



Case Report

# A rare case of an intramedullary metastasis of a myxopapillary ependymoma

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## ABSTRACT

**Background:** Myxopapillary ependymoma (MPE) is a benign slow-growing tumor, and it has been designated histologically as a Grade I neoplasm according to the 2016 World Health Organization classification. Despite the benign character, dissemination and metastasis have occasionally been reported. The retrograde dissemination to other levels of the neuraxis is extremely rare, being more frequent to the intracranial compartment.

**Case Description:** We hereby present a case of medullary metastasis of cauda equina MPE, with a history of having undergone a subtotal resection and postoperative adjuvant radiotherapy. The patient presents complaints of night dorsal pain attributable to intradural metastasis twenty-one years after the first surgical intervention.

**Conclusion:** The case reported highlights the importance of long follow-up in patients with MPE, since the possibility of secondary seeding to distant craniospinal sites or local spinal sites after surgery, and radiotherapy should be considered in metastatic disease.

**Keywords:** Ependymoma, intramedullary, metastasis, myxopapillary

## INTRODUCTION

Myxopapillary ependymoma (MPE) was first described as a distinct subtype of ependymoma by Kernohaw in 1932.<sup>[11,16]</sup> MPE is characterized as a slow-growing tumor and classified as Grade I according to the World Health Organization (WHO).<sup>[15]</sup> This subtype accounts for 0.5% of all ependymomas, thus having an incidence of 0.01 per one million inhabitants.<sup>[20]</sup> It constitutes 13% of all spinal ependymomas and up to 90% of all conus medullaris tumors.<sup>[4]</sup> MPE is located almost exclusively in the conus medullaris, cauda equina, or filum terminale region and is rarely found as a multifocal type, with only little potential for dissemination.<sup>[2]</sup> No specific risk factors have been identified although associations with neurofibromatosis type 2 have been suggested.<sup>[20]</sup> The prognosis of MPE is very good, with overall 1-year and 10-year survival rates of 100% and 93%, respectively.<sup>[19]</sup> The treatment of choice is total surgical excision; however, local recurrence can occur in up to 15% of the cases being the major cause of therapeutic failure. The retrograde

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dissemination to other levels of the neuraxis is extremely rare, being described more frequently to the intracranial compartment.<sup>[13]</sup> We report a case of medullary metastasis of cauda equina MPE and present a brief review of the literature.

## CASE REPORT

A 43-year-old Caucasian male started experiencing progressive dorsalgia, including nocturnal pain, and progressive resistance to analgesic therapy. He had previously undergone lumbar spine surgery 21 years ago for MPE of cauda equina. A subtotal resection of the tumor was done and postoperative radiotherapy was performed with follow-up scans showing no evidence of residual lesion or any new lesion in the spinal cord. He reported no motor, numbness, bowel, or bladder dysfunction. The patient's actual neurological examination was normal with no pyramidal or cauda equina compression signs. Magnetic resonance (MR) imaging studies showed an intramedullary lesion with expansive features extending from D5 to D10. The lesion had a cranial cystic and a caudal solid component. After the injection of gadolinium, there was an intense homogenous enhancement of the solid component and several small pachymeningeal lesions throughout the dorsal region and filum terminale. MR studies of the brain and cervical spine showed no abnormality [Figures 1 and 2]. The patient underwent surgical resection under intraoperative neurophysiologic monitoring, including somatosensory evoked potentials and motor evoked potentials. Bilateral D8 and D9 laminectomies were done, and a large, vascularized tumor was encountered intramedullary. We performed a subtotal resection of the solid component because the patient presented a decrease of motor evoked potentials during tumor resection [Figure 3].

Histologically, the lesion was composed of cells with medium-sized, oval nuclei with finely granular chromatin and occasional intranuclear pseudoinclusions. Also well defined eosinophilic cytoplasm with microcystic inclusions and basophilic myxoid material under Alcian-Blue staining. There were frequent hyalinized vessels. No mitotic activity, necrosis, or vascular proliferation was observed. Neoplastic cells expressed glial fibrillary acidic protein and were negative for cytokeratin AE1/AE3 and EMA. Ki-67 proliferation index was inferior to 2%. A diagnosis of MPE was made (2016 WHO grade I).

