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CASE OF MONTH JULY 2015 CASE 1

UNUSUAL SPINAL CORD TUMOR IN A 16-MONTH-OLD CHILD

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CLINICAL HISTORY

A 16-month-old boy presented to his pediatrician following a 3 week history of left head tilt and a 3 day history of cessation of crawling. Developmental history was significant for delays in sitting independently (8 months) and crawling (12 months), necessitating physical therapy for delayed gross motor milestones. Birth history and all other past medical history were unremarkable. Neurologic examination was positive for a mild left head tilt and lower extremity proximal muscle weakness on ventral suspension. Muscle bulk, tone, sensation, reflexes, and coordination were all within normal limits. MRI of the spine showed an expansile, enhancing, intramedullary mass from C2-T3 with an associated syrinx above and below the lesion (Figure 1). He subsequently underwent complete C3 to T3 laminectomies for spinal cord decompression and tumor resection.

MICROSCOPIC PATHOLOGY

Microscopic examination revealed small fragments of neuroglial tissue with increased cellularity in a heterogeneous distribution. Medium power-200x (Figure 2) and high power-600x (Figure 3) views demonstrated moderately cellular proliferation of monomorphic, process-forming cells in a basophilic proteinaceous background with angiocentric nuclei. Mitoses were not identified. **What is your diagnosis?**

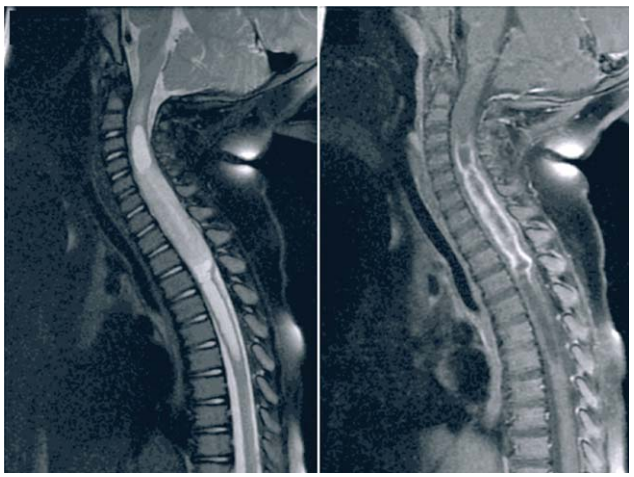

Figure 1.

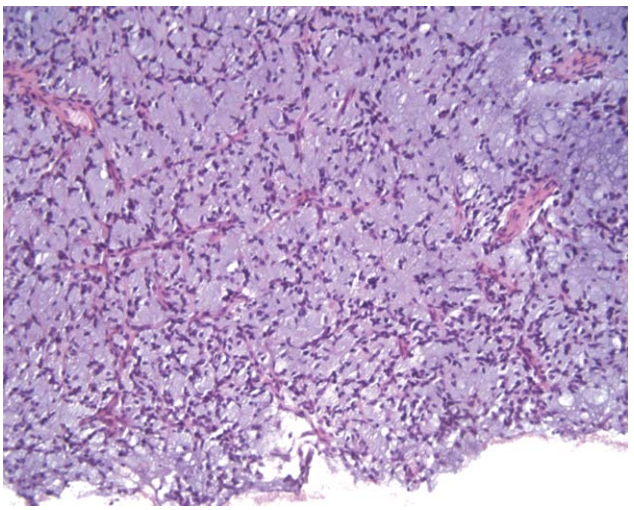

Figure 2.

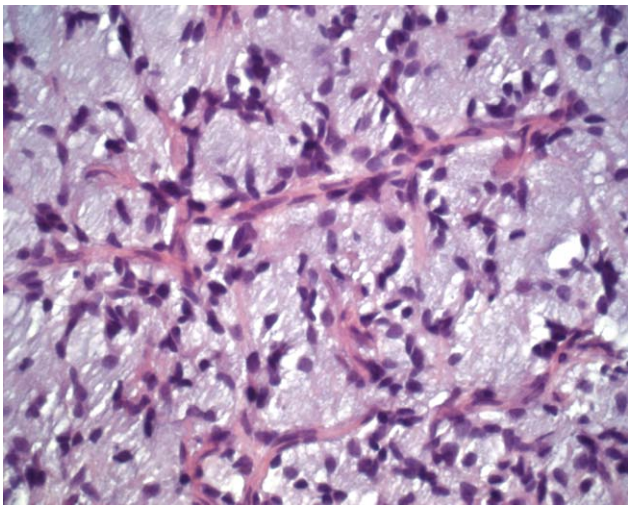

Figure 3.

DIAGNOSIS

Pilomyxoid Astrocytoma (WHO Grade II).

DISCUSSION

While brain tumors are the most common solid tumor in the pediatric population, spinal cord tumors are relatively rare, accounting for 1–10% of all pediatric central nervous system tumors. Due to their location and invasive nature, it is often difficult to achieve a complete resection which ultimately leads to an increased rate of recurrence and increased morbidity. Historically, the classification of spinal cord tumors is based on histopathologic characteristics of the tumor and is similar to the classifications for primary brain tumors. The differential diagnosis for primary intramedullary spinal cord tumors is relatively narrow. It includes low-grade astrocytomas (WHO grade I pilocytic astrocytoma or WHO grade II diffuse astrocytoma), high-grade or malignant astrocytomas (WHO grade III anaplastic astrocytoma or WHO grade IV glioblastoma), ganglioglioma, and ependymomas. Our patient's clinical history, physical exam findings and MRI findings demonstrating an infiltrating lesion with both enhancing and nonenhancing components were consistent with a differential diagnosis of either a low-grade astrocytoma or ependymoma. Among pediatric spinal cord tumors, astrocytomas are the most common histologic type. As part of the diagnostic workup, frozen tissue was sent for molecular analysis including high resolution single nucleotide polymorphism (SNP) DNA microarray and BRAF mutation analysis. BRAF V600E mutation and KIAA1549-BRAF fusion protein analysis, the most common molecular aberrations associated with low grade gliomas (1), were not detected. KIAA1549-BRAF fusion has been detected in >80% of pilocytic astrocytomas (2). Although KIAA1549-BRAF fusion is most commonly associated with pilocytic astrocytomas, it has also been detected in a few pilomyxoid astrocytomas including those involving the spinal cord (4). BRAF V600E mutations have been detected in 54% of diffuse low grade-gliomas (2).

SNP analysis of our patient's tumor revealed a gain of chromosome 8, a novel association with low grade glioma and in particular, pilomyxoid variant astrocytoma. Gain of chromosome 8 has been associated with some leukemias but has not been reported in CNS tumors (3). This represents a novel finding in pediatric spinal cord tumors, particularly astrocytomas.

The histopathologic features of this tumor are most consistent with a pilomyxoid astrocytoma, which presents at a median age of 10 months typically located in the hypothalamic/chiasmal region with rare reports of PMA in the spinal cord (4). While spinal cord PMA is rare, this tumor should be included in the differential diagnosis of intramedullary pediatric spinal cord tumors.

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