Case Report

Retinoblastoma in Adults: a Case Report and Literature Review

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Abstract

Purpose: To report a case of adult retinoblastoma with a wrong diagnosis of melanoma.
Case report: Herein, we present an adult retinoblastoma case who was misdiagnosed as melanoma in fine-needle aspiration biopsy with intravitreal hemorrhage and later neovascular glaucoma after biopsy. The diagnosis of retinoblastoma was confirmed after enucleation.
Conclusion: Retinoblastoma should be considered in the differential diagnosis of an intraocular mass in adults, especially when media haziness precludes adequate ophthalmoscopic visualization.

Keywords: Adult Retinoblastoma; Eye; Ocular Tumor; Retinoblastoma; Retinoma

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INTRODUCTION

Retinoblastoma is the most common primary intraocular malignancy in childhood.[1] The frequency of retinoblastoma ranges from 1 in 14,000 to 1 in 20,000 live births and about 90% of patients are diagnosed under 3 years of age.[1] In the majority of cases, the diagnosis is made before 5 years of age.[2] It is thought that retinoblastoma arises from retinoblasts, which are retinal precursor cells.[3] The literature pertaining to retinoblastoma affecting adults is scarce, however the vast majority of cases have been isolated reports.[4-13] Despite clinical improvements in the field of ocular oncology for establishing a preoperative diagnosis, a small number of atypical cases still defy accurate clinical diagnosis.

Herein we report a isolated of late presentation of retinoblastoma in a 29-year-old woman that was not diagnosed by cytology in a vitrectomy specimen but proved to be retinoblastoma tumor later in the enucleation specimen.

CASE REPORT

A 29-year-old woman with a complaint of diminished vision in her left eye since 7 months ago was referred to our clinic. She had a history of left eye redness which did not respond to topical medications. In past medical history, she had a seizure attack 4 years before and had received appropriate treatment.

Examination in the right eye (OD) was normal. In the left eye (OS), visual acuity was one meter finger count, anterior segment examination was normal, intraocular pressure was 14 mmHg, and relative afferent pupillary defect was 2+. In the posterior segment examination, there was a dome-shaped partially pigmented mass with vitreous hemorrhage obscuring tumor features.

Orbital magnetic resonance imaging (MRI) revealed an enhancing nodular mass lesion in the posterior aspect of the left globe protruding into the vitreous and associated with exudative or nearby hemorrhagic retinal detachment [Figures 1a, 1b and 1c]. B scan of left eye revealed a dome-shaped solid mass with high internal reflectivity 16.5 × 12.5 × 11 mm in size with point calcifications [Figures 1d and 1e].

Intraocular tumor, possibly retinoblastoma or aggressive astrocytoma, was considered as a provisional diagnosis and biopsy was suggested. Fine-needle

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aspiration biopsy (FNAB) was performed but the specimen lacked enough cells for definitive diagnosis. Vitrectomy (23 G) assisted biopsy was carried out. The sample was obtained from the vitreous after removing the vitreous hemorrhage and also from the tumor by high aspiration and low cut level.

With a histologic diagnosis of choroidal melanoma, enucleation was proposed but was refused by the patient. After one month, the patient presented with severe left eye pain, visual acuity was no light perception, anterior segment showed circumcilliary congestion, neovascularisation of the iris and angle with intraocular pressure of 60 mmHg. Due to severe pain and loss of vision, at the time, the left eye was enucleated.

In the pathology report, macroscopically, a blood filled globe cavity and a tumor with hypo and hyperpigmented areas and foci of hemorrhage 20 mm in diameter and 5 mm in thickness was shown [Figure 1f]. The microscopic section was composed of atypical proliferation of cellular elements with small round hyperchromatic nuclei and scant cytoplasm, arranged as closely packed cells forming a nodule occupying half of the posterior chamber. The neoplastic cells were differentiated in some areas accompanied by Flexner-Wintersteiner rosette formation [Figure 1g and 1h]. No calcification was reported. For a definite diagnosis immunohistochemistry (IHC) study was recommended. IHC stains were positive for neuron-specific enolase (NSE), retinoblastoma protein and synaptophysin and negative for human melanoma black 45 (HMB45) and leukocyte common antigen in the tumor cells and hence the final diagnosis was retinoblastoma.

