Article published online: 2022-09-14

Case Report

Pilocytic Astrocytoma with Gangliocytic Differentiation to Pilomyxoid Astrocytoma-expanding the Morphological Spectrum: Case Report and Literature Review

Abstract

We present a rare case of pilocytic astrocytoma (PA) with gangliocytic differentiation arising in the suprasellar/chiasmatic region in a young boy that showed a rapid regrowth after the 1st subtotal resection and "differentiated" into pilomyxoid astrocytoma (PMA) in subsequent recurrences. The clinical course, imaging, and histological features have been described with a review of the literature. While PA is well-circumscribed, biphasic tumors with bipolar piloid cells, those arising in the diencephalic region often contain myxoid stroma, angiocentric pattern, and "intermediate" features between PA and PMA. Examples of PMA "maturing" to PA are also on record; however, PA with gangliocytic component differentiating to PMA has not been described in the literature to the best of our knowledge.

Keywords: *Brain tumors, maturation, pilocytic astrocytoma, pilomyxoid astrocytoma*

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Introduction

Pilomyxoid astrocytoma (PMA), initially described as a variant of pilocytic astrocytoma (PA), over the years got recognition as a distinct entity with higher recurrence rate.[1,2] Until recently, these were regarded as the WHO Grade II neoplasms which reflected their increased tendency to leptomeningeal dissemination and thus the need for distinguishing its morphologic features. However, the recent updated WHO classification has questioned assigning it a higher grade in view of considerable variation in their outcome in different studies.[3] An interesting and rare phenomenon of "maturation" has been observed with examples of PMA undergoing "maturation" to PA in subsequent recurrences[4-6] which is more commonly observed in the "intermediate" lesions. "Intermediate" lesions are tumor displaying features of typical PMA admixed with areas resembling classic PA.[4] Herein, we describe a rare example of PA with gangliocytic component showing a rapid regrowth within 1½ years with differentiation to PMA on the third recurrence. While diencephalic tumors are well known to show intermediate features, PA with gangliocytic differentiation has not been described within the spectrum of "intermediate" lesions. Furthermore, morphologic distinction of PMA is important on account of its aggressive behavior as suggested in a few studies.

Clinical Summary and Imaging

A 3-year-old boy had presented with progressive visual diminution over 9 months. Radiology revealed a brilliantly enhancing large suprasellar mass with bilateral parasellar extension [Figure 1]. The child was operated through a right frontotemporal craniotomy. Partial excision was achieved, and histology revealed a PA with focal gangliocytic differentiation. His vision progressively worsened and he went blind. Repeat radiology showed significant residual component mainly in the left parasellar and suprasellar region. Six months later, the child was reoperated through the opposite side, and tumor was partially excised. At this stage, the tumor stage was characterized by classic PA features. No gangliocytic component was identified. Radiotherapy was deferred in view of young age. Postoperatively, the child required cortisol and thyroxine replacement. He developed excessive body hair and obesity. Gonadotropin-releasing hormone analogs was advised. Magnetic

How to cite this article: Gupta K, Tewari MK, Salunke P. Pilocytic astrocytoma with gangliocytic differentiation to pilomyxoid astrocytoma-expanding the morphological spectrum: Case report and literature review. Asian J Neurosurg 2018;13:1193-6.

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Access this article online

Website: www.asianjns.org

DOI: 10.4103/ajns.AJNS_247_17

Quick Response Code:

resonance imaging (MRI) 1½ years later showed a residual mass which was debulked through a right craniotomy. Histology at this stage revealed features of PMA. The postoperative MRI 6 months later [Figure 2] revealed a smaller residual mass. As the child is 5 years old now, the residual tumor is being irradiated.