The patient did not experience any new postoperative neurological deficits after surgery and he had an uneventful postoperative course. Adjuvant radiotherapy was planned after surgery.

## DISCUSSION

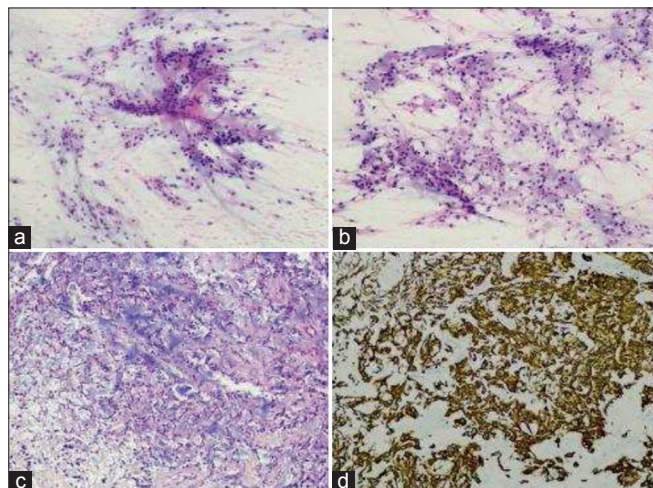
Ependymal tumors originate from ependymal cell rests and are uncommon central nervous system neoplasms with an incidence of 0.2/100,000 person-years and a slight predominance in men and Caucasians.<sup>[5,16]</sup> It has been described a slight upward trend over the past 35 years.<sup>[5]</sup> Ependymal tumors usually appear in the fourth decade of life, and in adults, 75% occur in the spinal



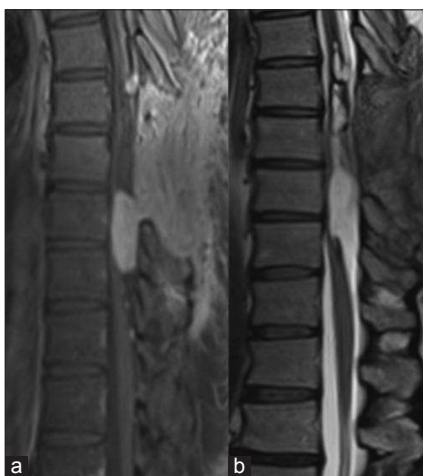
**Figure 1:** Preoperative magnetic resonance images (MRI). (a) Sagittal T1 sequence with gadolinium contrast showing an intramedullary lesion at D9–D10 level with homogeneous enhancement and several small dorsal implants. (b) Sagittal T1 sequence with contrast where there is no evidence of residual lesion in filum terminale of the first surgery. (c) Sagittal T2 sequence showing an intramedullary isointense lesion in D9–D10 level with hemosiderin focus. (d) Axial T1 MRI T1 with gadolinium contrast at D9 level where the lesion involves the whole spinal cord.

canal, making up 25% of intramedullary spinal cord tumors and 2% of primary central nervous system neoplasms.<sup>[3,6]</sup> No specific risk factors have been identified; however, associations with neurofibromatosis type 2, SV-40 polyomavirus exposure, and the lack of vitamin intake in the prenatal period by the mother have been suggested.<sup>[20]</sup>

Ependymomas are divided into three histological entities according to the 2016 WHO classification: ependymoma, subependymoma, and MPE.<sup>[14]</sup> Regarding their degree of malignancy and their histological appearance, the WHO defined three grades: MPE and subependymoma are Grade I lesions, the most benign in histologic appearance; Grade II ependymoma includes classic, cellular, papillary, clear cell, and tancytic subtypes, grouped together



**Figure 2:** Smears of the specimen showed a papillary pattern with myxoid background (a, H and E,  $\times 200$ ) and presence of globules of myxoid substance (b, H and E,  $\times 200$ ). The paraffin sections reflexed these findings, with a microcystic myxoid background (c, H and E,  $\times 200$ ) and intense glial fibrillary acidic protein (GFAP) expression (d, GFAP,  $\times 200$ ).



