Case report

Retinal anaplastic pleomorphic xanthoastrocytoma unassociated with phakomatosis

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Abstract

Purpose: To present a rare anaplastic form of retinal pleomorphic xanthoastrocytoma (PXA) unassociated with phakomatosis.

Methods: A 9-year-old girl, presented with a rapidly growing unilateral intraocular white mass unresponsive to intra-arterial chemotherapy, underwent enucleation with the clinical suspicion of retinoblastoma versus malignant astrocytoma.

Results: Histopathology revealed pleomorphic cells with Rosenthal fibers, mitosis, and necrosis. Immunohistochemistry confirmed the diagnosis of anaplastic pleomorphic xanthoastrocytoma (aPXA). The patient had no signs of phakomatosis.

Conclusion: Retinal PXA may occur in patients without phakomatosis and rarely progress toward malignant transformation.

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Keywords: Anaplasia; Pleomorphic xanthoastrocytoma; Retinal tumor

Introduction

Pleomorphic xanthoastrocytoma (PXA), the grade II of central nervous system tumors,1 has a favorable prognosis in children and young adults. It represents less than 1% of all brain astrocytic tumors,2 and retina is considered a rare site of its involvement.3 PXA has 75%–80% five-year survival rate, and 30% chance of recurrence after resection.4 However, malignant transformation may occur and anaplastic pleomorphic xanthoastrocytoma (aPXA), the grade III of central nervous system tumors, is a new name for the previous entity "pleomorphic xanthoastrocytoma with anaplastic features".1

Astrocytic tumors occur in 57% of patients with tuberous sclerosis (TSC) and 14% of neurofibromatosis cases while the remaining 29% are attributed to solitary tumors.5

Here, we add a case of retinal aPXA unassociated with phakomatosis to the previous 12 reported cases.6

Case report

Ophthalmic examination of a 9-year-old girl, with a 4-month history of decreased vision in her right eye, revealed an amelanotic retinal mass with glial tissue strands over the optic disc, areas of vitreous seeding, and serous retinal detachment (Fig. 1). Her vision was 2 m finger counting with + relative afferent pupillary defect. Her intraocular pressure was 16 mmHg.

The contralateral eye examinations were unremarkable. Considering the diagnosis of group D retinoblastoma versus activated astrocytoma, four sessions of intra-arterial
chemotherapy with Melphalan (5 mg) and Topotecan (1 mg) was performed. However, the rapid tumor growth was unresponsive to the above globe preserving therapy, and progression to neovascular glaucoma occurred within three weeks necessitating enucleation with the clinical suspicion of retinoblastoma versus malignant astrocytoma.

Histopathologic evaluation revealed spindle cells with elongated fibrillary processes and round cells with vesicular cytoplasm, bizarre nuclei, multinucleated giant cells and Rosenthal fibers as well as necrosis, and the presence of less than 5 mitoses in 10 high power fields (HPF) with calciospherites and a cystic space inside the tumor (Figs. 2 and 3).

Moreover, immunohistochemistry evaluation showed a diffuse immune reactivity for glial fibrillary acidic protein (GFAP) and S100 together with focal reactivity for CD34 and CD68. No immune reactivity was noted for P53, synaptophysin and neurofilament. Ki67 immunostaining showed 10% reactivity, respectively (Fig. 3).

Considering the above findings, the aPXA was diagnosed.

Brain MRI and physical examinations did not reveal any neurologic or dermatologic sign of phakomatosis.

**Discussion**

Our case is an extremely rare case of a rapidly growing anaplastic form of PXA in the retina of a 9-year-old girl with no evidence of phakomatosis.

PXA accounts for less than 1% of all brain astrocytic tumors and rarely transforms to anaplasia. Retina is an uncommon site for PXA and subsequently anaplastic PXA. Two-thirds of PXAs are associated with phakomatosis. Takafumi et al. have shown the total reported cases of retinal astrocytomas unassociated with TSC, regardless of being PXA or aPXA. However, Shields et al. have classified them and added two new cases of retinal aggressive PXA unassociated with TSC to the ten previously reported retinal aPXA cases.

No gender or racial predilection for PXA has been reported in the literature. There are many clinical and histopathological similarities between retinal aPXAs with and without TSC, except for enucleation at older ages in aPXA patients without TSC. Retinal astrocytic hamartomas associated with TSC generally show a low tendency to grow. Our case is similar to Shields’ review on acquired aPXAs in which most of their cases had unilateral and solitary tumors, and also that blind painful eye or progressive growth were the most common causes of enucleation. Our case also had a rapidly growing tumor unresponsive to the chemotherapy. A wide age range at the enucleation (i.e., between 1 and 56 years) has been reported for retinal aPXAs without TSC. Our case did not show the signs of TSC in systemic evaluation. However, later progression to TSC is unpredictable.

Histologically, PXA is composed of spindle cells, xanthomatosous cells, bizarre mononuclear or multinucleated giant cells, mitotic index (MI) less than five in ten HPF, eosinophilic granular bodies (Rosenthal fibers), and calciospherites with numerous reticulin fibers. The anaplastic form of PXA (aPXA), which is associated with shorter survival and more recurrence rate, is histologically defined as PXA with more than five MI in ten HPF, cellular anaplasia, high Ki67 labeling indices (LI), and decreased reticulin fibers with or without necrosis, but still maintains eosinophilic granular bodies, desmoplasia and xanthomatos changes which are characteristics for PXA and differentiate it from glioblastoma.
It is noteworthy that 1–5% of PXAs and 4–22% of aPXAs are immune-reactive for Ki67 LI\textsuperscript{12} which is a more reliable index than MI for proliferation potential estimation.\textsuperscript{12} The 10% immunoreactivity for Ki67 in our case is compatible with the reported Ki67 LI of aPXA in the literature.\textsuperscript{12} Regarding the Korshunov grading system for PXA,\textsuperscript{15} our case with the rapid tumor growth, moderately high Ki67 LI, greater nuclear pleomorphism and necrosis than conventional PXA could not be considered a benign PXA. Moreover, previous chemotherapies could affect the mitotic rate.

Both neuroglial and histiocytic features of PXA were detected in our case.\textsuperscript{11,12,16} Neural differentiation is important for PXA to differentiate it from astrocytoma or glioblastoma.\textsuperscript{12}

Only half of PXAs express CD34. This immunoreactivity is more apparent in PXA than in aPXA.\textsuperscript{12} Only few cells of our case expressed CD34.

PXA and aPXA do not show a significant difference in P53 expression.\textsuperscript{12} Generally, more than 50% of P53 immunoreactivity indicates the presence of TP53 mutation.\textsuperscript{17} In our case, immunoreactivity for P53 was negative.

Common clinical differential diagnoses for PXA include retinoblastoma, choroidal melanoma, Coat's disease, capillary hemangioma, and choroidal osteoma. Less dilated tortuous vessels, the presence of subretinal yellow exudation, and entirely amelanotic feature are in favor of astrocytic hamartomas.\textsuperscript{9,18}

Globe preserving therapies such as brachytherapy, endoresection and photodynamic therapy have vision threatening risks\textsuperscript{19–21} and chemotherapy, similar to our case, is generally ineffective for PXA and aPXA.\textsuperscript{8,22}

As a conclusion, diagnosis of aPXA should be kept in mind in the case of retinal white mass with an aggressive course in young children without phakomatosis.

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