Morphological Findings

First resection

The tumor was defined by regions composed of bipolar piloid cells dispersed in sheets. Rosenthal fibers and eosinophilic granular bodies (EGBs) were also noticed within the glial fragments, some of which were rimmed by linear vascular proliferation. No mitotic figures or necrosis was identified. Few tumor fragments distinctly revealed scattered dysmorphic ganglion cells with binucleation and nuclear irregularities in a background of coarse glial fibers [Figure 3a-d]. These were highlighted by synaptophysin and neuronal nuclear antigen [Figure 3e]. Glial fibrillary acidic protein (GFAP) immunostain highlighted the long, delicate processes of the bipolar piloid cell [Figure 3f]. The tumor was categorized as the WHO grade I neoplasm.

Second resection

The resected tumor demonstrated features of classic PA with occasional Rosenthal fibers and EGBs [Figure 4a and b].

Third resection

The tumor fragments demonstrated a monomorphous piloid neoplasm comprising spindle bipolar cells set in a dominant myxoid background [Figure 4c and d]. The cell processes were seen converging on the blood vessels giving an angiocentric arrangement [Figure 5a and b]. No fibrillar compact areas or microcystic areas were seen. Rosenthal fibers were absent and EGBs were occasionally encountered. No necrosis or mitoses was identified. GFAP stain highlighted the delicate cellular processes [Figure 5c]. Ki-67 labeling index was low [Figure 5d]. The tumor was classified as PMA, WHO grade II. The tumor did not harbor BRAF V600E mutation as evaluated on genomic deoxyribonucleic acid extracted from paraffin-embedded tissue.

Discussion

PAs are well-circumscribed, slow-growing tumors, morphologically defined by a biphasic component with cellular areas of bipolar cells and associated microcystic areas. The presence of Rosenthal fibers and EGBs are helpful clues in their morphological categorization.[1] A subset of PA arising in young children in the diencephalic region (including the hypothalamus, optic chiasm, and suprasellar) demonstrate a slight deviation from its characteristic features, including cytologic monomorphism, small bipolar cells, prominent myxoid matrix, angiocentric pattern, and the relative paucity of Rosenthal fibers and EGBs. These were given a distinct entity in 1999 by

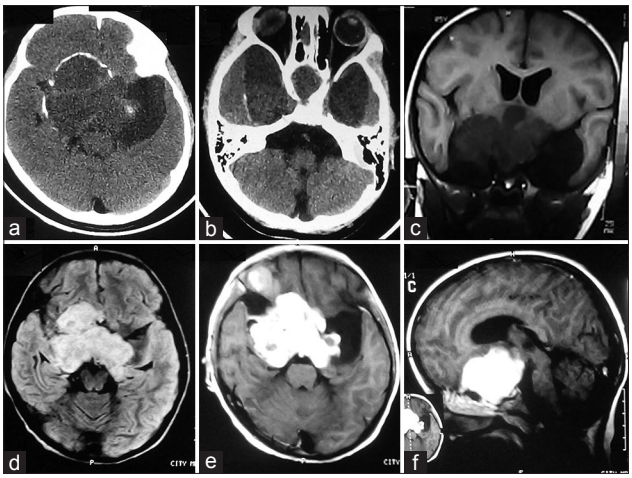

Figure 1: (a and b) Computed tomography scan showing iso-hyodense suprasellar mass with parasellar extension with expansion of skull base and rim calcification; (c) Coronal magnetic resonance imaging showing the bilateral parasellar extent of lesion; (d) Axial proton-density magnetic resonance imaging showing uniform lesion with increase intensity; (e and f) Axial and sagittal magnetic resonance imaging showing the brilliant and homogenous enhancement of lesion

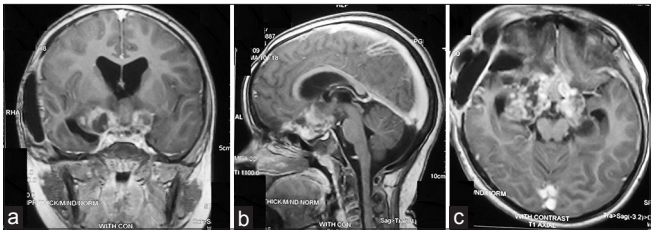

Figure 2: (a-c) Postoperative magnetic resonance imaging (coronal, sagittal and axial) after 3rd surgery showing reduction in tumor volume

