Pilomyxoid astrocytoma (PMA) is a rare, aggressive myxoid variant of pilocytic astrocytoma. In 2007, PMA was recognized as a variant of astrocytoma and classified as WHO Grade II. Typically, PMAs present in the suprasellar/hypothalamic region, although they have been reported throughout the neuraxis. These tumors represent approximately 1% of all astrocytomas, whereas 85% of pediatric astrocytomas are pilocytic (WHO Grade I) in nature. Pilocytic astrocytomas tend to present in slightly older children (mean age 6 years), but PMAs are largely seen in children younger than 4 years, with a median age at diagnosis of 18 months. In contrast, low-grade infiltrating astrocytoma, also classified as WHO Grade II, has a peak incidence at 20–45 years.

Optimal treatment strategies for PMAs are still being elucidated, but as with other primary CNS tumors, treatment options may vary considerably depending on tumor location. The surgical goal in treating intramedullary spinal cord tumors is maximal resection without compromising neurological function. Postoperative radiation therapy, chemotherapy, or both are administered in many cases, with either single-agent (carboplatin) or multiagent (carboplatin and vincristine or carboplatin and etoposide) platinum-based regimens.

Pilomyxoid astrocytomas were first reported in 1999 by Tihan et al., who described an intracranial glial tumor similar to a pilocytic astrocytoma but with distinct histopathological characteristics and more aggressive clinical behavior. It was not until 2005, however, that this lesion was reported to occur in the spinal cord as well. To date there have been fewer than 10 cases of spinal PMA reported in the pediatric literature. Even more rare is the presence of extraneural lesions, of which only 1 case has been reported.

We review the case of a previously healthy 11-year-old boy with back pain and rapidly progressive scoliosis who was found to have a thoracic spinal cord PMA. Magnetic resonance imaging of the thoracic spine also revealed multiple bilateral parenchymal and pleural lung nodules at the time of initial diagnosis. We review the existing literature describing PMAs to gain a better understanding of these rare lesions. Because of the small number of cases optimal treatment guidelines have not been established, but gross-total resection and adjuvant chemotherapy with alkylating agents appear to confer a better long-term prognosis. Pediatric patients with PMAs can remain recurrence free at least 5 years after surgery, although these tumors may disseminate or dedifferentiate into more malignant gliomas. Recognition of intramedullary PMA as a unique entity in children is vital to the development of specific surgical and adjuvant treatment regimens.

Case Report

**History and Presentation.** This 11-year-old boy was seen in an outpatient orthopedic clinic for the onset of scoliosis over the preceding year. The patient reported occasional back pain but was otherwise neurologically intact. A standing anteroposterior radiograph of the spine revealed an atypical right thoracolumbar curve measuring...
approximately 43°. An MRI scan of the thoracic spine was obtained for further evaluation, and an intramedullary, enhancing spinal cord tumor was discovered spanning the T5–10 levels (Fig. 1). There was a nonenhancing fluid collection superior to the enhancing portion of the lesion, which was thought to be an associated thoracic spinal cord syrinx. Multiple enhancing nodules in both lungs were also seen on the thoracic spine MR images, raising suspicion for extraneural metastatic disease (Fig. 2).

Operation. Our surgical approach was a T5–11 laminoplasty with an ultrasound-guided midline dorsal myelotomy. Analysis of an intraoperative frozen section was consistent with a low-grade astrocytoma; aggressive resection was pursued based on this finding. Neurophysiological monitoring including somatosensory and motor evoked potentials remained at baseline throughout the procedure. Postoperatively, the patient had some decreased motor strength in his lower extremities, with the left leg (4/5) more involved than the right (5+/5). Findings on MRI studies of the thoracic spine obtained on postoperative Day 1 were consistent with a near-total resection (Fig. 3).

