Case Report

Presumed Intraocular Lymphoma Masquerading as Age-Related Macular Degeneration: A Case Report

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Abstract

Purpose: To describe a case of primary vitreoretinal lymphoma (PVRL) that initially presented and managed as dry type age-related macular degeneration (AMD).

Methods: A 69-year-old male was referred to us by decreased vision.

Results: On funduscopy, a few small hard drusen at the posterior pole of the right eye and many large confluent drusen in the left eye were observed. Optical coherence tomography findings included the hyperreflective drusenoid materials in the subretinal pigment epithelium (sub-RPE) space which was similar to previous imaging records except for decreased area and height of pigment epithelial detachments and RPE and ellipsoid zone attenuation in some areas appeared. The thickness of the retina was normal, but the choroid appeared to be slightly decreased compared to the left eye. Patient has been followed up with the diagnosis of AMD for 1 year. After the right hemiparesis presentation, he underwent craniotomy and biopsy that made the diagnosis evident.

Conclusion: PVRL/primary central nervous system lymphoma may be one of the most important masquerades of AMD, but a significantly waxing and waning course may help to make correct diagnosis.

Keywords: Age-related macular degeneration, Masquaredes, Primary central nervous system lymphoma, Primary vitreoretinal lymphoma, Uveitis

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Submitted: 28-Jun-2019; **Revised:** 01-Dec-2019; **Accepted:** 05-Dec-2019; **Published:** 30-Apr-2020

Introduction

Clinical spectrum of age-related macular degeneration (AMD) includes a wide array of manifestations that may resemble the findings of other diseases. A correct diagnosis of these masquerades of AMD is crucial, not only for the patients' well-being but also from a prognostic point of view.[1]

Primary central nervous system lymphoma (PCNSL) is a large B-cell non-Hodgkin's lymphoma of the brain. It is estimated that PCNSL is responsible for 4–6% of primary brain tumors.[2] The incidence has tripled over the past years. Up to 25% of patients with PCNSL have or ultimately develop an ocular manifestation of the lymphoma. Primary vitreoretinal lymphoma (PVRL), as a subset of PCNSL, is a rare and fatal intraocular malignancy. PVRL frequently masquerades as chronic uveitis, especially in patients older than 60 years old, and the complexity of the management of samples obtained from ocular fluids poses a challenge.[3] Here, we describe a case of intraocular lymphoma that initially presented and was managed as a case of bilateral asymmetric dry type AMD to suggest that PVRL should be considered a masquerade of dry type AMD.

Access this article online

Quick Response Code:

Website: www.jcurrophthalmol.org

DOI: 10.4103/JOCO.JOCO_106_20

How to cite this article: Riazi-Esfahani H, Hassanpoor N, Ghassemi F, Zarei M. Presumed intraocular lymphoma masquerading as age-related macular degeneration: A case report. J Curr Ophthalmol 2020;32:207-10.

Case Report

A 69-year-old male was referred to the retina service of Farabi Eye Hospital. He was a diagnosed case of PCNSL with the right hemiparesis, for which he underwent craniotomy about 3 weeks ago.

The patient's visual complaints had started almost 1 year earlier. At that time, ophthalmic examination by an ophthalmologist was performed, and a best corrected visual acuity (BCVA) of 20/25 in each eye and mild bilateral cataract were documented. No cellular reaction in the anterior chamber and anterior vitreous was noted. Intraocular pressure (IOP) was within the normal limits bilaterally. Funduscopy revealed small-to-medium size drusen, more prominent in the left eye. Optical coherence tomography (OCT) demonstrated multiple subretinal pigment epithelium (sub-RPE) and subretina deposits compatible with drusen and subretinal drusenoid deposits [Figure 1]. Fluorescein angiography (FA) presented tiny hyperfluorescent spots with the areas of blockage due to vitreous organization [Figure 1]. The patient was followed with the diagnosis of dry type AMD.

Six months later, the vision was decreased to 20/50 in his left eye, and the patient was evaluated in another center.

