Indian Journal of Pathology & Microbiology

CASE REPORT
Year : 2021 | **Volume** : 64 | **Issue** : 2 | **Page** : 354–357

A rare case of cerebellar pilomyxoid astrocytoma associated with neurofibromatosis-1 in a young female; case report highlighting immunohistochemical features

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Abstract

Pilomyxoid astrocytoma (PMA), a distinct clinico-histopathological entity in the World Health Organization classification 2007, tends to be locally aggressive, with higher chance of leptomeningeal dissemination, recurrence, and poor prognosis. PMA is generally seen in young children and tend to occur in the hypothalamic-chiasmatic region. Their presence in other parts of the brain in the non pediatric age group is uncommon. To the best of our knowledge we are presenting first case of cerebellar PMA associated with neurofibromatosis 1 (NF1) in a 40-year- old female, with immunohistochemical study.

How to cite this article:
Sinai Khandeparkar SG, Gosavi SS, Gogate BP, Talathi N. A rare case of cerebellar pilomyxoid astrocytoma associated with neurofibromatosis-1 in a young female; case report highlighting immunohistochemical features.Indian J Pathol Microbiol 2021;64:354-357

How to cite this URL:
Sinai Khandeparkar SG, Gosavi SS, Gogate BP, Talathi N. A rare case of cerebellar pilomyxoid astrocytoma associated with neurofibromatosis-1 in a young female; case report highlighting immunohistochemical features. Indian J Pathol Microbiol [serial online] 2021 [cited 2021 May 4];64:354-357
Available from: https://www.ijpmonline.org/text.asp?2021/64/2/354/313274

Full Text

Introduction

Pilomyxoid astrocytoma (PMA), is a rare central nervous system (CNS) tumor once considered as a subtype of pilocytic astrocytoma (PA), has been recently characterized as a distinct clinico-histopathological entity in the World Health Organization (WHO) classification 2007.[1] In contrast to the PA (WHO grade I), this tends to be locally aggressive, with higher chance of leptomeningeal dissemination, recurrence, and poor prognosis.[2] The PMA is more common in infants and young children and usually at hypothalamic-chiasmatic region.[3] To the best of our knowledge, we are presenting first case of cerebellar PMA associated with neurofibromatosis 1 (NF1) in a 40-year-old female.

Case Report

Forty-year-old female, a known case of NF1, [Figure 1]a presented to the neurosurgery outpatient department with history of headache, vomiting, and difficulty in walking since 15 days. On clinical examination, she was having gait imbalance, right dysdiadochokinesia, and horizontal gaze nystagmus. Cerebrospinal fluid examination was unremarkable. Magnetic resonance imaging (MRI) brain showed irregular, lobulated, altered signal intensity, and heterogeneously enhancing mass lesion of size 2.5 × 2.6 × 2.9 cm [Figure 1]b. The lesion was heterogenously hyperintense on T2W images, whereas hypointense on T1W images. It showed heterogenous intense enhancement on postcontrast study with small central non enhancing areas suggestive of liquefactive change. It was not crossing the midline. Mild perifocal edema was seen extending into the cerebellar peduncles. On the basis of clinico-radiological findings, differentials offered were pilocytic astrocytoma, pleomorphic xanthoastrocytoma, and hemangioblastoma.{Figure 1}

Patient underwent gross total resection of the tumor through transcortical approach. Intraoperatively, the tumor was infiltrating into the adjacent brain parenchyma. Tissue was sent for frozen section examination. Operating neurosurgeon communicated differentials of tumor of vascular nature due to hemorrhage and glial tumor likely of grade II/III. Frozen sections study showed numerous RBCs and few bits showed monomorphic cells against fibrillary background. Primary diagnosis of low grade glial tumor was given. On gross examination, multiple soft gelatinous brain tissue with blood clots were obtained showing brownish-white areas total aggregating to 3 cc. Microscopic examination revealed oval monomorphic cells typically arranged around blood vessels giving rise to pseudorosettes. Fibrillary cytoplasmic processes embedded in myxoid matrix with focal microcystic spaces formation was seen. Some of the cells showed atypia in the form of nuclear pleomorphism and binucleation. Normal bipolar and abnormal uni and multipolar mitotic figures (10/10 high power fields), occasional foci of necrosis, focal hyalinized endothelial hyperplasia, linear endothelial hyperplasia, and infiltration into the surrounding cerebellar parenchyma was observed. Cells with rounded nuclei surrounded by clear space sitting in myxoid free background were noted giving rise to oligodendroglioma like areas [Figure 2]a,[Figure 2]b,[Figure 2]c,[Figure 2]d,[Figure 2]e. No Rosenthal fibers or eosinophilic granular bodies were seen. Areas of hemorrhage were observed. Diagnosis of pilomyxoid astrocytoma was considered. Pilocytic astrocytoma, ependymoma, and hemangioblastoma were considered as close differentials. immunohistochemical (IHC) analysis was performed with the following panel of antibodies viz. glial fibrillary acid protein (GFAP), CD31, CD34, neuron specific enolase (NSE), synaptophysin, epithelial membrane antigen (EMA), p53, and Ki67. The tumor cells expressed strong glial fibrillary acidic protein (GFAP) immunoreactivity, showed positive NSE and synaptophysin expression, Ki67 labelling index (Ki67LI) of 7% and were negative for EMA, CD31, CD34 and p53 [Figure 2]f,[Figure 2]g,[Figure 2]h,[Figure 2]i,[Figure 2]j. Diagnosis of pilomyxoid astrocytoma was confirmed. Postoperatively the patient is disease free at six month's follow-up.{Figure 2}

