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Case Report

Pilomyxoid astrocytoma showing malignant transformation in adult male

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ABSTRACT
Pilomyxoid astrocytomas are type of tumors rarely seen in the central nervous system as a variant of pilocytic astrocytoma. They are often localized in hypothalamic-chiasmatic area and seen in early childhood. They exhibit different histological characteristics and more aggressive behaviors compared to pilocytic astrocytomas. Although cases with malignant transformation were reported in pilocytic astrocytomas, no pilomyxoid astrocytoma patients was reported with malignant transformation. We have presented a pilomyxoid astrocytoma patient, since it is rarely seen in adulthood and shows malignant transformation histopathologically.

Keywords: pilomyxoid astrocytoma, malignant transformation, adult patient

INTRODUCTION

Pilomyxoid astrocytoma (PMA) was described as a variant of pilocytic astrocytoma (PA) by Tihan et al. in 1999 (1). PA is one of the most common indolent WHO Grade-I astrocytoma in the pediatric population. Its prognosis is excellent and 20 years of survey with reaching up to 70-80% was defined even in subtotal resection (2). PMA has different histopathological characteristics, more aggressive behaviors and earlier age of onset compared to PA (3). Therefore, in the classification of WHO, it was included within the group of Grade-II astrocytic tumors. These tumors are most frequently seen in the hypothalamic and chiasmatic areas (4). They are seen as well-demarcated and solid masses with cystic components (5). PMA often occurs during early childhood (6, 7). In PA; a small number of patients with malignant transformation in recurrent masses after radiotherapy (RT) were reported, and no PMA case with malignant transformation was seen in the literature.

CASE REPORT

A 46-year-old male patient, suffering from nausea and vomiting for 2 months, admitted to our neurosurgery clinic. Preoperative magnetic resonance imaging (MRI) showed a tumoral lesion which had solid and cystic components in the pontocerebellar angle (Figure 1 a-c). The patient underwent surgery via an ordinary retrosigmod approach in sitting position and the tumor excised in subtotal fashion due to intensive cohesiveness to surrounding vital brain stem and vascular structures. In gross pathological appearance the tissue has a gray and gelatinous consistency. Histopathologically, there were atypical glial cell clumps with fibrillary cytoplasm containing myxoid degeneration areas. Tumor cells had pseudorosette and rosette formations and aligned as a tape. Necrosis was seen in 2 areas, but no palisade-like arrangement was seen. In several areas of the tumor growth was seen in pleomorphism, cellularity and vascularity. In 10 high power fields; while the number of mitosis was 7, it was only 1 in conventional areas. Tumor cells are GFAP (+), S-100 (+) as a result of immunohistochemical staining, whereas EMA, pancytokeratin and synaptophysin (-). Ki-67 proliferation index was 40% in areas, where pleomorphism was pronounced, and 1% in other areas respectively (Figure 2 a-i). The patient was diagnosed with "pilomyxoid astrocytoma including malignant transformation areas".

DISCUSSION

PMA is defined as an aggressive variant of PA. It often appears in hypothalamic-chiasmatic areas especially in early childhood (6, 7, 9). It is important to draw a distinction between PMA and PA since PMA emerges at younger ages with a more aggressive course, higher local recurrence rates and tendency to spread into cerebrospinal fluid (3). PA is seen in the 58-month old babies and PMA is seen in the 18-month old babies in average. PMA has higher recurrence rates even with the same resection rates (2). In a study, long-term clinical follow ups of 42 PA and 21 PMA cases in the same localization were compared and the survey with no progression was found as 26 months in PMA and 147 months in PA ($p < 0.001$), respectively. On the other hand, the survey was found as 63 months in PMA and 213 months in PA ($p < 0.001$), respectively. In addition, deaths from the disease were reported as 33% and 17%, respectively. Cerbrospinal fluid dissemination was 14% in PMA, whereas no dissemination was seen in PA (2).

Although PMA often appears in the childhood, there is a small number of patients diagnosed with PMA in adulthood period in the literature (3, 12-17). Our case was a 46-years old male patient.

In these tumors, findings related to parenchymal compression and increased intracranial pressure was found clinically (2). In our case, the patient admitted to our hospital with complaints of nausea and vomiting due to increased intracranial pressure.