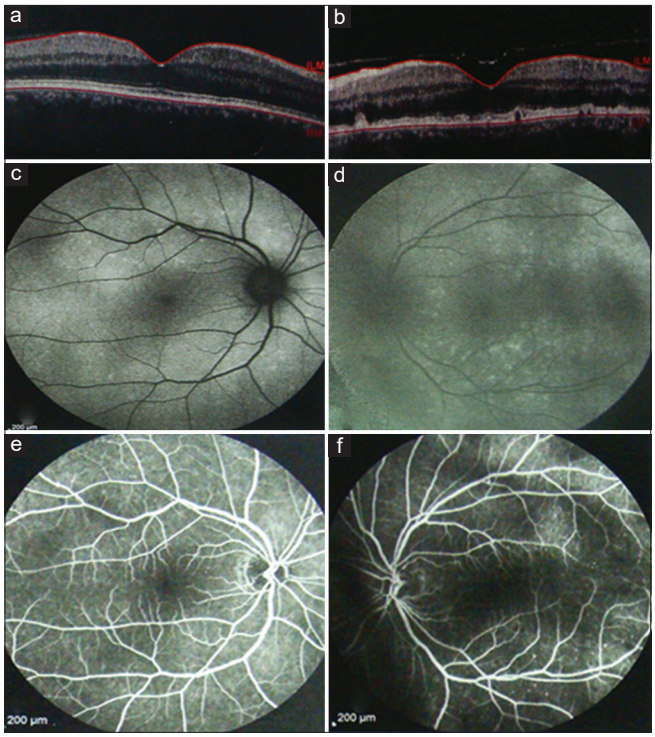

Figure 1: Images from the first ophthalmic evaluation. Optical coherence tomography of the right (a) and left (b) eyes show subretinal pigment epithelium/pre-Bruch's deposits resembling small-to-medium size drusen, more prominent in the eft eye. Multiple tiny hyperautofluorescent spots are evident in the right (c) and left (d) fundus autofluorescence images. Multiple tiny hyperfluorescent dots are seen in fluorescein angiography (e and f) with areas of blockage that is caused by vitreous organization

A new OCT showed that the sub-RPE/pre-Bruch's deposits had become more confluent and larger [Figure 2]. Subretinal hyperreflective materials had also increased. Intravitreal bevacizumab was injected in the left eye for a presumed diagnosis of wet type AMD. Three months later, the vision improved to 20/32, but hemiparesis developed, and after neuroimaging, a brain biopsy confirmed the diagnosis of PCNSL. Three weeks later, while recovering from craniotomy, and before receiving any chemo/radiation treatment, the patient was referred to the retina service in Farabi Eye Hospital.

On examination in our hospital, patient had no pain and redness in eyes. BCVA was 20/25 in the right eye and 20/32 in the left eye. Slit-lamp examination of the left eye revealed +2 cells in the anterior vitreous with some degree of organization in vitreous. Right eye slit-lamp examination was unremarkable except for mild cataract. IOP was17 mmHg in the right and 19 mmHg in left eye. On funduscopy, a few small hard drusen at the posterior pole of the right eye and many large confluent drusen in the left eye with yellowish subretinal plaque-like lesion temporal to macula were observed.