Discussion

In 1999, Tihan and colleagues described a subtype that was clinically and histologically different from classic PA, which they later named PMA.[4] The 2007 WHO classification described PMA as a grade II tumor. It mentioned that PMA histologically reveal angiocentric cell arrangement and exhibit more aggressive biological behavior than typical PA.[4] However, a more recent 2016 WHO classification does not provide a specific grade for PMA. The rationale for this being extensive histological and genetic overlap shown by the PMA and PA, with some

of the former maturing into the latter over time and less certainty that the PMA always follows a more aggressive course than a more classic appearing suprasellar PA.[5]

In adults, PMA are occasionally seen with very few reports in literature.[3],[4],[6],[7],[8],[9] Other than the usual hypothalamic-chiasmatic region, few cases have been reported in the posterior fossa, spinal cord, and sporadically in the supratentorial location (parietal, temporal, and basal ganglia region).[3] In females these are exceedingly rare.[4],[6] Our patient was 40-year-old female. The first reports of PMA described this lesion as a strictly pediatric tumor, occurring at a mean age of 18.[9] However, review of all subsequent PMA cases reported in the literature revealed a larger age range.[3],[4],[6],[8],[9] Our patient was a case of NF-1. The association of PMA with NF-1 has been reported in literature.[8] This suggests that PMA may be another NF-1 associated tumor. In our case, the tumor was located in the cerebellar hemisphere. Handful of cases are reported in the cerebellum.[6] To the best of our knowledge, we are presenting first case of cerebellar PMA associated with neurofibromatosis 1 (NF1) in a 40-year-old female.

It is difficult to reliably differentiate PMA from PA due to its shared common location and a similar radiological picture.[3] Certain subtle clues such as predominantly a solid tumor with increased propensity to bleed than their PA counterpart could suggest the PMA diagnosis as in present case. No feature is unique to PMA, and hence the diagnosis is confirmed only by histopathological studies. In present case, one of the clinico-radiological differentials was hemangioblastoma owing to increased vascularity. Spontaneous intratumoral hemorrhage is predominantly a feature of high-grade tumors and metastasis, more so in children. Intratumoral hemorrhage has been reported in up to 25% of PMA in one series, which is higher than reported for PA. The etiology underlying the bleed in low-grade neoplasms is less understood. In recent times, studies have attempted to identify the abnormal vasculature that predisposes to hemorrhage in these low-grade neoplasms. They have noted thick-walled densely hyalinized vessels, glomeruloid endothelial hyperplasia, and thin-walled ectatic vessels in such cases.[3] Present case showed presence of such areas, which could explain the suspicion for vascular tumor and presence of hemorrhagic areas in the frozen squash smears.

Frozen sections showing typical areas of tumor cells arranged in pseudorosettes against myxoid background could suggest accurate diagnosis of PMA.[1] In our case lack of myxoid areas and pseudorossette made accurate diagnosis difficult. Routine histopathological sections in our case characteristically revealed pseudorossette arrangement of the tumor cells microscopically against myxoid background. PMA tumor deviate from conventional pilocytic histology in containing pseudorossette-like formations of neoplastic cells that appear to radiate from stromal blood vessels.[1] We saw oligodendroglioma like areas focally, the same finding has been reported by Ding et al.[10] Features such as brisk mitotic activity and foci of necrosis seen in our case has been reported by Pruthi et al.[9] Occasional glomeruloid vascular tufts and infiltration of tumor cells into surrounding neuropil at the tumor periphery was seen in our case, which has been observed by other studies as well.[10] Rosenthal fibers or eosinophilic granular bodies, both characteristic of pilocytic astrocytoma were conspicuously absent in our case.[4]

The tumor cells and fibrillary background showed strong immunopositivity for GFAP, synaptophysin, and NSE, which confirmed the astrocytic nature of the tumor.[1],[11] Pilocytic astrocytoma was ruled out due to absence of biphasic fascicular and microcystic pattern and presence of pseudorosettes and myxoid background. Absence of CD31 and CD34 immunoexpression ruled out clinico-radiological differential of vascular tumor.[3],[11] Ependymoma was considered as a differential diagnosis due to the presence of pseudo-rosettes, but its location, prominent fibrillary background, absence of true rosettes, and dot like EMA expression, and synaptophysin positivity excluded possibility of ependymoma.[11]