Histological Evaluation. Final pathological analysis indicated that the tumor was consistent with a WHO Grade II PMA. Histologically the tumor was found to be hypercellular, with a myxoid background, rare mitotic figures, and several focal areas of increased vascularity (Fig. 4). There was no evidence of necrosis or hemorrhage, and no Rosenthal fibers or eosinophilic granular bodies were seen on permanent sections. The patient was taken for a CT-guided lung biopsy approximately 3 weeks after the initial surgery, but complete resolution of his previously noted bilateral lung nodules was seen on CT scans and the biopsy was abandoned. This finding suggested a postinfectious or inflammatory cause of the patient’s lung nodules, although rapid regression after primary tumor removal and postoperative steroid administration is also a possibility. The patient was discharged home soon afterward with plans to reserve adjuvant therapy in favor of radiographic surveillance.

Postoperative Course. Fourteen months later the patient presented with worsening scoliosis, and MRI sequences demonstrated a significant recurrence (Fig. 5). After extensive discussion at the meeting of the tumor board, radiation therapy was recommended and he completed a 4-week course of involved-field radiation therapy. Over the 4-week treatment period, the patient received 22 fractionated doses of 180 cGy to his thoracic spine as well as 4 sessions of boost therapy (180 cGy per session). The radiation was tolerated extremely well; the only side effect was a mild sore throat. Given the patient’s older age (> 10 years) and the desire for a rapid response, chemotherapy was deferred in favor of radiation treatment. Unfortunately, an MRI study performed approximately 6 months after the completion of radiation treatment again showed recurrence in the resection cavity, and the patient is now planning to undergo dual-agent chemotherapy with a carboplatin and vincristine–based regimen.

Discussion

This case demonstrates a rare example of a pediatric spinal intramedullary PMA. Because of the rarity of this diagnosis, particularly in the spine, PMA was not included on our initial differential diagnosis for this lesion. However, PMA should be included on the list of possibilities for an intramedullary spinal cord mass, particularly in pediatric patients. Our goal in reviewing this case was to outline the presentation, natural history, and variably aggressive nature of this disease, and the treatment options available for this rare spinal cord lesion.

Previous Case Reports

A literature review of the PubMed database performed using the key words “pilomyxoid,” “astrocytoma,” “pediatrics,” “children,” and “spinal cord” identified 4 papers published between 2005 and 2011 (Table 1).
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1) Komotar et al. described a series of 3 male pediatric patients with diagnoses of intramedullary spinal PMAs; the patients ranged in age from 3 weeks to 8 years. Presenting symptoms included back pain and scoliosis in the older patients, and a flaccid left arm and hypotonic lower extremities in the neonatal patient. The tumors were located in the lower thoracic spine in the 2 older patients, and throughout the entire spinal cord, with enhancement of the fourth ventricle and medulla, in the neonate. The patients underwent thoracic laminectomy for exploration, biopsy, and partial resection or GTR. All patients were still alive at follow-up ranging from 9 months to 5 years; however, the 6-year-old patient had undergone 6 subsequent resections for symptomatic tumor recurrence as well as chemotherapy and radiation. The other 2 patients were monitored with serial imaging. The 8-year-old patient who underwent GTR of his tumor remained neurologically intact without evidence of disease recurrence.

Arulrajah and Huisman reported an intramedullary spinal PMA with CSF and extraneural dissemination in a 13-year-old girl who presented with headaches, papilledema, lethargy, and neck pain. The MRI sequences of the brain and spine revealed hydrocephalus and a mass in the cervical cord spanning C2–7, with multiple areas of intracranial enhancement. Histological findings from a biopsy were consistent with a PMA. Ventriculoperitoneal shunt placement was required for treatment of her symptomatic hydrocephalus. The patient then underwent induction and maintenance chemotherapy with vincristine and carboplatin. Craniospinal irradiation was initiated after 2-year follow-up imaging revealed diffuse leptomeningeal disease. Three years after her initial presentation, the patient was readmitted with urosepsis and abdominal pain, and a diagnosis of peritoneal seeding (presumably from her shunt) was made. After extensive family discussion, the patient was discharged home with hospice services.

