Pilomyxoid astrocytoma with high proliferation index

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Abstract

Pilomyxoid astrocytoma (PMA) is an uncommon aggressive piloid neoplasm, closely related to pilocytic astrocytomas and typically presents in the very young but can occur in older children and rarely in adults. A 12-years-old male presented with focal seizures, headache and vomiting of 10 days duration. Computed tomogram showed a hypo- to hyperdense and peripherally enhancing, solid-cystic lesion in the left temporal lobe. Histopathological examination revealed a characteristic tumor composed of bipolar cells arranged in dyscohesive sheets, angiocentric pattern in a loose myxoid background, with brisk mitotic activity and foci of necrosis. No Rosenthal fibers or eosinophilic granular bodies were seen. The tumor cells showed strong GFAP and scattered p53 positivity, but were negative for EMA. Ki-67 positivity ranged from 30 to 40%, highest reported till date. The patient was treated with radiotherapy and concurrent temozolomide and the tumor recurred after two years.

CASE REPORT

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Introduction

Pilomyxoid astrocytoma (PMA) is an uncommon progressive piloid neoplasm, closely related to pilocytic astrocytoma (PA). [1] Originally described by Janisch et al,[2] in 1985 as ‘diencephalic pilocytic astrocytoma with clinical onset in infancy’, the term pilomyxoid astrocytoma was introduced in 1999 by Tihan et al. [3] It has been recognized as a separate entity in WHO classification of Central Nervous System Tumors in 2007 because of its distinct histological features and labeled grade II tumor owing to its aggressiveness. [1] This tumor typically presents in young children (median: 10 months), but can also occur in older children and is rare in adults. [1]

Case Report

A 12-years-old male presented with focal seizures, headache and vomiting of 10 days duration. On clinical examination there were no neurological deficits or papilledema. Computed tomogram (CT) scan of the brain showed a solid-cystic lesion in the left temporal lobe, which was hypo- to hyperdense with peripheral contrast enhancement [Figure 1]. Gross total resection of the tumor was done and sent for histopathological examination. Immediate post-operative period and further recovery was uneventful. [Figure 1]

Microscopic examination showed a cellular tumor, composed of monomorphic, bipolar cells arranged in dyscohesive sheathing pattern [Figure 2a], interspersed with microcyclic spaces and abundant myxoid matrix [Figure 2c]. The tumor cells were small to medium-sized, with scant cytoplasm and bipolar, short cytoplasmic processes arranged in an angiocentric fashion, forming pseudorosettes [Figure 2b]. Brisk mitotic activity and foci of necrosis [Figure 2c] was seen. However, no Rosenthal fibers or eosinophilic granular bodies were noted. Immunohistochemical studies showed strong glial fibrillary acid protein (GFAP) positivity [Figure 2a inset], p53 positive in occasional tumor cell nuclei [Figure 2f] and Ki-67 labeling index varied from 30-40% [Figure 2e] in different areas of the tumor. Tumor cells were immunonegative for epithelial membrane antigen (EMA) [Figure 2d inset],[Figure 2f inset].

The patient had received 50Gy radiation with concurrent temozolomide (TMZ) over a period of 5 weeks at 75 mg/m². The patient presented with recurrence after two years. Histological examination of the repeat gross total excision specimen showed radiation-induced geographic necrosis [Figure 1g and h], ghost outlines of angiocentric tumor pattern [Figure 1h], with preserved tumor islands, retained angiocentricity and myxoid matrix [Figure 1g inset], and Ki-67 labeling index of 40-50% [Figure 1h]. The patient had received 50 Gy radiation with concurrent TMZ over a period of 5 weeks at 75 mg/m², followed adjuvant TMZ at 150 mg/m² from day 1 to day 5, cycles repeated every 4 weeks.

Discussion

The review of literature shows less than 100 cases of pilomyxoid astrocytoma being reported till date (PubMed search as on 12 th June 2013). The mean age at diagnosis for patients with PMA has been documented to be 18 months. [4] Apart from the commonest site of hypothalamic/chiasmatic region, this entity has also been described in thalamus, cerebellum, brain stem, temporal lobe and spinal cord. [1] Pilomyxoid astrocytoma most commonly presents with symptoms of raised intracranial pressure or parenchymal compression. [4] The presenting symptoms of hypothalamic juvenile PMA are vomiting, feeding difficulties, developmental delay and failure to thrive. [2]

On magnetic resonance imaging, these tumors are well circumscribed without evidence of peritumoral edema or parenchymal infiltration. [5] The majority (84.6%) are solid, with the remainder showing a minimal cystic component. Radiographic evidence of central necrosis is rare and PMA tends to enhance homogeneously on contrast. [4] [5] Presentation at younger age, more frequent occurrence in the suprasellar area, mainly solid mass containing non-enhancing portion and more frequent leptomeningeal dissemination, are helpful differential features of PMAs as compared to PAs. [6]

Angiocentric pattern of arrangement of tumor cells and myxoid matrix are characteristic histologic features. Rosenthal fibers or eosinophilic granular bodies, both characteristic of pilocytic astrocytomas are conspicuously absent in PMA. Mitotic figures and glomeruloid vascular tufts can be present and Ki-76 labeling index ranges from 2-20%. [1] The high Ki-76 labeling index of 30-40%, as recorded in this case has hitherto not been reported. The tumor cells and fibrillary background shows strong...
immunopositivity for GFAP, S-100 and Vimentin. [1] Though the angiocentric/pseudorosette pattern may mimic ependymoma, but absence of perinuclear dot expression of EMA in the present case of PMA differentiated it from ependymoma. Poor prognostic indicators in gliomas, that is necrosis, mitotic figures and vascular proliferation, are not uncommon in PMAs. [7]

The occurrence in the setting of neurofibromatosis type 1 (NF-1) and KIAA1549:BRAF fusions have been reported in PMA. [8],[9] Patients with PMA experience shorter progression free survival and higher local recurrence than those with juvenile PA. [4] Intra-cerebral metastasis of an intramedullary PMA, [10] leptomeningeal dissemination [11] and rapid progression to glioblastoma [12] have also been reported. A greater extent of surgical excision is associated with favorable outcome. But gross total excision may not be achievable in hypothalamic PMA and in such cases chemotherapy is instituted. [13] Kim et al., have used cisplatin and vincristine to treat juvenile PMA of the optochiasmatic region. [14] Terasaki et al., successfully treated leptomeningeal gliomatosis of pilomyxoid astrocytomas with concurrent radiation and TMZ after failed frontline chemotherapy with carboplatin and vincristine. [15]Adjuvant therapy with TMZ was incorporated in the present case, as the tumor’s biological behavior was akin to high grade astrocytomas.

It is important to separately recognize PMA from PA due to its propensity to involve younger age group, aggressiveness, higher local recurrence, metastasis, CSF spread and progression. Increased mitotic activity, proliferation index and necrosis or endothelial proliferation necessitates adjuvant therapy. Further follow-up and larger studies are needed to more accurately determine the prognosis of these tumors.

References