of the brain, cervical, and thoracic spine. These demonstrated additional lesions at the time of diagnosis, including bilateral internal auditory canal enhancement, a small focus of enhancement in the left tectum, and an apparent drop metastasis to the sacrum [Figure 1a-c].

Operation

A lumbar laminectomy at the level of L2-L3 was performed with gross total resection of the dominant lumbar tumor achieved. At surgery, the tumor appeared to be grossly necrotic, appeared to arise from the filum terminale, and had a solid component in addition to the soft or necrotic areas.

Histopathological examination

Low-grade areas of tumor [Figure 2a] have classic histology of ependymal cells surrounding blood vessels producing a somewhat papillary appearance. Perivascular myxoid material between the blood vessels and ependymal cells create the classic myxopapillary appearance.

High-grade anaplastic areas of tumor [Figure 2b] show hypercellularity, brisk mitotic rate, and vascular proliferation. Pleomorphic cells and atypical mitotic figures are frequently seen. The MIB-1 index is high. Immunohistochemical profile is as follows: Positive for vimentin and GFAP [Figure 2c]; Negative for EMA, CAM5.2, CK7, CK20 (not shown); MIB-1 index (Ki-67) 8–38% [Figure 2d].

The combination of areas of typical MPE-appearing tumor interspersed with areas of ependymoma with anaplastic or high-grade features was consistent with a diagnosis of MPE with anaplastic features.

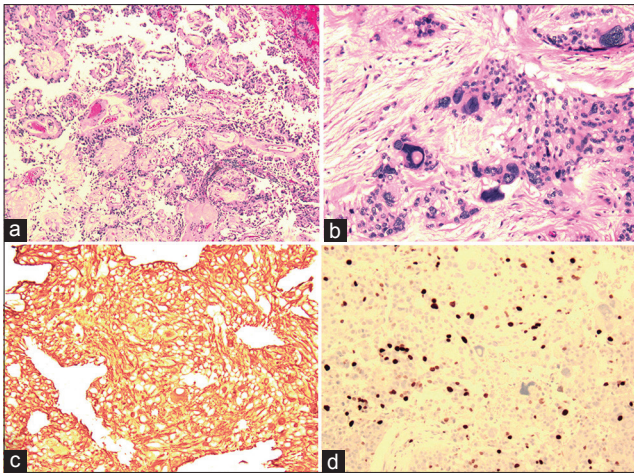


Figure 2: Low magnification view (panel a) demonstrating typical low-grade myxopapillary ependymoma including papillary appearance and fibrovascular cores. Other areas of tumor (panel b, shown under high magnification) demonstrate anaplasia and cellular atypia typical of high-grade tumor. Tumor specimen was diffusely positive for GFAP staining, indicating a neuronal differentiation, and demonstrated a high Ki-67 index (panels c and d, respectively)

Postoperative course

Postoperatively, the patient did well without any new neurologic deficits; bladder and bowel functions were intact, and the patient had full motor strength in bilateral lower extremities. Postoperative MRI confirmed gross total resection of the tumor.

Given the presence of anaplastic or malignant-appearing tumor on histopathology, and the presence of disseminated metastases at presentation, craniospinal radiation was recommended. However, the patient refused, and proceeded with external beam radiation to the tumor bed in the lumbar spine only. Initially, she refused any treatment for her cranial metastases, until progression of intracranial disease was documented on follow-up MRI. Again, the patient refused craniospinal radiation, opting for stereotactic radiosurgery to the growing lesions. Ten months after her surgical resection, the patient therefore underwent CyberKnife radiosurgery to five intracranial lesions: (1) the lesion in the hypothalamus, (2) the lesion in the right internal auditory canal, (3) a new left pontine lesion, (4) the left tectum lesion, and (5) a new left medial temporal lesion. The hypothalamic lesion was treated with a dose of 25 gray in 5 fractions, and the remainder of the lesions were treated in 3 fractions of 8 gray each. The patient was followed with serial MRIs every 3 months and again demonstrated progression of both intracranial and spinal disease. At 18 months postoperation from her initial surgery, the patient underwent thoracic laminectomy for a large metastasis at T6 and T8 [Figure 3]. At surgery, it was evident that multiple leptomeningeal metastases had coalesced into a larger tumor, however, there were also

