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Primary Uveal Lymphoma: Report of Three Cases with Histopathology Proven

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Abstract

Purpose: To describe three cases of primary uveal lymphoma with histopathology proven and summarize the clinical and imaging characteristics of this rare disease.

Methods: Clinical description of three patients with primary uveal lymphoma.

Results: Our three cases have characteristics of primary uveal lymphoma both clinically and on imaging evaluation, except that two cases were bilateral involvement. Case 1 and case 3 showed conjunctival lesion when they presented to us, thus immediate biopsy was done and resulted in correct diagnosis with subsequent radiotherapy with favorable outcome. As for case 2, we had ignored a crescent acoustically empty lesion adjacent to scleral posteriorly on B scan. Preoccupied with the diagnosis of metastatic choroidal tumor initially, the patient lost the opportunity to be appropriate diagnosed and managed. The eye progressively lost all vision, neo-vascular glaucoma ensued and the eye had to be enucleated.

Conclusion: Through literature review and our own experiences, we recognized that the disease has many characteristics both clinically and on imaging evaluation, timely diagnosis can achieve, so long as highly suspicious is raised and meticulous inspection be performed.

Keywords: Primary uveal lymphoma; Primary intraocular lymphoma; Diagnose; Clinical characteristics; Histopathology

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Introduction

Most intraocular lymphoma is a Primary Vitreoretinal Lymphoma (PVRL) involving the retina and vitreous associated closely with Primary Central Nervous System Lymphoma (PCNSL) and with dimmed prognosis [1,2]. Uveal lymphoma is relatively rare, with secondary type metastatic from systemic lymphoma. Primary uveal lymphoma even rarer [3,4]. Our understanding has undergone three periods.

Firstly, Triefenstein in 1920, call it uveal lymphosarcoma [4]. In the second period, Crookes and Mullaney [5] and Ruan introduced the term lymphoid hyperplasia [6], while Gass [7] called it inflammatory pseudo tumor, denoting its benign nature. With the development of immunohistochemistry and molecular biology, uveal lymphoproliferative infiltration of the uveal now has been widely accepted as a low grade malignant lymphoma [8,9]. Because of its low incidence, and the lack of awareness, diagnosis is usually delayed. Herein, we report three histopathologic proved cases with quite different outcome and some lessons can be learned from it.

Case Presentation

Case 1

A 51-year-old man, presented to local hospital in November 2007 with painless visual loss and redness in his right eye. Examination showed 20/20 vision in both eyes with mild hyperopia. The main finding was KP (+) and elevated IOP. Topical steroids and anti-glaucoma eye drops were given but were in effective. He then went to two other hospitals with the same diagnosis, managements and similar results. Since vision deteriorated progressively, one half years later, the patient visited to the fourth tertiary hospital. Visual acuity at that time was 0.4 OD, 0.6 OS, Slit lamp revealed hyperemia of conjunctiva and scleral, mutton fat KP (++) present in both eyes. Dilated fundus examination showed vitreous cells (+), optic disc edema and exudative retinal detachment inferiorly. Bilateral scleritis were diagnosed and the patient was treated with prednisone 80 mg orally. Three

