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Case Report

Single-Agent Carboplatin for a Rare Case of Pilomyxoid Astrocytoma of the Spinal Cord in an Adult with Neurofibromatosis Type 1

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Keywords

Spinal cord tumor · Astrocytoma · Pilomyxoid astrocytoma · Neurofibromatosis type 1 · Carboplatin

Abstract

Introduction: Pilomyxoid astrocytoma (PMA) is a rare and more aggressive variant of pilocytic astrocytoma, which usually affects young children and is most often located in the hypothalamic/chiasmatic region. The association of PMA with underlying genetic disorders is not well known. ***Methods:*** We identified a 23-year-old woman with a PMA of the spinal cord who was simultaneously diagnosed with neurofibromatosis type 1. Diagnosis of neurofibromatosis type 1 was made clinically and confirmed with genetic testing that revealed a heterozygous one-amino-acid deletion (c.2970–2972 delAAT) in exon 17 of the NF1 gene, which is correlated with a milder phenotype. The patient underwent a partial surgical resection of the spinal cord tumor followed by adjuvant carboplatin 560 mg/m^2 every 4 weeks. Radiation was avoided due to risks associated with neurofibromatosis type 1. ***Results:*** At the 11-month follow-up, the patient maintained a partial radiographic response as well as complete resolution of her neurologic deficits. ***Conclusion:*** To our knowledge, this is the first reported case of an adult patient with neurofibromatosis type 1 and a spinal cord PMA. Single-agent carboplatin was effective and well-tolerated.

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Introduction

Pilomyxoid astrocytoma (PMA) is a rare primary central nervous system tumor that shares characteristics with pilocytic astrocytoma (PA) and was first described in the 1990s. In 2007, it was recognized by the World Health Organization (WHO) as a distinct astrocytoma variant and was designated a WHO grade II. However, due to considerable overlap with PAs, the updated 2016 WHO guidelines have retracted designation of a specific grade until more information is obtained regarding their behavior [1]. PMAs can be distinguished from classic PAs due to their monomorphous appearance, myxoid background, angiocentric patterning, paucity of Rosenthal fibers and rare eosinophilic granular bodies, as well as a tendency to be more aggressive [2]. PMAs most often occur in very young children and are frequently located in the hypothalamic/chiasmatic region and are only rarely found in the spinal cord. The association of PMA with neurofibromatosis 1 (NF1) is even less common. Here, we report a unique case of a spinal cord PMA in an adult patient with NF1 and discuss the relevant literature.

Case Report

A 23-year-old Caucasian woman with a 12-year history of severe scoliosis and migraine headaches presented to her primary care physician with complaints of an acute onset of back pain and numbness in her lower extremities followed by progressive gait difficulty over several days. Spinal magnetic resonance imaging (MRI) was obtained and revealed an intramedullary T1–T12 enhancing lesion with cystic changes (fig. 1). The patient was referred to our institution for surgery, and a T4–T8 laminectomy was performed with subtotal excision of the lesion. Grossly, the tumor was soft, almost mucoid-like and had extremely large blood vessels. Microscopic analysis revealed a low-grade glioma with prominently thickened blood vessels, rare Rosenthal fibers, abundant myxoid areas, and low Ki-67 labeling index, consistent with a diagnosis of PMA (WHO grade I–II) (fig. 2). Isocitrate dehydrogenase 1 mutation and BRAF:KIAA 1549 fusion were not detected.

The patient presented to our clinic for consultation. Postoperatively, she experienced persistent numbness in her lower extremities and mild back pain but with improvement of her gait. Upon further history taking, we learned that the patient suffered from failure to thrive during infancy, had recurrent infections throughout childhood and a mild developmental delay. Pertinent physical examination findings included a subtle speech impediment, mild hypertelorism, and short stature. Multiple café-au-lait macules were noted on the patient's trunk and proximal bilateral lower extremities, along with inguinal freckling. Neurologically, the right lower extremity was mildly weak and had reduced pin prick sensation, while the left lower extremity had diminished vibratory sensation. An initial clinical diagnosis of NF1 was corroborated by further genetic analysis, which revealed a heterozygous one-amino-acid deletion in exon 22 in the NF1 gene (c.2970_2972delAAT). The patient was then treated with intravenous carboplatin 560 mg/m^2 administered every 4 weeks. At the 11-month follow-up, the patient maintained a partial radiographic response and had returned to her neurologic baseline.