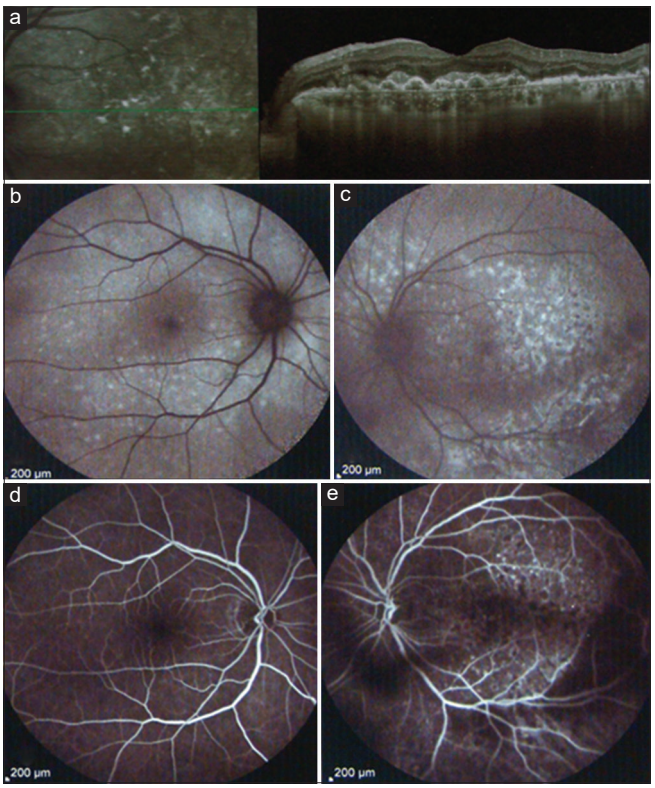

Figure 2: Images, 6 months after initial presentation. In the left eye, optical coherence tomography, (a) subretinal pigment epithelium/pre-Bruch's deposits have become more confluent and larger than previous images. There are pigment epithelial detachments and subretinal deposits with accompanying irregularities in retinal layers. Tiny hyperfluorescent dots are increased in fundus autofluorescence and fluorescein angiography images, especially in the left eye (starry sky appearance) (b-e). At this stage, patient received intravitreal bevacizumab injection in his left eye for presumed wet type age-related macular degeneration