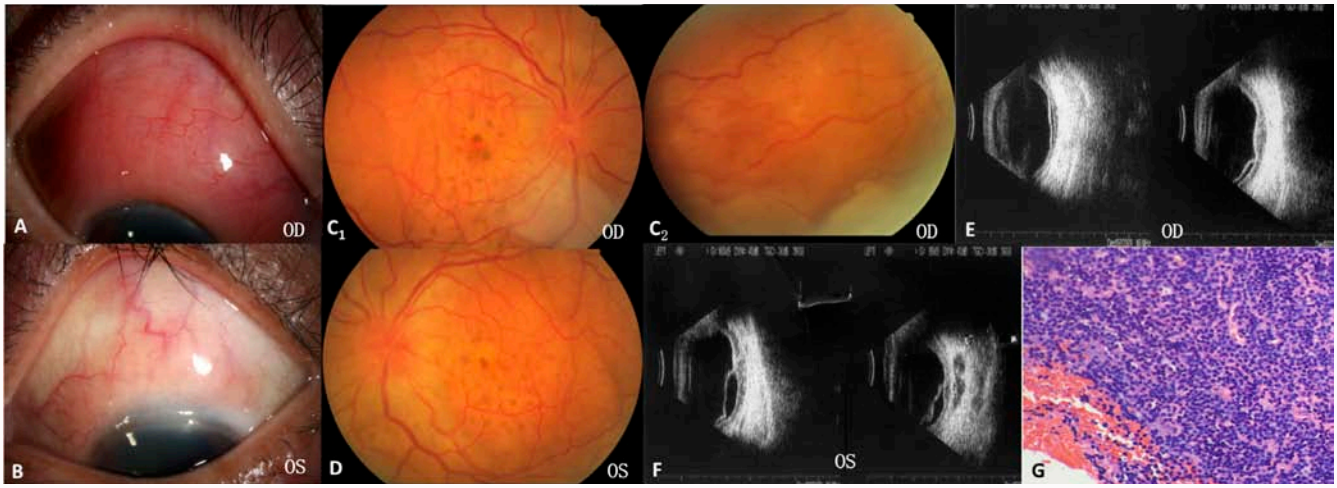

Figure 1: Case 1: Anterior segment photograph, fundus photographs, B-scan ultrasound and pathological section of the conjunctiva tissue. (A, B) Anterior segment photograph presented hyperemia and swollen conjunctiva in both eyes. (C1, C2, D) Fundus photographs presented exudative retinal detachment, swollen optic disc with subretinal scattered brown pigment spots in both eyes. (E, F) B-scan ultrasound showed diffuse choroid thickening with low to medium internal reflectivity and similar hyporeflectivity lesion behind eyeball adjacent to sclera in both eyes. (G) Pathological section of the conjunctiva tissue.

days later, VA improved in both eyes. While on tapering the steroid, visual acuity deteriorated. Oral prednisone 80 mg resumed with retrobulbar triamcinolone injection administered additionally, however, improvement was little. Bone marrow aspiration showed no abnormalities.

When the patient came to our hospital in December 2009, BCVA was 0.4 in the right eye and 0.3 in the left eye. Ocular movement was full with no proptoses. Hyperemia and swollen conjunctiva were present in both eyes (Figure 1A, 1B), more prominent in the right. KP was absent. Iris looked normal and vitreous was clear. Exudative retinal detachment, swollen optic disc with sub-retinal scattered brown pigment spots were observed in both eyes (Figure 1C, 1D). Break was not detected. B-scan ultrasonography showed diffuse choroid thickening with low to medium internal reflectivity in both eyes. Similar hypo-reflectivity lesion was seen behind eyeball adjacent to sclera (Figure 1E, 1F). MRI also showed thickening of eye wall in both eyes. Conjunctival biopsy was done on the right eye, pathology (Figure 1G) and PCR gene rearrangement showed lymphoid cell hyperplasia, consistent with primary uveal lymphoma.

Low dose radiotherapy administered to both eyes, visual acuity stabilized at 0.4 and 0.3 in right and left eye respectively till the last follow-up visit 6-years later. No recurrence was seen. Retina was attached with atrophic and proliferative pigmental changes.

Case 2

A 63-year-old man complained visual loss in his left eye for more than half a year, came to our hospital in 8/24/2014. Past medical history had controlled hypertension and diabetes mellitus. VA was 20/20 OD and HMOS. IOP measured 13 mmHg and 11 mmHg in the right and left eye, respectively. Except mild cataract in both eyes, the right was normal. In the left eye, there was pigmented KP and mild flare in the anterior chamber. Dilated fundus examination revealed pigment granules in the vitreous. An amelanotic subretinal mass located temporal peripherally was disclosed with inferior retinal detachment. In addition, whitish exudation was seen in the macula area. Laboratory investigations of serum were unremarkable except positive IgG results for *Herpesviridae* family. B scan ultrasonography showed choroidal mass temporally with undulating surface and secondary retinal detachment (Figure 2A). Metastatic choroidal carcinoma was diagnosed. The patient went back to hometown for evaluating the primary tumor.

Here turned back in December 14th, 2015 with progressing vision loss and pain in his eye for more than one month. Systemic evaluation, imaging of brain, chest, abdomen and PET-CT done in other hospital were all unremarkable. On examination, VA was 20/20 OD and no light perception OS. IOP was 14.3 mmHg in right eye, plus 2 to digital palpation in the left eye. Bio-microscopy revealed diffuse cornea edema pigmented KP, one plus flare, normal anterior chamber depth and iris neovascularization in the left eye. Mature cataract precluded visualization of the fundus. The right was unchanged.

