

Case Report

Pilomyxoid astrocytoma of the cerebellar vermis in an elderly patient

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Received: 12 October 13 Accepted: 25 November 13 Published: 27 February 14

This article may be cited as:

Skovrlj B, Pain M, Bederson JB, Fowkes M. Pilomyxoid astrocytoma of the cerebellar vermis in an elderly patient. *Surg Neurol Int* 2014;5:29.

Available FREE in open access from: <http://www.surgicalneurologyint.com/text.asp?2014/5/1/29/127968>

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Abstract

Background: Pilomyxoid astrocytoma (PMA) has recently been accepted as an aggressive variant of pilocytic astrocytoma with distinct histopathological features. PMAs have been frequently described in the pediatric population with a predilection for the hypothalamic/chiasmatic region.

Case Description: A 72-year-old African American male presented with 6 months of memory loss, difficulty expressing himself, and a progressively worsening gait. Magnetic resonance imaging of the brain demonstrated a heterogeneously enhancing cystic mass centered within the cerebellar vermis with mass effect on the fourth ventricle and ventriculomegaly. The patient underwent placement of a ventriculoperitoneal shunt followed by a surgical resection of the lesion, which after immunohistopathologic evaluation, was diagnosed as a World Health Organization grade II PMA. The patient refused further treatment of the lesion and expired 11 months after initial symptom presentation and 4 months after surgery.

Conclusion: To our knowledge, this is the first report of PMA of the cerebellar vermis in a previously unreported age group. This case report describes the natural history of this type of tumor in a patient who refused adjuvant therapy following surgical resection.

Key Words: Cerebellar vermis, elderly patient, natural history, pilomyxoid astrocytoma

Access this article online

Website:

www.surgicalneurologyint.com

DOI:

10.4103/2152-7806.127968

Quick Response Code:



INTRODUCTION

Pilomyxoid astrocytoma (PMA) represents a new clinical entity within neuro-oncology. First described in 1999, Tihan *et al.* identified a subset of 18 pilocytic astrocytomas with a distinctive pilomyxoid histological pattern as well as a higher recurrence rate than similar tumors with more classical pilocytic astrocytoma characteristics.^[15] The majority of tumors in this new

category occurred in infants and children and involved the hypothalamic/chiasmatic region. In contrast to the biphasic pattern, Rosenthal fibers and eosinophilic granules characteristic of pilocytic astrocytoma (PA), PMAs typically lack Rosenthal fibers and eosinophilic granules. PMAs are defined by their myxoid matrix with small, compact, piloid, and highly monomorphous cells arranged radially around blood vessels in a pattern that resembles the perivascular rosettes seen in

ependymomas.^[8] Because of these differences, PMAs are thought of as an aggressive variant of the classic pilocytic astrocytoma. As such, PMAs are classified as World Health Organization (WHO) grade II while pilocytic astrocytomas are assigned to the WHO grade I group.^[11]

To our knowledge, this is the first report of PMA of the cerebellar vermis in an elderly patient. Moreover, this case report describes the natural history of this type of tumor in a patient who refused additional medical treatment following surgical resection.

CASE REPORT

A 72-year-old male with a distant history of alcohol abuse presented with approximately 6 months of memory loss, difficulty expressing himself, and a progressively worsening gait. A magnetic resonance imaging (MRI) of the brain revealed a $2.5 \times 3.7 \times 2.5$ cm heterogeneously enhancing cystic mass centered within the cerebellar vermis with mass effect on the fourth ventricle and mild ventriculomegaly [Figure 1a and b] as well as an $8 \times 6 \times 4$ mm satellite lesion within the right superior cerebellar peduncle [Figure 1c and d]. On examination at an outpatient clinic, the patient had a slight expressive aphasia but was otherwise neurologically intact. At that time, the differential diagnosis of the lesion included primary glioma versus metastatic or granulomatous disease and the decision was made for surgical resection of the lesion.