**Figure 3:** Postoperative magnetic resonance images. (a and b) Sagittal T1 sequence with gadolinium contrast and T2 sequence showing residual solid lesion in the lower portion of the tumor. Surgery was early terminated by the intraoperative decrease of the evoked potentials.

for their similar biologic behavior and Grade III are anaplastic ependymomas, which the most malignant behavior.<sup>[14]</sup> The grades differ between them in terms of tendency of recurrence, ease of surgical resection, and most usual locations within the spinal cord.<sup>[6]</sup> However, recent studies demonstrated that supratentorial location, younger age, genetic markers, and failure to achieve gross total resection may be more accurate predictors for prognosis than histologic grade.<sup>[17,18,22]</sup>

As already mentioned, 75% of ependymomas in the adult population occur in the spinal cord, and 50% of these lesions are MPE.<sup>[15]</sup> The conus medullaris and cauda equina region were identified as exclusive sites of MPE.<sup>[14]</sup> In the reported

case, the tumor was initially located at the cauda equina but then presented as a multifocal type at dorsal segment at time of progression. As a Grade I tumor, MPE is considered to be a slow-growing lesion with benign behavior. Despite these facts, recurrence after both subtotal and gross total resection is well documented.<sup>[9,12]</sup> Sonneland *et al.* reported a recurrence rate of 10% for completely resected tumors and 19% for subtotally removed or fragmented tumors, in a population of 77 cases with MPE.<sup>[21]</sup> Metastatic behavior has also been reported in the literature, with the intracranial compartment being the most frequent spread site. Metastases have been reported up to 20 years after initial treatment,<sup>[10]</sup> emphasizing the role for long-term follow-up in patients treated for MPE. Previously reports of drop metastases in pediatric and adult patients with MPE were reported,<sup>[8,9]</sup> being a well-established way of dissemination. A recent review by Chakraborti *et al.*<sup>[7]</sup> in 2012 described 19 cases with a variety of intracranial spread sites including the telencephalon, brainstem, and cerebellum, showing the tendency of MPE to spread rostrally in the central nervous system. Although dissemination to the intracranial compartment is well known, the same phenomenon is not established for spinal metastasis. To our knowledge, there are only three reports of secondary spinal dissemination, a single pediatric case, and two adults, described by Libório *et al.* in 2001.<sup>[13]</sup> These appear to be the only reports documenting spinal metastasis of an MPE. Our case is an additional report supporting the possibility of this extremely rare phenomenon.

Despite the benign histology and slow-growing nature of most MPE tumors, some behave in an aggressive manner, with local recurrence, primary seeding, and metastasis. In the management of these patients, radiation therapy and chemotherapy are a treatment option after surgery.<sup>[22]</sup> The gold standard first-line therapy for all spinal ependymomas is gross total resection, but when this resection is not possible, adjunctive radiotherapy is recommended.<sup>[6]</sup> Sonneland *et al.* found in an adult series that radiotherapy improves outcome in cases of subtotal resection or metastases.<sup>[21]</sup> However, this treatment efficacy is not clear in cases of gross total resection.<sup>[21]</sup> Fassett *et al.*, in 2005, describe progression of disease with local recurrence of metastatic behavior in patients treated with radiotherapy.<sup>[9]</sup> The explanation for this event is probably due to the localized treatment that would not prevent the spread of the disease, like in our case. Craniospinal irradiation can be considered for patients with disseminated or metastatic disease despite studies are few in number and report mixed results.<sup>[6]</sup> The role of chemotherapy is even clearer than radiation, and some studies suggest this treatment as salvage therapy for recurrence if both surgery and radiotherapy fail.<sup>[6]</sup> Histologically, MPE metastasis does not show features indicative of the malignancy,<sup>[1]</sup> and Ki-67 labeling indices have always been low,<sup>[7]</sup> like our case. Therefore, they cannot be used as predictive markers for disease progression.

## CONCLUSION

Neurosurgeons should be aware of the possibility of secondary seeding of an MPE to distant craniospinal sites or local spinal sites after surgery and should consider craniospinal imaging as part of preoperative workup and postoperative follow-up. Our case highlights the importance of long follow-up in patients with MPE. Although the limited data, radiotherapy should be considered in patients with metastatic disease.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his 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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