Brain and orbit MRI showed a mass lesion on the top of the posterior wall and retinal detachment in the left eye. In addition, there was enlargement of the optic nerve and lacrimal gland. Both orbital roof and floor were thickened with infiltrates, suggesting choroidal melanoma with orbit extension (Figure 2B).

In view of loss of all visual acuity and choroidal melanoma could not be ruled out, the eye was enucleated with orbital mass resection. Histopathologic examination showed lymphocytic malignant tumor invading the iris, ciliary body, choroid, optic nerve, as well as orbital tissue. Immunohistochemistry showed (LCA(+), CD20(+), CD3(-), CD5(-), BCL-2(+), Ki-67 (60%+)) (Figure 2C, 2D). A final diagnosis is primary uveal lymphoma with orbital extension.

Case 3

A 73-year-old male presented with two years history of increasingly blurry vision and 1 year of redness of conjunctiva in his right eye. He was diagnosed retinal detachment outside without special treatment. On presentation at our hospital in July, 2013 V.A. was 0.2 OD and 0.6 OS. Slit lamp revealed a pinkish swollen conjunctiva of right eye (Figure 3A) and thickened lacrimal caruncle in the left eye (Figure 3B). Fundoscopy revealed thickened choroidal with exudative retinal detachment in the right, and a few scattered white spot lesions nasally in the left eye. B scan ultrasonography showed diffuse thickening of choroid with low to medium internal reflectivity. Two retrobulbar lesions adjacent to the sclera were seen with similar echo reflectivity