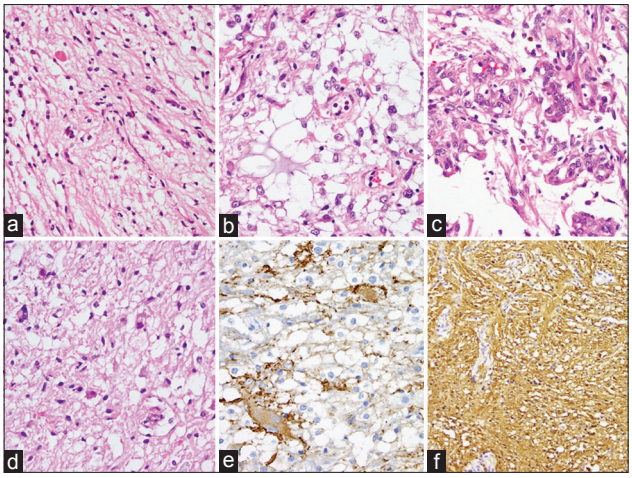

Figure 3: (a) Bipolar cells set in a densely fibrillar background (H and E, ×400); (b) Loose spongy tissue with microcysts (H and E, × 400); (c) Endovascular proliferation rimming tumor fragments (H and E, × 400); (d) Dysmorphic ganglion cells with bi-nucleation in a coarse glial background (H and E, × 200); (e) Neuronal component highlighted with synaptophysin (immunoperoxidase × 200); (f) densely compact fibrillar tissue immunoreactive with glial fibrillary acidic protein (immunoperoxidase × 200)

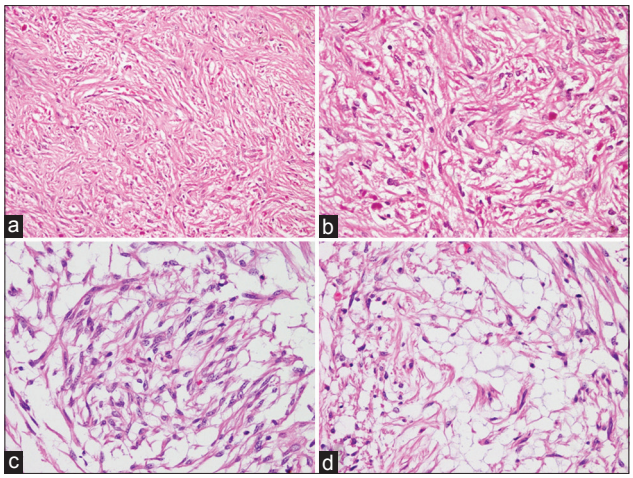

Figure 4: (a) Densely fibrillar bipolar cells predominates this resection (H and E, ×200); (b) High magnification depicting scattered Rosenthal fibers and eosinophilic granular bodies (H and E, ×400); (c) Small uniform bipolar cells with fine processes seen in third resection. The dense fibrillar background is missing (H and E, ×400); (d) Uniform cells in a rich basophilic myxoid background (H and E, ×400)