In 2010, Matsuzaki et al. described the case of a 15-month-old girl with a 3-month history of dysphagia and failure to thrive. Imaging revealed an intramedullary mass extending from the craniocervical junction to the C-6 level. A suboccipital craniotomy and C1–6 laminectomy resulted in partial tumor removal because of unclear tumor margins at the time of surgery. Final diagnosis was consistent with a PMA. The patient subsequently underwent chemotherapy with cisplatin and etoposide, and interval MRI studies revealed no evidence of tumor progression at the time of last follow-up, 64 months after symptom onset.

Fig. 2. Axial (A and B) and coronal (C) T1-weighted MRI studies obtained after addition of contrast material showing enhancing nodules (arrows) in both lungs and thoracic dextroscoliosis secondary to the intramedullary tumor.

Fig. 3. Sagittal T1-weighted (A) and T2-weighted (B) MRI studies obtained without contrast, and a T1-weighted (C) MRI study obtained after addition of contrast material showing no residual areas of nodular enhancement, decreased size of cord syrinx, but with mild enhancement of the cavity wall (C).
Paraskevopoulos et al.\textsuperscript{13} reported a case of a 12-year-old girl who presented 3 months after a near-total resection of a PMA with glioblastoma multiforme transformation and an acute neurological decline. Despite surgery and chemotherapy, she died 1 year after diagnosis.

**Presentation and Natural History**

These case reports demonstrate the variability in presentation and course of spinal PMAs. In older children, thoracic location and scoliosis with back pain are common. In younger children, cervical location and neurological deficits at the time of presentation appear to be more prevalent. Given the large size of these tumors, GTR, although desirable, can be very challenging. It appears that long-term survival is possible with a STR; however, several of the reported cases demonstrate the ability of PMAs to recur and even to seed extraneural sites.\textsuperscript{2,6} Periolo et al.\textsuperscript{14} quoted a 5%–10% rate of dissemination of low-grade gliomas (for example, juvenile pilocytic astrocytomas) to other sites throughout the neuraxis, although metastatic disease was most often found at the time of progression rather than after the initial diagnosis. Suspected intramedullary PMAs should therefore be approached in a similar fashion to other aggressive pediatric CNS tumors, including presurgical MRI of the entire neuraxis and lumbar puncture for CSF sampling. Postoperatively, the possibility of CSF dissemination mandates close radiographic follow-up.

**Origins of PMA**

Although the cause of PMAs remains unclear, some of these tumors have shown reactivity to synaptophysin, suggesting a possible mixed glioneural origin.\textsuperscript{5} There has been no clear evidence of *TP53* gene mutations involved with this tumor; however, there have been several sporadic cases of intracranial PMAs associated with chromosome 17 abnormalities and neurofibromatosis Type 1.\textsuperscript{4,5} In one Spanish case report, a 4-month-old child with a suprasellar PMA was found to have a chromosome 17 gene insertion leading to alteration of the Bcr-Abl tyrosine kinase protein. Alteration of this protein is a known cause of chronic myeloid leukemia via its activation of the Ras signaling pathway and upregulation of platelet-
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No consistent genetic alterations have been found with PMAs, but further studies may elucidate the molecular changes associated with this tumor.

**Histopathological and Radiographic Findings**

Pilomyxoid astrocytomas are distinguished histologically from pilocytic astrocytomas by the absence of several findings characteristic of pilocytic astrocytomas, including Rosenthal fibers, eosinophilic granular bodies, microcysts, and biphasic architecture with solid and loose cell areas. Instead, PMAs consist of monomorphic piloid cells embedded in a mucopolysaccharide-rich (myxoid) matrix. The pilomyxoid variant can also display marked vascular proliferation and infiltration into adjacent brain parenchyma. The tumor cells stain positive for both glial fibrillary acidic protein and vimentin.