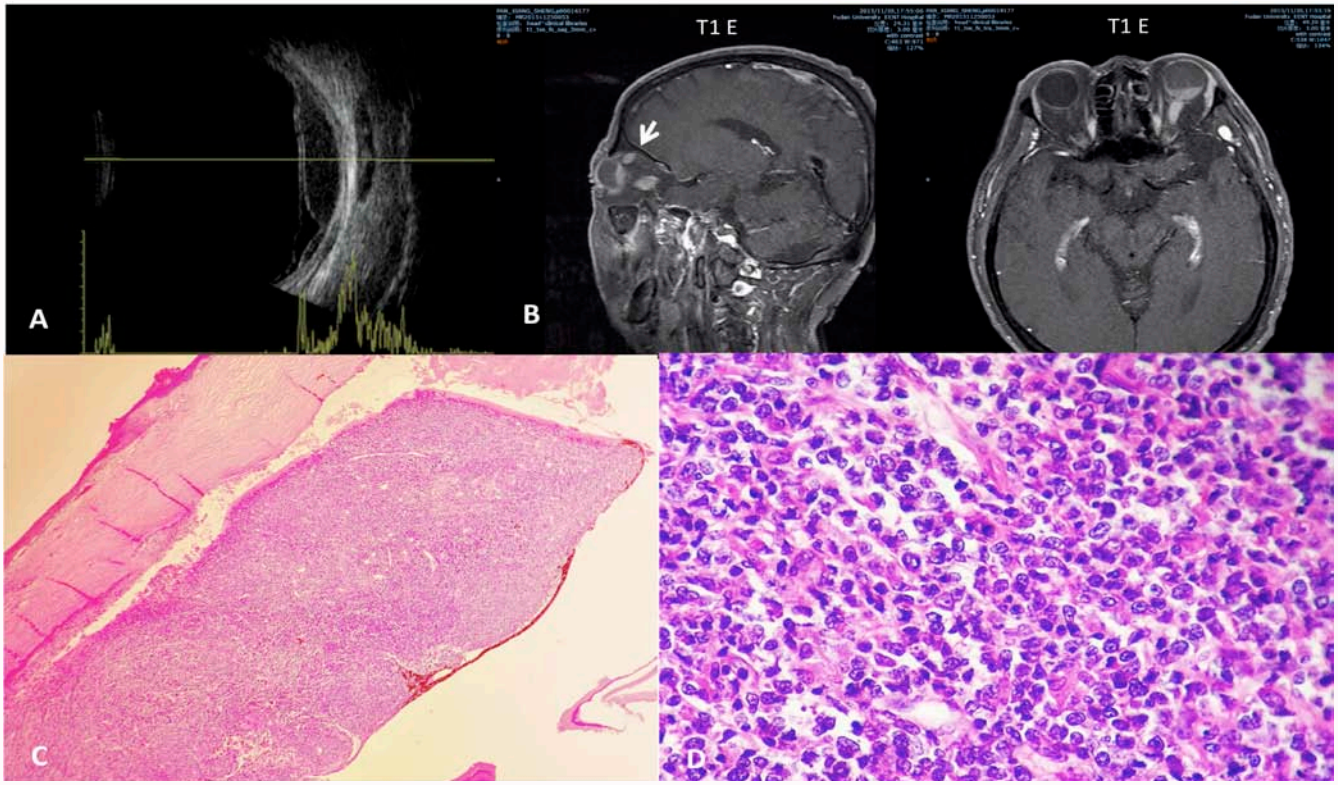

Figure 2: Case 2: B-scan ultrasound of the left eye, MRI, and pathological section of the tissue outside the left eye scleral. (A) B scan ultrasonography showed choroidal mass temporally with undulating surface and secondary retinal detachment, (B) Brain and orbit MRI showed a mass lesion on the top of the posterior wall and retinal detachment in the left eye. In addition, there was enlargement of the optic nerve and lacrimal gland. Both orbital roof and floor were thickened with infiltrates, Trans-scleral tumor specimen. (C) 40 times magnification of the lesion, (D) 400 times magnification of the lesion.