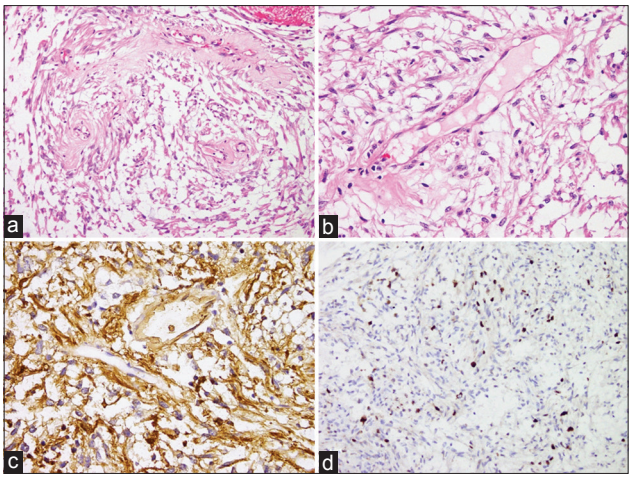

Figure 5: (a and b): Angiocentric arrangement of tumor cells in a myxoid background ([a] H and E, ×200, [b] ×400); (c) Perivascular processes immunoreactive for glial fibrillary acidic protein (immunoperoxidase ×400); (d) Ki67 immunostain depicts a low labelling index (immunoperoxidase ×200)

Tihan *et al*.[2] and were called PMA. The histological distinction is crucial for prognostic significance as these are known for an aggressive biological behavior with higher rates of recurrence as compared to classic PAs in some studies.[1,2,4] Leptomeningeal dissemination is also more frequent in PMA than PA.[7] However, the recent WHO update has questioned assigning it a higher grade and agreed on assigning it grade I on account of considerable variation in their behavior, in various studies.[3] These almost always arise in young children with mean age at diagnosis around 3 years.[1] While hypothalamus and the chiasmatic region is the favored location, their occurrence at other sites such as cerebellum,[7,8] spinal cord[9] has also been documented rarely. Interestingly, a curious phenomenon of "maturation" has been described in a small subset of PMA with recurrent tumors "maturing" into PA-like neoplasms.[4-6] This is more frequently observed in tumors with "intermediate" features between PMA and PA designated as "intermediate pilomyxoid forms".[3,6] The novelty in the present case is the presence of dysmorphic ganglion cells in PA in the 1st resection with recurrent lesions depicting PMA-like features, an observation which is reverse of "maturation". Moreover, gangliocytic differentiation within the spectrum of "intermediate forms" has not been earlier described in the literature. While the recurrence in the index case was mainly attributed to the unfavorable hypothalamic/chiasmatic location, the rapid regrowth in this case somehow makes it imperative to assign a definite grade to this tumor.

Activation of mitogen-activated protein kinase pathway by tandem duplication and in-frame fusion of *KIAA1549:BRAF* and BRAF V600E activating mutation are the most common mechanisms for pathway activation.[10,11] *KIAA1549:BRAF* fusion, *NF1* and BRAF V600E mutations have been detected in minority of PMA also.[5,12-14] Earlier reports have indicated their aggressive behavior with frequent recurrences and cerebrospinal fluid dissemination.[15,16] Investigators have recently observed an increased expression of insulin-like growth factor 2 (IGF2BP) gene, besides developmental genes and extracellular matrix collagens in PMA and have attributed the shorter progression-free survival in these tumors to increased expression of IGF2BP mRNA binding protein 3.[17] Although an isolated and early finding, but a recent report of successful treatment of PMA by vemurafenib is promising.[13] The tumor in index case, however, was negative for BRAF V600E mutation.

Conclusion

The finding of this case expands the morphologic spectrum of "intermediate" forms of PA/PMA arising in chiasmatic region and calls for a close follow-up and may be an aggressive treatment. Their location in the hypothalamic/chiasmatic region presents greater surgical challenge for complete excision and thereby accounts for their local recurrence, as seen in the present example. Nevertheless, a careful assessment of morphologic features and a close follow-up is essential for all diencephalic tumors due to their unpredictable clinical behavior.

