Spinal Pilomyxoid Astrocytoma in A 17-Month-Old Twin

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Introduction

Pilomyxoid astrocytoma (PMA) is a rare type of brain tumor that primarily affects young children. It typically arises in the hypothalamic-suprasellar region of the brain as a well circumscribed lesion with very little or no peritumoral edema. In contrast to Pilocytic astrocytoma (PA), they are predominantly solid masses, rarely have cystic components, and may extend into the temporal lobes. Unlike PA, PMA is characterized by a more aggressive clinical course and distinct histopathological features. Histologically, PMAs are cellular monomorphic lesions with angiocentric architecture within a myxoid background. The lesion cells show a hyperchromatic pleomorphic elongated nuclei and fibrillary processes and are focally infiltrative into the surrounding brain. These tumors show lack of biphasic pattern, Rosenthal fibers and eosinophilic granular bodies, which are typically seen in PAs.

Case Presentation

A 17 months old patient with a history of twin-to-twin transfusion born at 36 weeks was brought to the hospital with complaint of motor regression, compared to his twin. Spinal CT and MRI images (Figure 1) revealed an intradural intramedullary thoracic spinal mass with no intracranial mass. The spinal mass tissue biopsy was sent to pathology.

Results

Intraoperative smear preparation of the mass showed a hypercellular tumor consisting of monomorphic bipolar cells with a fibrillary background (Figure 2). The permanent tissue hematoxylin and eosin sections revealed a moderately cellular, relatively monomorphic glial neoplasm composed predominantly of the elongated cells with round to oval nuclei, delicate chromatin, and long, thin pyloric process. Some areas show microcystic spaces and a prominent myxoid stroma with a rich, branching capillary network. Rare perivascular pseudorosettes were present. No definite Rosenthal fibers or eosinophilic granular bodies are found (Figure 3a).

The tumor cells were diffusely positive with GFAP, highlighting the pyloric process and rare perivascular pseudorosettes (Figure 3b). Neurofilament highlighted the entrapped axons in some but not all fragments of tumor (not shown). Sox-10 was diffusely positive, synaptophysin was weakly patchy positive in tumor cells (not shown). NGS panel showed duplication involving FGFR1 (Figure 4). With the combination of histomorphology, immunohistochemical and molecular findings, the tumor was diagnosed as Low-grade glioma, most suggestive of pilomyxoid astrocytoma.

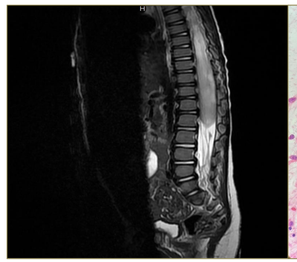

Figure 1: MR image showing thoracic spinal mass.

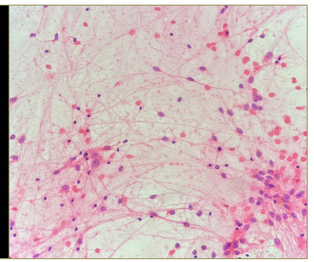

Figure 2: Smear preparation (H&E @ 40x) shows bipolar monomorphic cells in a fibrillary background.

Results (Continued)

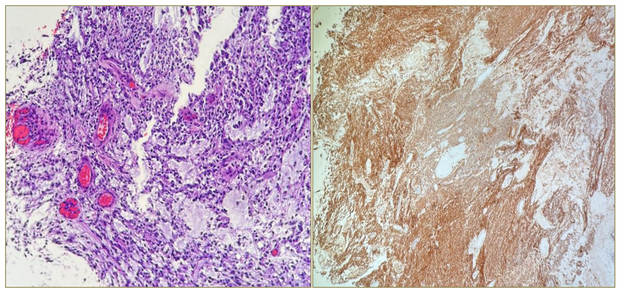

Figure 3: (a) H&E @ 20x shows a moderately cellular neoplasm composed of a relatively monomorphous bipolar population of glial cells in a myxoid background with occasional vascular proliferation. There is striking absence of Rosenthal fibers and eosinophilic granular bodies. (b) GFAP (glial fibrillary acidic protein) immunostain @ 20x shows strong staining in tumor cells.