Radiographically, PMAs are hyperintense on T2-weighted MRI and iso- or hypointense on T1-weighted imaging, and they exhibit variable enhancement after contrast administration. Eighty-five percent of PMAs are solid, with the remainder displaying a cystic component as well. These tumors tend to lack peritumoral edema and central necrosis, and up to 20% will display intratumoral hemorrhage. In comparison, pilocytic astrocytomas rarely hemorrhage, and low-grade diffuse astrocytomas often display no enhancement after contrast administration.

**Aggressiveness of PMAs**

Of the 6 cases of intramedullary PMA in the pediatric literature, 2 patients died of their disease. Only 1 of the other 4 was able to undergo a GTR. Two patients experienced a recurrence of tumor within 3 months of surgery. One of these patients was 12 years old at the time of recurrence and the other was a neonate. Therefore, it is unclear whether these tumors are more aggressive in older or younger patient populations.

PMAs may metastasize both within the CNS and to extraneural sites. In the case described by Arulrajah and Huisman it appears that the shunt was the cause of disease spread to the abdomen. The incidence of extraneural metastases in patients with a spinal PMA is unknown. Although it was thought that our patient ultimately did not have lung metastases, a review of the incidence of extraneural metastases revealed only scarce case reports of dissemination of intracranial low-grade gliomas to such sites as cervical lymph nodes and the osseous skeleton. As described by Paraskevopoulos et al., malignant transformation of a PMA is also possible. The overall estimated risk of malignant transformation of a low-grade glioma in children is estimated at 10%. Paraskevopoulos et al. even raised the possibility of a sampling error at the time of first surgery.

**Treatment Options**

Because this lesion is so rare in the spine, effective therapeutic treatment options are still being elucidated. With low-grade gliomas, complete resection is often desired; however, of the 6 reported cases of pediatric spinal cord PMA, only 1 patient was able to undergo GTR.
Since complete resection is not always feasible because of tumor location, postoperative chemotherapy and radiation should be considered as adjuvant treatment options. In patients with intracranial PMAs who are younger than 3 years old, however, chemotherapy is often the only adjuvant option because of the deleterious neurocognitive effects of radiation in this age group. Effective treatment options for low-grade gliomas include single-agent carboplatin as well as dual-agent chemotherapy with carboplatin and vincristine or cisplatin and etoposide. Cisplatin boplatin as well as dual-agent chemotherapy with carboplatin and vincristine or cisplatin and etoposide. Cisplatin etoposide were used by Matsuzaki et al.,11 and this platinum-based chemotherapy regimen has previously been shown to reduce tumor volume by 70% in childhood low-grade gliomas.10 Only 1 of the 6 pediatric patients with confirmed spinal cord PMA underwent postoperative radiation. This 6-year-old patient described by Komotar et al.5 was also treated with chemotherapy, although the regimen was not recorded. He experienced a partial remission of his tumor and was still alive with disease at the 60-month follow-up.

Conclusions
Pilomyxoid astrocytoma is a recently described glial tumor that is similar to pilocytic astrocytoma, although with distinct histopathological characteristics and the potential for a more aggressive clinical course. Our case is the seventh reported pediatric case of intramedullary spinal PMA. With such small numbers, optimal treatment guidelines for spinal PMAs have not yet been established, although GTR and adjuvant chemotherapy with alkylating agents appear to confer a better long-term prognosis. Pediatric patients with PMAs can remain recurrence free at least 5 years postoperatively, although these tumors also have the ability to disseminate via the CSF and to extraneurial sites, as well as to dedifferentiate into a more malignant glioma. More cases are needed before effective treatment guidelines can be established. Nevertheless, the more aggressive nature of these lesions when compared with WHO Grade I pilocytic astrocytomas can be neither understated nor overlooked when making clinical decisions.

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