DISCUSSION

Retinoblastoma, a tumor originating from the sensory retina, is the most common primary intraocular tumor in childhood. According to Shields et al only 8.5% of patients with retinoblastoma are older than 5 years at the time of diagnosis and all reported cases were sporadic.[5] Due to its low frequency, retinoblastoma in adults creates a diagnostic dilemma.[4,5] The presence of vitreous hemorrhage, inflammation, and cataract further complicate the diagnosis[6] as in our patient in whom vitreous hemorrhage was the presenting sign precluding careful funduscopy and B scan revealed the point calcified mass. Although late presenting retinoblastoma is uncommon, there are a number of case reports of these cases (30 cases).[7,8]

Calcification is not an important finding in adult onset retinoblastoma cases. Ultrasonography and computed

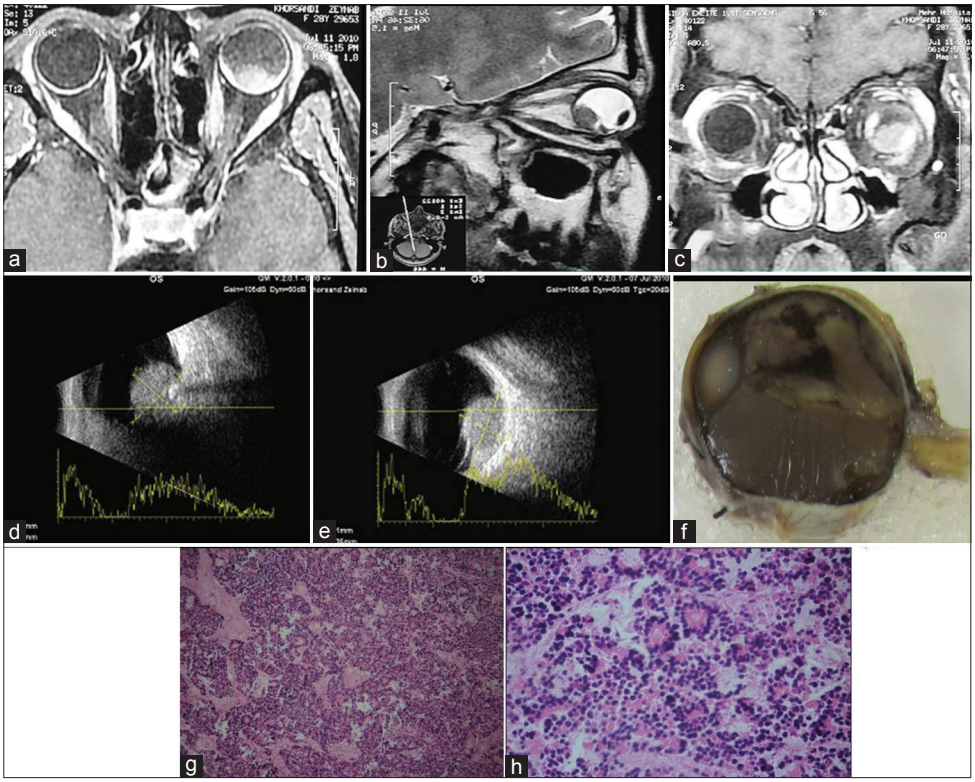

Figure 1. Imaging and histologic findings of an adult onset retinoblastoma. (a) Magnetic resonance imaging (MRI) T1 image shows a hyperintense lesion in the posterior part of the left globe that is hypointense in T2 MRI image (b). (c) The lesion is intensifying by gadolinium injection. (d and e) B-scan echography reveals a dome-shaped lesion with a calcification area associated with retinal detachment. (f) Gross pathology of the enucleated eye shows partly a pigmented lesion in the posterior and inferior part of the globe occupying >50% of the globe. (g and h) The microscopic appearances of well-differentiated retinoblastoma in our case.