Routine preoperative testing found the patient to be in rapid atrial fibrillation and he was sent to the emergency room. While undergoing evaluation of

the arrhythmia, his rhythm converted to a junctional bradycardia, necessitating placement of transvenous pacemaker. In the absence of other identifiable etiologies for his sudden bradycardia, his cardiac symptoms were attributed to intracranial hypertension secondary to the obstructive hydrocephalus caused by the vermian lesion. A computed tomography (CT) scan of the head revealed ventriculomegaly but no frank hydrocephalus and the patient was taken to the operating room for placement of a ventriculoperitoneal (VP) shunt. Intraoperatively, he was found to have elevated intracranial pressure. His postoperative course was notable for immediate resolution of the cardiac arrhythmia.

Two days following placement of the VP shunt, the patient underwent a suboccipital craniectomy for resection of the cerebellar lesion. Intraoperatively, the lesion was found to be soft and mildly vascular with clean margins relative to the surrounding brain. Pathology specimens were sent for frozen histological analysis and were thought to be most consistent with a diagnosis of glioma. A postoperative MRI revealed a subtotal resection of the lesion. Permanent section of the lesion demonstrated a glial neoplasm composed of astrocytes with elongated, bipolar cytoplasmic processes, forming fascicles and focally, loose perivascular patterns, dispersed within an abundant myxoid background [Figure 2a and b]. The tumor cells had round to irregular, hyperchromatic nuclei, with prominent perinuclear halos infiltrating the molecular layer of the adjacent cerebellar folia. They were strongly immunoreactive for GFAP and WT-1 with a MIB-1 labeling index of greater than 5% [Figure 2c and d]. The lesion was diagnosed as a WHO grade 2 PMA. Postoperatively, the patient did well

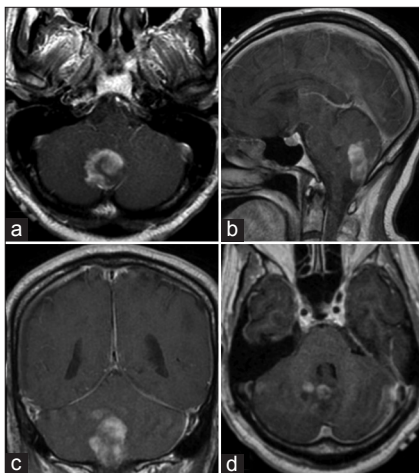


Figure 1: Preoperative (a) axial and (b) sagittal T1-weighted contrast enhanced magnetic resonance imaging demonstrating a $2.5 \times 3.7 \times 2.5$ cm heterogeneously enhancing cystic mass centered within the cerebellar vermis causing marked mass effect on the fourth ventricle. Preoperative (c) coronal and (d) axial T1-weighted contrast enhanced magnetic resonance imaging demonstrating an $8 \times 6 \times 4$ mm satellite lesion within the right superior cerebellar peduncle

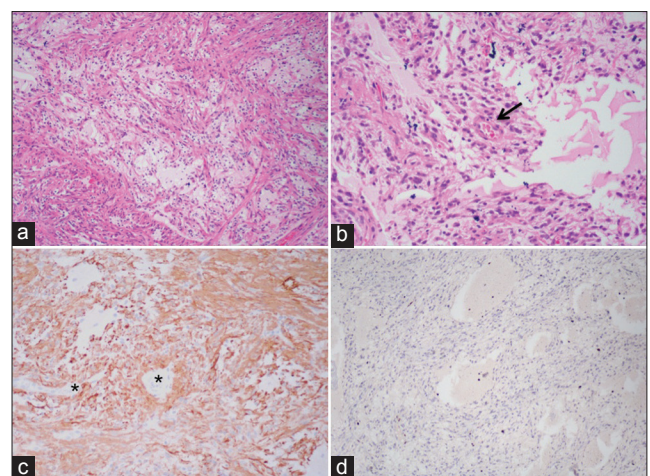


Figure 2: Specimen resected at surgery demonstrating: (a) piloid tumor cells within a myxoid background (hematoxylin and eosin, $\times 10$); (b) tumor cells with a perivascular orientation, lack of Rosenthal fibers identified (arrow) (hematoxylin and eosin, $\times 20$); (c) nonreactive blood vessels surrounded by reactive tumor cells (glial fibrillary acidic protein (GFAP), $\times 20$); (d) tumor cells with low proliferative index (Ki-67 (MIB-1), $\times 10$)