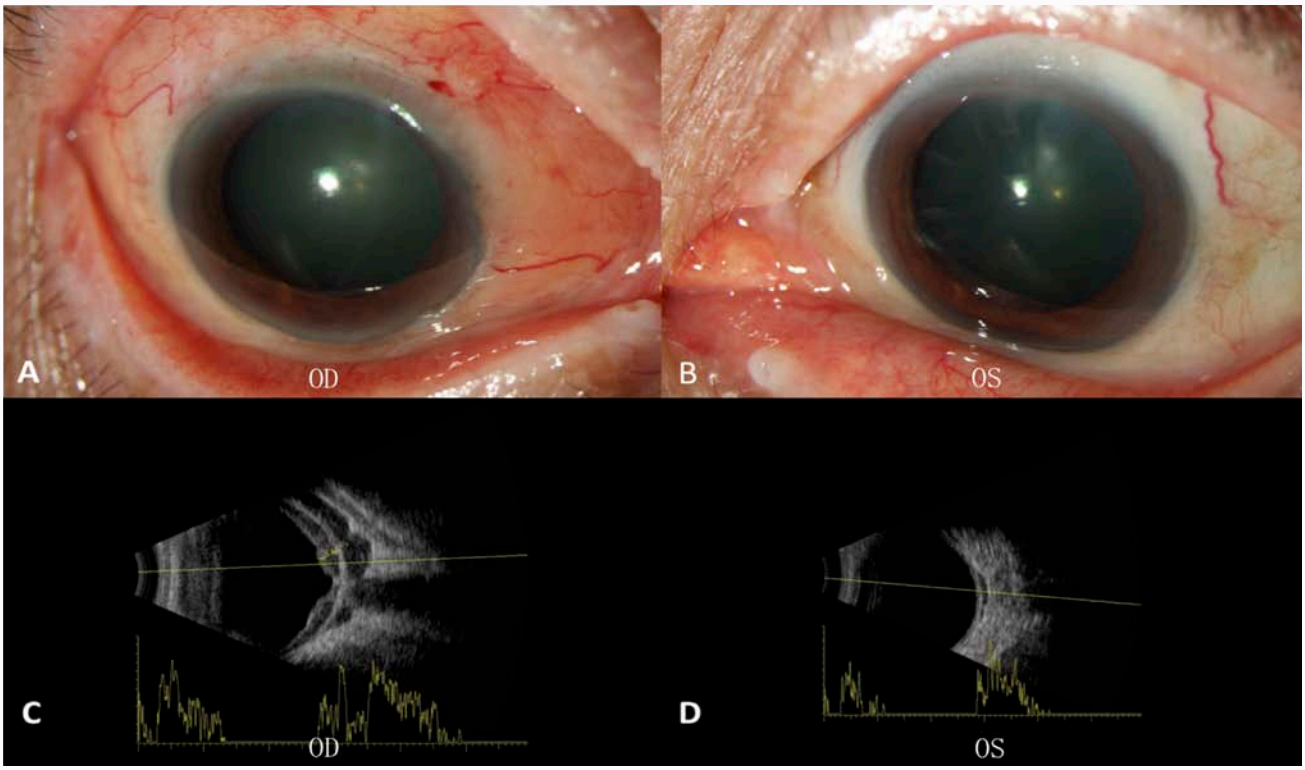

Figure 3: Anterior segment photograph and B-scan ultrasound of both of the eyes. Anterior segment photograph of the right (A) and left (B) eye revealed a pinkish swollen conjunctiva of right eye and thickened lacrimal caruncle in the left eye, B-scan ultrasound of right eye (C) and left eye (D) showed diffuse thickening of choroid with low to medium internal reflectivity, and two retrobulbar lesions adjacent to the scleral with similar echo reflectivity.

(Figure 3C, 3D). Conjunctival biopsy and immunohistochemistry staining showed B-cell lymphoma (LCA(+), CD20(+), CD3(-), CD79a(+), bcl2(+)). Additional blood analysis, chest, abdomen CT were unremarkable.

External radiotherapy was given to the right eye with good response. Conjunctival lesion reduced as well as the retrobulbar mass. Disappearance of choroidal thickening and retinal detachment were also noted.

Discussion

Primary uveal lymphoma has characteristic of clinical manifestations including old age, male gender, unilateral, slowly progressive clinical course, diffuse choroid thickening about 3 mm high [3] or a isolate whitish choroidal mass with retinal detachment. Extraocular extension presents pink fleshy conjunctival lesion anteriorly, which observed in more than half of the cases [3,10-12]. Imaging investigation also had characteristic of findings, especially on B scan ultrasonography, which included diffuse choroidal thickening with low internal reflectivity but without excavation. Round or crescentic shape peripapillary nodule adhering to scleral with similar low internal reflectivity [3,13,14], further confirmed by orbit MRI imaging. Our three cases have characteristics of primary uveal lymphoma both clinically and on imaging evaluation, except that two cases were bilateral involvement. However, bilateral case had been reported in the literature [3,4]. In the first and the third case, because the present of conjunctival lesion, which is most accessible and less invasive for biopsy [10,15], immediate biopsy was done and resulted in correct diagnosis with subsequent radiotherapy with favorable outcome. The first case had refractory glaucoma as one of his initial presentation, the high intraocular pressure resisting to conventional pressure lower eye drops. The mechanism of glaucoma may be due to lymphoma cells blocking the chamber angle and the trabecular meshwork as reported by Cockerham et al. [8] in his pathologic study. The elevated IOP could only be resolved with pathogenic eradication. The first case has been followed up for 6 years with free recurrence and maintained relevant vision until the latest visit. Similar situation has been seen in the third case, long term follow up was lacking though. As for the second patient, although in many aspects, it resembles the characteristics of primary uveal lymphoma. Unfortunately, we had ignored a crescent acoustically empty lesion adjacent to scleral posteriorly on B scan, which is one of the most diagnostic features described by many authors [10-12,16,17]. Preoccupied with the diagnosis of metastatic choroidal tumor initially, even no primary tumor was found. The patient lost the opportunity to be appropriate diagnosed and managed as a result. The eye progressively lost all vision, neo-vascular glaucoma ensued and the eye had to be enucleated. If we had paid enough attention to this extra-scleral lesion to do biopsy [11,16] or even move forward to perform choroidal biopsy in case of absence of retro-bulbar mass, correct diagnosis may be achieved [18-20] and this eye would be saved.

For the management, though steroids have been used by some [6,21], immune-chemotherapy with rituximab has been reported [22]. Low dose radiation has been the most frequently used modality with good response and low complications [23], as evidence backed by our patients too. Our second patient already had extensive orbit involvement as well as the presence of tumor cells in the cutting edge of the optic nerve, further interventions with radiation or chemotherapy should be seriously considered and long term follow up is needed.

In conclusion, primary uveal lymphoma is a rare disease, diagnosis is usually delayed resulting in poor prognosis, and otherwise the overall prognosis is usually benign. Through literature review and our own experiences, we recognized that the disease has many characteristics both clinically and on imaging evaluation, timely diagnosis can achieve, so long as highly suspicious is raised and meticulous inspection be performed.

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