Consent

The consent for publication was obtained from patient's guardian.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Burger PC, Jouvet A, *et al.* The 2007 WHO classification of tumours of the central nervous system. Acta Neuropathol 2007;114:97-109.
2. Tihan T, Fisher PG, Kepner JL, Godfraind C, McComb RD, Goldthwaite PT, *et al.* Pediatric astrocytomas with monomorphous pilomyxoid features and a less favorable outcome. J Neuropathol Exp Neurol 1999;58:1061-8.
3. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, *et al.* The 2016 World Health Organization classification of tumors of the central nervous system: A summary. Acta Neuropathol 2016;131:803-20.
4. Johnson MW, Eberhart CG, Perry A, Tihan T, Cohen KJ, Rosenblum MK, *et al.* Spectrum of pilomyxoid astrocytomas: Intermediate pilomyxoid tumors. Am J Surg Pathol 2010;34:1783-91.
5. Kleinschmidt-DeMasters BK, Donson AM, Vogel H, Foreman NK. Pilomyxoid astrocytoma (PMA) shows significant differences in gene expression vs. pilocytic astrocytoma (PA) and variable tendency toward maturation to PA. Brain Pathol 2015;25:429-40.
6. Ceppa EP, Bouffet E, Griebel R, Robinson C, Tihan T. The pilomyxoid astrocytoma and its relationship to pilocytic astrocytoma: Report of a case and a critical review of the entity. J Neurooncol 2007;81:191-6.
7. Forbes JA, Mobley BC, O'Lynnger TM, Cooper CM, Ghiassi M, Hanif R, *et al.* Pediatric cerebellar pilomyxoid-spectrum astrocytomas. J Neurosurg Pediatr 2011;8:90-6.
8. Okano A, Oya S, Fujisawa N, Tsuchiya T, Indo M, Nakamura T, *et al.* Significance of radical resection for pilomyxoid astrocytoma of the cerebellum: A case report and review of the literature. Childs Nerv Syst 2013;29:1375-9.
9. Sajadi A, Janzer RC, Lu TL, Duff JM. Pilomyxoid astrocytoma of the spinal cord in an adult. Acta Neurochir (Wien) 2008;150:729-31.
10. Qaddoumi I, Orisme W, Wen J, Santiago T, Gupta K, Dalton JD, *et al.* Genetic alterations in uncommon low-grade neuroepithelial tumors: BRAF, FGFR1, and MYB mutations occur at high frequency and align with morphology. Acta Neuropathol 2016;131:833-45.
11. Forshew T, Tatevossian RG, Lawson AR, Ma J, Neale G, Ogunkolade BW, *et al.* Activation of the ERK/MAPK pathway: A signature genetic defect in posterior fossa pilocytic astrocytomas. J Pathol 2009;218:172-81.
12. Khanani MF, Hawkins C, Shroff M, Dirks P, Capra M, Burger PC, *et al.* Pilomyxoid astrocytoma in a patient with neurofibromatosis. Pediatr Blood Cancer 2006;46:377-80.
13. Skrypek M, Foreman N, Guillaume D, Moertel C. Pilomyxoid astrocytoma treated successfully with vemurafenib. Pediatr Blood Cancer 2014;61:2099-100.
14. Ho CY, Mobley BC, Gordish-Dressman H, VandenBussche CJ, Mason GE, Bornhorst M, *et al.* A clinicopathologic study of diencephalic pediatric low-grade gliomas with BRAF V600 mutation. Acta Neuropathol 2015;130:575-85.
15. Enting RH, van der Graaf WT, Kros JM, Heesters M, Metzemaekers J, den Dunnen W, *et al.* Radiotherapy plus concomitant and adjuvant temozolomide for leptomeningeal pilomyxoid astrocytoma: A case study. J Neurooncol 2006;80:107-8.
16. Komotar RJ, Burger PC, Carson BS, Brem H, Olivi A, Goldthwaite PT, *et al.* Pilocytic and pilomyxoid hypothalamic/chiasmatic astrocytomas. Neurosurgery 2004;54:72-9.
17. Barton VN, Donson AM, Birks DK, Kleinschmidt-DeMasters BK, Handler MH, Foreman NK, *et al.* Insulin-like growth factor 2 mRNA binding protein 3 expression is an independent prognostic factor in pediatric pilocytic and pilomyxoid astrocytoma. J Neuropathol Exp Neurol 2013;72:442-9.