Discussion

This case depicts an unexpected presentation of an already rare primary central nervous system tumor. Notably, the patient is an adult, significantly older than the average age of PMA diagnosis. Additionally, the tumor's location in the spinal cord rather than in the diencephalon is also remarkable. Furthermore, the patient was also found to have NF1, a condition that predisposes patients to the development of certain tumors such as neurofibromas, optic pathway PAs, and malignant peripheral nerve sheath tumors, but not typically PMAs.

In reviewing the literature, we found 10 other reported cases of spinal cord PMAs, which are summarized in table 1. These cases varied widely according to age, spinal cord location and outcome [3–10]. In these cases, various treatment regimens were administered and often involved combinations of surgery, radiotherapy, vincristine and/or platinum-based chemotherapy with mixed success rates. Another observation is that in contrast to the more common diencephalic PMAs, spinal cord PMAs tended to not have such a young age predilection.

Additionally, we identified two accounts of PMA in the setting of NF1. In the first example, Khanani et al. [11] described a 9-year-old girl who presented with signs of increased intracranial pressure and was found to have obstructive hydrocephalus secondary to a third ventricular PMA diagnosed via partial resection. She was treated with weekly vincristine and carboplatin and showed good clinical and radiographic response. In the second instance, Jiménez et al. [12] also report a 9-year-old girl with NF1 who was diagnosed with PMA within the left lateral ventricle. With regard to NF1 in our case, another noteworthy feature is that the patient's particular NF1 mutation is not frequently encountered and unlike many NF1 mutations that cannot reasonably predict phenotypic severity, this mutation is generally correlated with a mild clinical manifestation, including absence of plexiform neurofibromas [13].

Unfortunately, due to the low incidence of spinal cord PMAs, clinical trials and treatment recommendations are lacking. Furthermore, another therapeutic challenge encountered in our case was due to the patient's new NF1 diagnosis. Because the patient has NF1, our goal was to avoid radiotherapy due to the propensity for NF1 patients to develop malignant peripheral nerve sheath tumors and other secondary malignancies following radiation [14]. However, less is known about the impact of radiotherapy on patients with the c.2970_2972delAAT NF1 mutation. Our decision to treat the patient with carboplatin was extrapolated from a phase II study that evaluated carboplatin for pediatric patients with low-grade glioma. This study demonstrated a 3-year overall survival of 84% and a subgroup analysis found that NF1 patients had even significantly superior outcomes [15].

In summary, this report supports a link between PMA and NF1 as well as contributes to our knowledge of PMA in the spinal cord. Even though PMA is considered similar but more aggressive than classic PA, its behavior and sensitivity to treatment in NF1 patients is not yet known. Further reporting is thus imperative to characterize this tumor in the setting of NF1 in order to better define successful management.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

Dr. Dunn-Pirio, Ms. Howell and Dr. McLendon declare no conflicts of interest. Dr. Peters participates on the advisory boards of Agios and Novocure and receives research support for Agios, Amgen, Eisai, Genentech and Merk.

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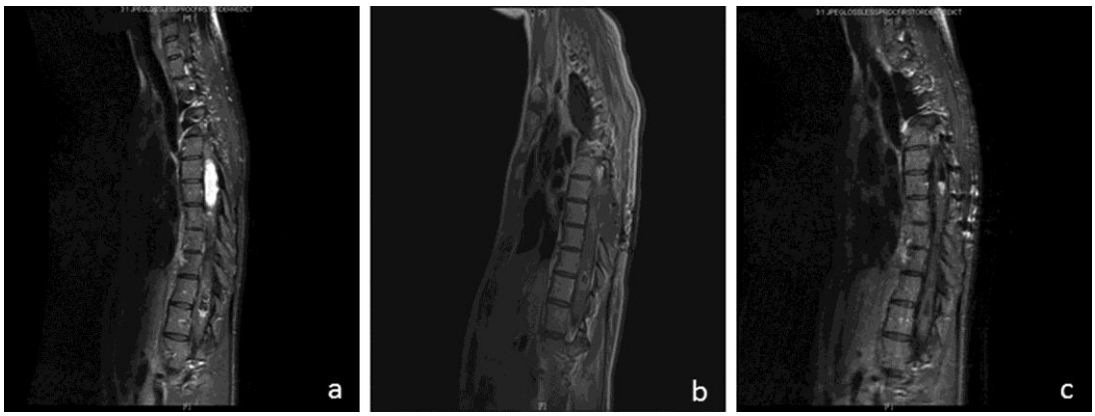

Fig. 1. Sagittal T1 with gadolinium thoracic MRI depicting PMA. **a** One month before partial resection. **b** Immediately postoperatively. **c** Nine months after initiating chemotherapy.