Our experience with present case highlights the rarity of lesion, its association with NF1, and a high index of suspicion in presence of pseudorosettes with immunohistochemical analysis for ruling out the differential diagnosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Figure 1: (a) Clinical photograph showing cutaneous nodules in Neurofibromatosis.1 patient, (b) MRI brain showing irregular, lobulated, altered signal intensity, heterogeneously enhancing mass

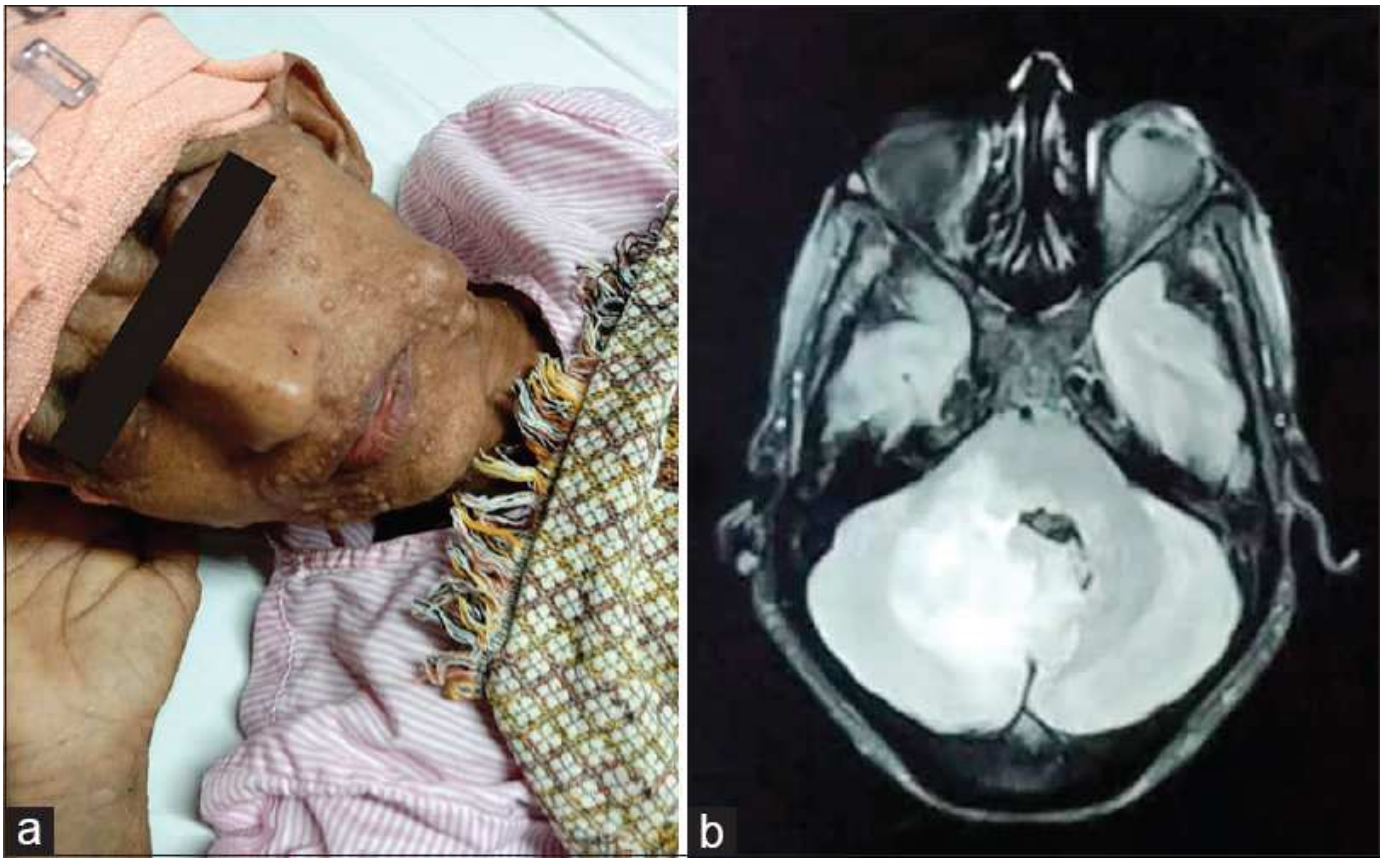

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Figure 2: Photomicrograph of pilomyxoid astrocytoma showing (a) pseudorosettes, myxoid matrix, and microcystic spaces (H and E, x400), (b) hyalinized endothelial hyperplasia (H and E, x100), (c) linear endothelial hyperplasia (H and E, x400), (d) necrosis (H and E, x100), (e) oligodendroglioma like areas (H and E, x400), (f) mitosis (H and E, x400), (f inset) mitosis (H and E, x1000), (g) GFAP (x100), (h) synaptophysin (x400) and (i) NSE immunoreactivity (x400), (j) CD34 positivity in linear endothelial hyperplasia (x400), (k) CD31 negativity (x400), (l) Ki67LI = 7% (x400)