Histologically, PA exhibits biphasic pattern consisting of loose and cystic areas in addition to cellular areas. Specifically, rosenthal fibers and eosinophilic granules are seen (2). Angiogenesis is present, but tumor cells are not located around vessels and mitotic figures cannot be seen in most of the cases

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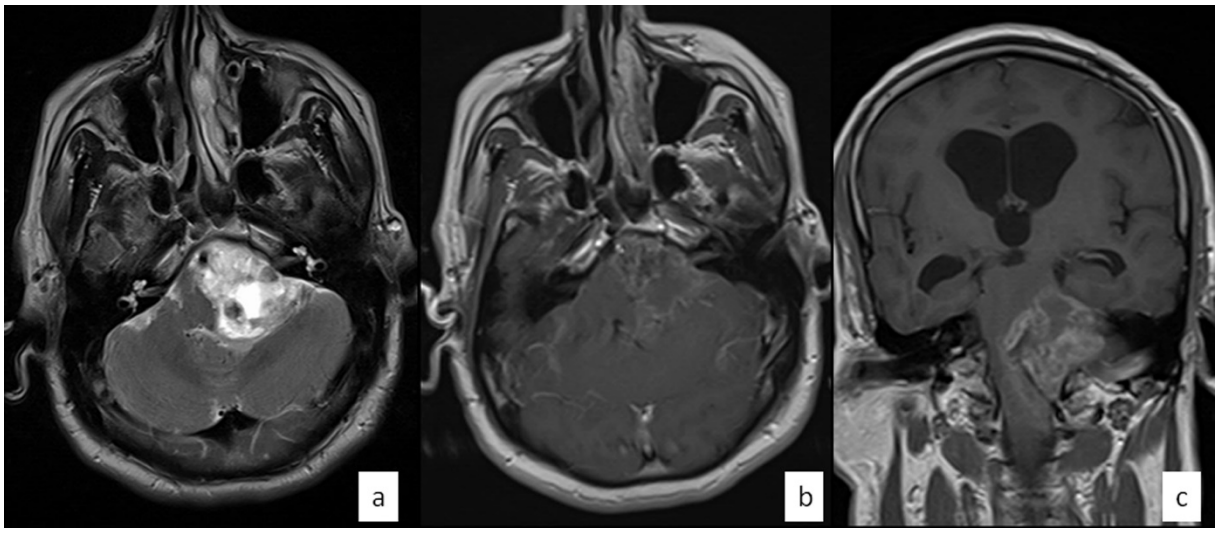

Figure 1: *Preoperative magnetic resonance imaging (MRI) scans.* ***a*** *T2-weighted axial MRI section shows a heterogeneous hyperintense lesion which contain solid and cystic areas at left ponto-cerebellar angle. The lesion significantly compresses the fourth ventricle and brain stem, also surrounds the basilar artery but not spread to internal acustic canal.* ***b*** *Contrast enhanced axial T1-weighted MRI section shows irregular enhancement.* ***c*** *T1-weighted coronal MRI section with gadolinium shows irregular enhancement and heterogenous hyperintense and hypointense areas within the lesion with brain stem compression*