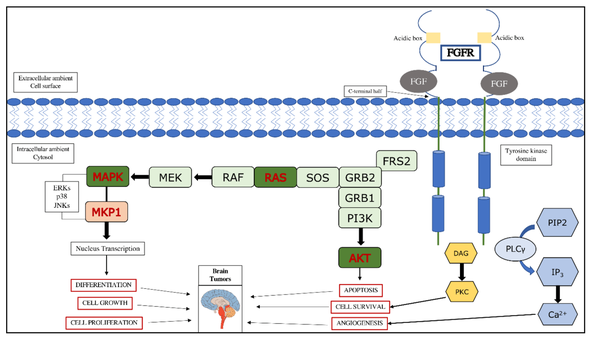

Figure 4: Figure 4: Activation of FGFRs, at the plasma membrane, involves the transduction of biochemical signals through a process known as dimerization. Receptor dimerization is essential for activation, as it brings the two tyrosine kinase domains into close proximity, thus allowing each other to phosphorylate the tyrosine in their activation circuits. This process activates kinases, which in turn bind adapter proteins and phosphorylated cytoplasmic substrates, thus triggering downstream signaling cascades that control cell growth and differentiation*.

*Ardizzone A, Scuderi SA, Giuffrida D, Colarossi C, Puglisi C, Campolo M, Cuzzocrea S, Esposito E, Paterniti I. Role of Fibroblast Growth Factors Receptors (FGFRs) in Brain Tumors, Focus on Astrocytoma and Glioblastoma. Cancers (Basel). 2020 Dec 18;12(12):3825. doi: 10.3390/cancers12123825. PMID: 33352931

Discussion

Pilomyxoid astrocytomas are an aggressive subtype of astrocytoma, first described by Tihan and friends in 1999. They have distinct clinical and histopathological features, typically presenting in younger patients (18 months old in average). The 2016 WHO classification of tumors of the central nervous system does not assign a grade to PMAs, but these neoplasms often have a more aggressive clinical course, higher recurrence and dissemination or cerebrospinal fluid spread rates, and shorter progression free survival than PAs.

PMAs are most commonly located in the hypothalamic/chiasmatic regions, however other locations, such as spinal cord, temporal lobe, occipital lobe, and sellar-suprasellar region were also reported. There are only 10 thoracic PMA cases published in the English literature.

From the genomic perspective, these tumors often harbor mutations affecting MAPK pathway (BRAF p.V600E) and FGFR signaling (FGFR1), mutations in IDH1 (p.R132), IDH2 (p.R17), NF1 and PTPN11, BRAF-KIAA fusions due to tandem 7q34 band duplication, and copy number alterations in chromosomes 5,7 and 11. While tumor genetics may not clearly differentiate PMAs from typical PAs, tumor genomic studies are indicated in the work up of these tumors due to the high frequency of targetable molecular alterations and to gain a better understanding of the molecular drivers behind their biology.

The treatment options for PMA include surgical resection, followed by radiotherapy with or without chemotherapy. It is important that PA and PMA are mostly indolent tumors and may exhibit a protracted clinical course and regression. Therefore, caution in treatment to avoid overtreatment, particularly in younger patients is recommended.

Conclusion

We present an uncommon tumor, pilomyxoid astrocytoma in an uncommon location, thoracic spinal cord. Pilomyxoid astrocytomas are not limited to the hypothalamic/chiasmatic region and should be included in the differential diagnosis for spinal cord masses. The histologic pattern is very important to differentiate pilomyxoid astrocytomas from pilocytic astrocytomas. The development of genetic studies for these rare cases will help us understand the biology of the tumor and improve the treatment options.

References

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