and was discharged to the inpatient rehabilitation service on postoperative day 4 and discharged home 12 days later with residual dizziness and gait imbalance. Following discharge, the patient refused further medical or surgical treatment. His neurologic status and overall health gradually deteriorated and he expired 11 months after initial symptom presentation and 4 months after surgery.

DISCUSSION

PMA has been recently described and accepted as a more aggressive variant of classical PA. Although both the PAs and PMAs present throughout childhood and can occur anywhere in the neuraxis, PMAs have a predilection for the hypothalamic region and tend to afflict very young children.^[1,3,7] The mean age at diagnosis for patients with PMA is 18 months, compared with 58 months for patients diagnosed with PA.^[7] There are very few reports of PMA in adults described in the literature,^[2,4-6,10,12,14,16] and only one with a lesion in the posterior fossa.^[9] To date, there have been no reports of PMA arising from the cerebellar parenchyma in an elderly person.

Clinically, PMAs have been shown to behave more aggressively than PAs. Komotar *et al.*^[7] compared the long-term outcomes for 21 patients with hypothalamic PMAs with the outcomes in 42 patients with PAs in the same location with a mean follow-up of 26 months. They found that patients with PMA had a higher rate of local recurrence than those with PA (76% and 50%, respectively). They also noted that the PMA group had a 14% tumor dissemination rate into the cerebrospinal fluid while this was not reported in a single patient in the PA group. More importantly, patients with PMA demonstrated significantly shorter progression-free (mean duration 26 and 147 months for those with PMA and PA, respectively; $P < 0.001$) and overall (mean duration 63 and 213 months, respectively; $P < 0.001$) survival times than those with PA. When matched for age, patients with PMA continued to exhibit significantly shorter progression-free and overall survival times than those with PA. The study also demonstrated that 33% of patients with PMA died of their disease, compared with 17% of those with PA.

There is currently no consensus on the standard of care for the management of PMAs. At present, PMAs are managed in a similar manner to PAs. Gross total resection (GTR), when possible, is the primary treatment strategy. GTR has been demonstrated to be the most reliable predictor of outcome in children with low-grade gliomas when surgery can be performed without excessive morbidity.^[17] Adjuvant therapy, either chemotherapy or radiotherapy, is instituted if tumor recurs following GTR, neurologic deficits remain following subtotal resection and in cases of subtotal resection with evidence of tumor growth on postoperative imaging, even in the absence of symptoms.^[13] With less

than a dozen reported cases of PMA in adults, there is no level 1 evidence to guide management of PMA in this population. Instead, recommendations are based on experience and expert opinion derived from individual cases published in the literature. In one center, unless GTR is achieved, adjuvant chemotherapy is started immediately after surgery, without waiting for tumor growth or recurrence and concomitant radiotherapy is recommended in adult patients.^[13] In cases of refractory or disseminated PMA, some authors recommend the use of tyrosine kinase inhibitors as an alternative treatment.^[9] As more cases of PMA emerge and clinicians gain more experience with PMA in the future, more definitive guidelines are certain to emerge.

CONCLUSION

To our knowledge this is the first report of PMA presenting in the cerebellum of an elderly patient. Our patient underwent subtotal surgical resection of the lesion and refused postoperative adjuvant therapy. He died from complications secondary to disease progression 11 months after initial diagnosis and 4 months following surgery. This report outlines the occurrence of PMA in the adult population and emphasizes the need for aggressive postoperative adjuvant therapy in adults with subtotal tumor resection. The current treatment recommendations based on a small sample of case reports suggests that aggressive surgical resection followed by adjuvant therapy with either chemotherapy and/or radiation therapy should be tailored to individual patients based on their age and disease characteristics.

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