tomography scan may not reveal calcification, which is characteristic of retinoblastoma in children.[4]

Until date, in the reported cases the presentation age of retinoblastoma in adults ranged from 16 to 74 years. Fifteen patients were women. The third decade of life was the most common presenting age for adult retinoblastoma cases (13 patients). Flexner-Wintersteiner rosettes were reported in 10 patients, Homer-Wright's rosettes in 6 patients, non-specified rosettes in 6 patients, no rosettes in 7 patients, and in 2 patients the reports did not state the existence of rosettes.[4,6-13]

The use of FNAB and IHC (with NSE)[14] may be helpful and confirmatory. In our case, vitrectomy assisted biopsy led to a diagnosis of choroidal melanoma. In general, preoperative FNAB is not routinely performed in retinoblastoma to minimize the theoretical risk of tumor seeding,[15] however occasionally, FNAB could be a useful diagnostic procedure, when the diagnosis is clinically uncertain.[16] Despite the rare use of FNAB in the diagnosis of intraocular tumors, the risk of tumor recurrence in enucleated eyes was not increased after enucleation according to the literature.[15,17] Shields et al stated some risks of retinoblastoma dissemination after vitrectomy in eyes with unsuspected retinoblastoma, in older pediatric patients.[18]

There are a number of explanations for the late presentation of retinoblastomas. Persistence of rare embryonal retinal cells may lead to malignant transformation in later life.[19] The tumor may also arise from previously undiagnosed, spontaneously regressed/arrested retinoblastomas which have been reactivated.[20] Gallie et al suggested a modification in the original mutation model of oncogenesis proposed by Knudson[21] to explain the presence of retinoma and low penetrance *retinoblastoma 1 (RB1)* mutations in some families.[22] It is well-accepted that inherited retinoblastoma with germinal mutation will arise if a second event (mutation) occurs in susceptible immature (primitive) retinoblasts, whereas retinoma will be likely if a second event occurs in almost mature retinoblasts.[23,24]

This proposal states that *RB1* mutations are necessary, but not sufficient to induce retinoblastoma and some mutations in *RB1* do not inactivate the *RB1* protein completely, leading to partial penetrance.[22] Normal fundi were not previously documented in the reported patients and hence perhaps they did harbor a retinoma in which additional oncogenic mutations eventually occurred, leading to retinoblastoma tumor. Retinomas are clinically well-characterized quiescent retinal masses, clearly linked to *RB1* gene mutation, but they do not generally progress to malignant growth. There are few reports of retinoblastoma arising from previously documented retinoma or quiescent retinoblastoma.[23]

If retinoblastoma could be diagnosed in its early stage, less aggressive treatment modalities such as chemotherapy, photocoagulation, cryotherapy, brachytherapy, external beam radiation, and diathermy would be extremely useful.[25] Management of retinoblastoma should be guided by the objectives save life, retain anatomical integrity of the eye, preserve vision, and obtain good cosmetic results.[26] Enucleation is indicated for unilateral retinoblastomas which fill most of the globe and when there is little hope of salvaging vision.[27] Enucleation was the primary treatment modality in the majority of reported adult cases of retinoblastoma, as the lesions were detected at a fairly advanced stage and each patient had one normal unaffected eye. Few patients underwent external beam radiotherapy.[8]

Risk factors for orbital and/or metastatic disease from retinoblastoma include massive choroidal invasion, tumor invasion into extrascleral tissue, the retrolaminar optic nerve and the optic nerve resection line, which in turn correlate with poorer survival.[28-30] The question regarding the long-term survival of adults with retinoblastoma compared with usual retinoblastoma in children remains to be answered.

In the case reported herein, the difficulty in establishing the diagnosis of retinoblastoma in adults was illustrated. In conclusion, retinoblastoma should be considered in the differential diagnosis of an intraocular mass in adults, especially when media haziness precludes adequate ophthalmoscopic visualization and any amelanotic or partially melanocytic lesion in the fundus of a patient at any age should raise the suspicion of retinoblastoma.

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