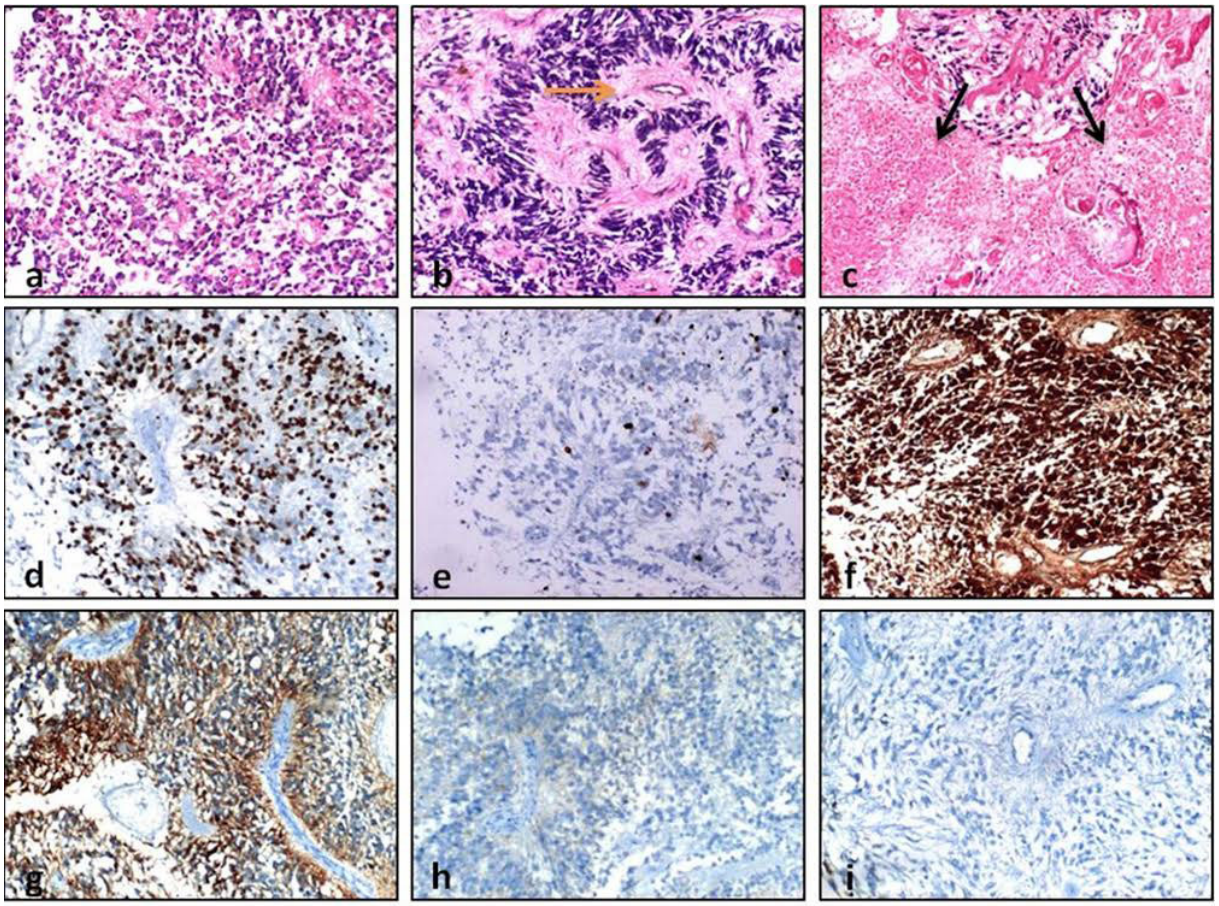

Figure 2: *Representative pathological images of the tumoral lesion.* ***a*** *tumoral lesion (H&E x100).* ***b*** *The arrow indicate the rosette formation (H&E x200).* ***c*** *The arrows indicate a necrosis area (H&E x100).* ***d*** *In some regions the lesion shows 40% Ki-67 positivity (x100).* ***e*** *The lesion shows 1% Ki-67 positivity in some areas (x100).* ***f*** *Positive immunostaining for S-100 (x100).* ***g*** *Positive immunostaining for GFAP (x100).* ***h*** *Negative immunostaining for synaptophysin (x100).* ***i*** *Negative immunostaining for EMA (x100)*

(2, 5). On the other hand, PMA exhibits monomorphic patterns. In the myxoid ground, piloid cells have angiocentric arrangements and they create pseudorosette-like structures around the vessels. There are no rosenthal fibers and eosinophilic granules (10). Tumor cells show positive expression with GFAP, S-100 and vimentin immunohistochemically (4).

In PA, the cases reported with malignant transformation can be seen. In a publication, histologically increased cellularity, cellular atypia and extensive necrosis in PA was defined as malignant transformation (19). According to some publications, malignant transformation is mostly seen after RT treatment and radiation is a key factor in malignant transformation (8). In

another article, anaplastic characteristics were identified in 34 of 2200 PA cases and only 4 of these patients had a history of RT. Therefore, RT therapy was not considered to be an effective factor by itself. In the same article, malignant transformation in PA with no history of RT was considered to be a controversial issue and it was emphasized that the underlying mechanisms should be clarified (20).

The poor prognostic indicator necrosis in gliomas, mitotic figures and vascular proliferation are rare in PMA (11). No PMA case with malignant transformation was found in the earlier studies in the literature. In PMA cases in the literature, Ki-67 index ranges from 2% to 20% (4). Only 1 case was reported with 40% Ki-67 index and focal necrosis and mitotic activity was also seen in the case, but the number of mitosis was not mentioned (18). In our case, Ki-67 index was 40% in areas defined as malignant transformation and it was 1% in conventional areas. In these areas, there is a hypercellularity, increased vascularity and cellular pleomorphism. Also necrosis was observed in 2 areas and 7 atypical mitosis were identified in 10 high power fields.

Gianni et al. emphasized that the Ki-67 indexis important to determine tumor grades and prognosis in astrocytomas. On the other hand, they have emphasized that Ki-67 is not sufficient alone in prognostic factors and histopathological characteristics are also important (21). In line with these findings; we have diagnosed our patient with PMA showing malignant transformation by considering many characteristics such as cellular pleomorphism, hypercellularity, increased vascularity, presence of necrosis, high mitotic count and Ki-67 index as a whole.

There is no common consensus in the PMA treatment yet and they are managed like PA cases. Total resection of the tumor is applied as the primary treatment strategy. Adjuvant treatment (chemotherapy or radiotherapy) is applied in recurrence cases after total resection if there are neurological deficits after subtotal resection or there is even an asymptomatic increase in the residual tumor size radiologically after subtotal resection (22). There are also some other studies suggesting that adjuvant therapy should be applied after surgical resection due to more aggressive behaviors of PMA patients compared to PA cases (12). On the other hand, some studies suggest that adjuvant therapy should be applied by considering the age of patient and different characteristic symptoms of the disease (23).

Our patient has unfortunately died due to sitting position related air embolism for a month after surgery. And also could not receive adjuvant therapy in this one-month period. Therefore, the clinical data obtained after the surgery is insufficient and we need more clinical data and more work done in these cases.

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