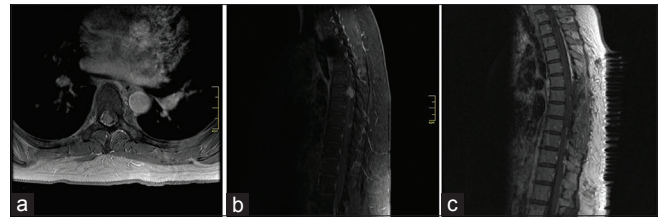


Figure 3: Axial and sagittal contrast enhanced T1-weighted MRI showing large enhancing mass within the thoracic spine causing compression of the thoracic spinal cord (a and b, respectively). Postoperative sagittal MRI demonstrates gross total resection of enhancing mass (panel c) MRI, magnetic resonance imaging

multiple additional leptomeningeal foci of disease noted. The patient was again referred for craniospinal radiation and/or potential chemotherapy.

DISCUSSION

MPE with anaplastic features is a rare occurrence, with only three case reports in the literature [Table 1].^[3-5] Similar to the previous three reports, the present case shows a dominant mass arising from the spinal column. However, widespread presence of metastases at diagnosis as well as rapid progression is noteworthy in our case. It is unclear as to why this present case had such aggressive progression of disease. The MIB-1 (Ki-67) index of 8–38% is similar to the previous three reports, two of which had no recurrence.

The immunohistochemical description of MPE has been reported, which consist of positivity for GFAP and vimentin, consistent with the present case.^[2,7,20]

Conventional MPE have a favorable overall survival, but despite their low-grade designation, almost half of all patients experience local recurrence (2–15 years after operation), irrespective of adequate excision.^[1,10,20] Recurrences can be accompanied with dissemination, with most metastases restricted regionally within the spine, although rare cranial metastases have been reported.^[1] Many of these patients can undergo salvage therapy with radiation. As a result, frequent surveillance scanning of patients with MPE is recommended to identify recurrent disease early.

The 5-year survival rate of patients with anaplastic ependymoma, on the other hand, has been reported to be less than 20%. Radiotherapy following partial excision is then recommended.

Grading of ependymoma is currently difficult and of questionable clinical utility under the current WHO guidelines.^[9] For anaplastic ependymoma specifically, Ho *et al.* had put forward a prognostic calculator based on a histopathologic score that takes into account mitoses ($\geq 4/10$ per high-power field), hypercellularity, endothelial proliferation, necrosis. They furthermore

Table 1: Clinical findings and outcomes in three previously reported cases of myxopapillary ependymoma with anaplastic features

Authors (reference)	Age (years)/sex	Location	Special aspect	Clinical presentation (duration if reported)	Treatment	Recurrence	MIB-1 (Ki-67)	Follow-up (months)	Survival (at last F/U)
Chakraborti <i>et al.</i> , 2012 ^[5]	11 months/F	Subcutaneous - sacrococcyx	-	Subcutaneous sacrococcygeal mass (1 month)	GTR + coccygectomy	6 weeks (pre-sacral deposit and inguinal lymph node metastasis)	4-70%	12	Alive
Beschorner <i>et al.</i> , 2007 ^[4]	3/M	Subcutaneous sacrococcyx	SGS, ependymoblastic features	Developmental delay, seizures, hypotonia, facial dysmorphism, bilateral inguinal hernia, bilateral cryptorchid testes, pelvic mass	GTR	No	40%	11	Alive
Awaya <i>et al.</i> , 2003 ^[3]	15/M	12 th thoracic to 2 nd lumbar spinal cord	-	Hip pain (7 months)	GTR	No	10.1%	18	Alive

SGS: Schinzel-Giedion syndrome, GTR: Gross total resection

proposed that anaplastic ependymoma could be diagnosed by the presence of two of those parameters.^[11] However, the classification of CNS tumors is moving toward a more molecularly oriented classification scheme, as reflected in the 2016 WHO classification of CNS tumors.^[15] So far, the RELA fusion-protein positive ependymoma is the only molecularly classified ependymoma. Determination of the RELA fusion-protein status in this present case was not feasible.

CONCLUSIONS

MPE is a benign tumor that has the potential for malignant degeneration. Although MPE is a WHO grade I tumor, cerebrospinal fluid metastases at the time of initial diagnosis is well reported. In contrast, other features of malignancy, including high-grade anaplastic histology, are rare, but when occurring is associated with an aggressive clinical course similar to that of nonmyxopapillary (high grade) ependymoma. The management of patients with myxopapillary ependymoma should take into account the possibility of malignant transformation/degeneration.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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