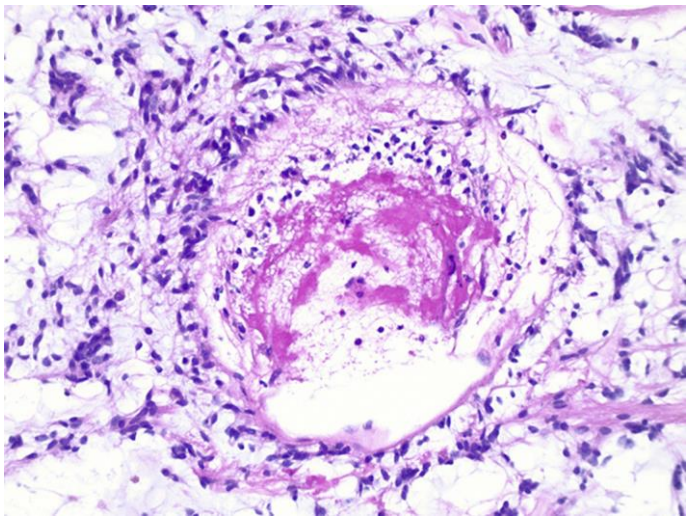

Fig. 2. H&E pathology image depicting a low-grade glioma with a monotonous, myxoid appearance and angiocentric patterning.

Table 1. Summary of spinal cord PMA cases

Age	Gender	Tumor location	Surgery	Adjuvant treatment	Outcome	Reference
23 years	female	thoracic	STR	carboplatin	maintained a PR at 6-month follow-up	Our case
40 years	female	thoracolumbar	STR	RT	at 3-year follow-up, no evidence of tumor regrowth	Wu et al. [3]
11 years	male	thoracic	near-total resection	RT; the plan at the time of report was to treat with carboplatin and vincristine	14 months after surgery had tumor recurrence; initially had good response to RT but six months later, tumor recurred again	Garber et al. [4]
12 years	female	cervical	initial GTR then had STR after progression	vincristine, etoposide and carboplatin following STR	12 weeks following GTR developed a rapid progression, which led to STR and histological analysis showed transformation to a GBM; died 1 year after initial diagnosis	Paraskevopoulos et al. [5]
15 months	female	cervical	STR	cisplatin and etoposide	CR even at 64 months	Matsuzaki et al. [6]
45 years	female	cervical	biopsy	RT	quickly developed tetraparesis and died of respiratory compromise	Sajadi et al. [7]
13 years	female	cervical	biopsy and VP shunt	vincristine and carboplatin; radiation	2 years after diagnosis had PD, and then treated with RT; 1 year after RT, developed peritoneal metastasis (likely from the shunt) and entered hospice	Arulraja and Huisman [8]
29 years	female	intradural, extramedullary cervical-lumbosacral	STR	RT	outcome not documented	Mendiratta-Lala et al. [9]
6 years	male	cervicothoracic	initial laminectomy and STR; required further laminectomies for cyst decompression and recurrent disease	RT and chemotherapy after recurrences	several weeks after surgery, developed sudden weakness in the lower extremities and MRI showed new cystic lesion in the conus medullaris requiring laminectomy for cyst decompression; neurologic symptoms did not improve with multiple cyst decompressions and required radiation therapy; did well for 2 years following RT, then developed a cervicomedullary cyst resulting in addition surgery followed by chemotherapy; at 5-year follow-up, neurologically stable and with residual enhancement	Komotar et al. [10]
8 years	male	thoracic	GTR		at 9-month follow-up, neurologically stable but concern for new enhancement and continued to be monitored off therapy	Komotar et al. [10]
3 weeks	male	holocord, as well as leptomeningeal enhancement at the medulla	biopsy and laminectomy		stable disease at 3.5 years but with significant disability	Komotar et al. [10]

CR = Complete response; GTR = gross total resection; PR = partial response; RT = radiation therapy; STR = subtotal resection; VP = ventriculoperitoneal.

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