Ocular Central Nervous System Lymphoma Mimicking Choroidal Neovascularization

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ABSTRACT
Two patients evaluated for metamorphopsia were noted to have inferotemporal retinal pigment epithelium elevations formed by a yellowish lesion. Fluorescein angiography showed granular hyperfluorescence with late leakage, which was interpreted as an occult choroidal neovascularization. One patient underwent photodynamic therapy. In both patients, neither vitreous cells nor neurologic manifestations were evident on presentation. Subsequent neurological signs appeared that prompted performance of brain imaging, which confirmed a space-occupying lesion. In both patients, the tumor was proven on histopathologic examination of brain tissue to be central nervous system lymphoma. Awareness of other possible underlying pathologies is warranted in cases of atypical choroidal neovascularization. [Ophthalmic Surg Lasers Imaging 2008;39:146-149.]

INTRODUCTION
Primary central nervous system lymphoma is a form of non-Hodgkin’s lymphoma, which is mostly large B-cell lymphoma,1 that occurs primarily in the sixth decade of life.2-4 We report an unusual presentation of ocular–central nervous system lymphoma in two patients.

CASE REPORTS
Case 1
A 75-year-old man was referred because of micropsia and metamorphopsia in his left eye. Visual acuity...
was 20/20 in the right eye and 20/40 in the left eye. Ocular examination revealed a mild nuclear cataract in the right eye and a posterior chamber intraocular lens in the left eye. The vitreous was clear, with no cells in both eyes. Fundus examination of the left eye demonstrated a subfoveal yellowish subretinal lesion with retinal pigment epithelial elevation inferotemporally (Fig. 1A), demonstrating early granular hyperfluorescence with late staining on fluorescein angiography. The differential diagnosis included occult choroidal neovascularization, although no drusen were noted in either eye. Follow-up was recommended.

One month later, visual acuity had deteriorated to 20/60 in the left eye. Repeat fluorescein angiography showed an area of subfoveal granular hyperfluorescence with evident leakage, interpreted as occult subfoveal choroidal neovascularization (Fig. 1B). The patient underwent photodynamic therapy. Due to persistence of leakage over the subsequent months, the patient underwent three additional photodynamic therapy treatments.

Eight months after presentation, the patient experienced mental deterioration. Brain imaging revealed a space-occupying lesion. Histopathologic examination of a biopsy specimen taken during craniotomy demonstrated large B-cell lymphoma of the brain (Fig. 2). The patient was treated with systemic chemotherapy but died.

Case 2

A 58-year-old man noticed a decrease in vision and metamorphopsia in his left eye. Best-corrected visual acuity was 20/40 in the right eye and 20/60 in the left eye. Examination of both eyes revealed an elevation of the retinal pigment epithelium inferotemporal to the fovea with late staining on fluorescein angiography (Fig. 3). There were no cells in the vitreous in both eyes. An ultrasound examination performed to rule out scleritis showed bilateral mild chorioretinal thickening with some fluid around the optic nerve, which was more prominent in the left eye. No evidence for vitreous haze or cells was demonstrated. Therefore, the differential diagnosis of ocular lymphoma was not raised and diagnostic vitrectomy was not considered.

Subsequent appearance of severe headaches prompted performance of magnetic resonance imaging. A large tumor around the tuberculum sellae with posterior extension beyond the optic chiasm, mainly on the left side, was demonstrated. Histopathologic examination of a specimen taken during craniotomy revealed solid sheets of medium-large atypical cells positive for B-cell marker CD20 (Fig. 4). The diagnosis of primary large B-cell central nervous system
lymphoma was established. The patient’s disease deteriorated rapidly into deep coma and he died a few months later.

DISCUSSION

Primary ocular–central nervous system lymphoma defines a rare variant of primary central nervous system lymphoma in which the malignant cells are initially present only in the eyes. Between 60% and 80% of patients subsequently develop central nervous system disease within a mean period of 29 months (range: 7 to 108 months).1-3

The common clinical presentation of primary ocular–central nervous system lymphoma, termed the vitreoretinal4 form, is the appearance of visual “floaters” and a painless decrease in vision. The presence of vitreous cells is typical, and yellowish-white infiltrates deep to the sensory retina in a focal, multifocal, or diffuse pattern are also characteristic.5 Exudative retinal detachment may occur infrequently,6,7 usually as a late finding. Rarely, the disease may present as a solitary intraocular mass, simulating amelanotic melanoma.6

Primary ocular–central nervous system lymphoma should be distinguished from a metastatic spread of systemic non–Hodgkin’s lymphoma to the uveal tract.4 This uveal form, which is bilateral in 80% of cases, presents with red or painful eyes. Posterior uveitis is typical, with or without associated anterior uveitis.8

Fluorescein angiography findings of ocular lymphoma previously described in the literature include hyperfluorescent white spots,9 retinal vasculitis with disc edema,9 window defects,10,11 and early blockage with late staining of lesions.10 The presence of hypofluorescent retinal pigment epithelium detachments is considered characteristic, corresponding histopathologically to tumor infiltrates.11 In a report of 31 eyes with primary ocular–central nervous system lymphoma, typically presenting with vitreous cells, the most prominent fluorescein angiography findings were disturbances at the retinal pigment epithelium level,10 defined as granularity, “mottling,” and late staining, noted both within and outside the arcades. Hyperfluorescent retinal pigment epithelium detachments were noted in three eyes, probably representing a different viable tumor cell density within the pigment epithelial detachment.10

In our two patients, the absence of vitreous cells and the clinical finding of inferotemporal masses, which showed granular hyperfluorescence intensifying in late frames of fluorescein angiography, led to the erroneous diagnosis of occult choroidal neovascularization. The delay in establishment of the correct diagnosis of lymphoma resulted in performance of unnecessary craniotomy in one patient. We suggest that awareness to other possible underlying disease may be warranted in cases of atypical occult choroidal neovascularization.

REFERENCES