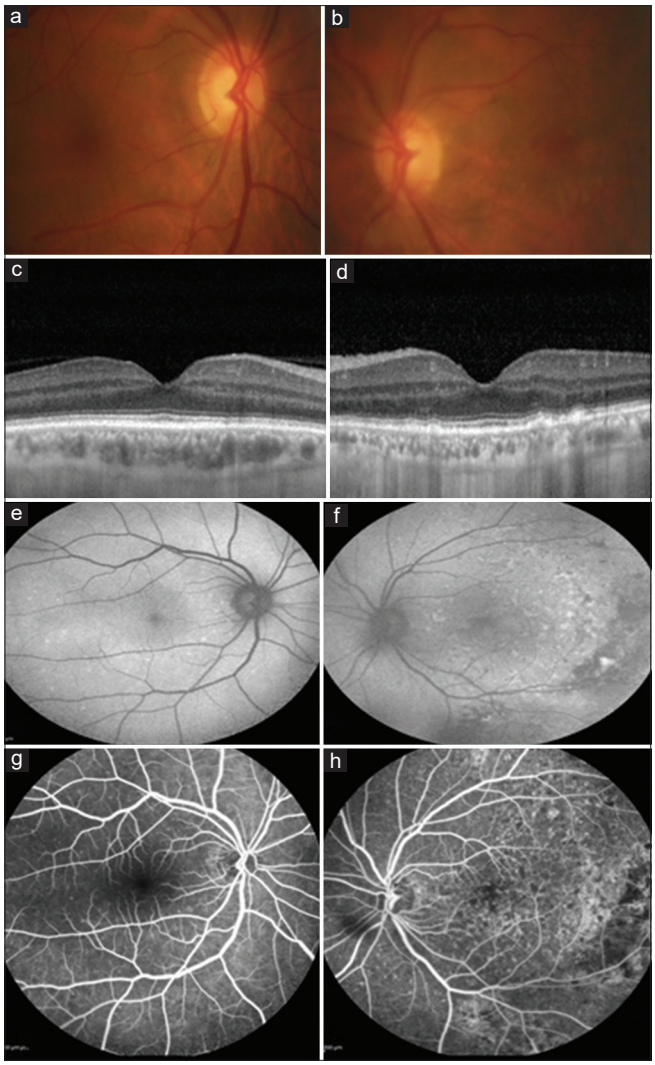

Figure 3: Patient's images at the time of referral to our center (1 year after initial presentation). Fundus of the right (a) and left (b) eye are poorly visible due to hazy media but show multiple drusen more prominent in the left eye and also a faint yellowish subretinal plaque-like lesion temporal to the macula of the left eye. Optical coherence tomography findings include hyperreflective drusenoid materials in subretinal pigment epithelium (sub-RPE)/pre-Bruch's area, that show decrease in size from earlier images with some areas of RPE and ellipsoid zone attenuation (c and d). Although retinal thickness appears not to be affected, choroid is slightly thin, especially in the left eye. Fundus autofluorescence (e and f) showed areas of hypoautofluorescence due to RPE atrophy and blocking infiltrates and hyperautofluorescence indicating stress on RPE. Fluorescein angiography showed multiple early hypofluorescent spots on a background of hyperfluorescence at the posterior and equatorial fundus corresponding to the subretinal deposits. There was evidence of some window defect in some areas of the left fundus (g and h)

OCT findings included hyperreflective drusenoid materials in sub-RPE/pre-Bruch's space, which compared to previous imaging records, showed decreased area and height and RPE and ellipsoid zone attenuation in some areas [Figure 3]. The thickness of retina was normal, but the choroid seems to be slightly thinned, especially in the left eye. FA showed multiple early hypofluorescent lesions on a background of hyperfluorescence on the posterior and equatorial fundus corresponding to the subretinal deposits. There was also evidence of window defects in some areas of the left fundus.

As the diagnosis of PCNSL with ocular involvement was established by brain biopsy, systemic, and intravitreal chemotherapy was initiated for the patient.

As there was a histopathologic confirmation for the central nervous system (CNS) involvement of PCNSL, based on our literature review, it seemed that there was no need to do vitrectomy and confirm the eye involvement. We decided to start intravitreal chemotherapy based on CNS biopsy report. Unfortunately, due to unstable systemic condition, the patient did not come back to us for intravitreal chemotherapy, and we have been informed that he has passed during the first chemotherapy session. Informed consent was obtained from the patient's son to report this case.

Discussion

This case shows that the diagnosis of intraocular lymphoma requires a high degree of clinical suspicion and should be suspected in the presence of confluent drusen, especially when they are asymmetric between two eyes or have a waxing and waning course.

On initial presentation, vitreous organization and sub-RPE/pre-Bruch's deposits – resembling small-to-medium-size drusen – were present simultaneously. This was followed by an increase in the number and extent of lesions that caused a rippled appearance of RPE, parallel with the accumulation of subretinal materials. The lymphoma cells in the primary ocular-CNS lymphoma appear to arise primarily in the sub-RPE/pre-Bruch's membrane space and/or vitreous. Patients show a wide variety of pictures that may simulate many ocular disorders.

RPE dysfunction may be the cause for this accumulation.[4] In this case, the location of these subretinal materials is consistent with sub-RPE infiltration.

There are some possible clues to differentiate this case from dry type AMD. In this case, symptoms at presentation were blurred vision and/or floaters, but visual acuity was better preserved than that expected. Vitritis and vitreous organization are not usual findings in a patient with AMD.[3,5,6]

The large and confluent solid pigment epithelial detachments (PEDs) were regressed in this case during follow-up period. There are some reports of a remarkable tendency of sub-RPE lesions to be spontaneously resolved in primary ocular/CNS lymphoma,[7] but this does not occur usually in dry type AMD.[7] When such regression occurs, RPE atrophy, ellipsoid zone attenuation, and subretinal fibrosis may develop, similar to what was seen in our case.[6] Of note, regression of the sub-RPE lesions was not synonymous with regression of the underlying lymphoma.[4]

Primary ocular lymphoma frequently reported to be a masquerade of both infectious and non-infectious uveitis, such as acute retinal necrosis syndrome, tuberculosis, retinochoroidal toxoplasmosis, syphilitic retinitis, endophthalmitis, sarcoidosis, punctuate inner choroiditis (PIC), and idiopathic uveitis.[5,8] Herein, we report a case of presumed primary CNS/ocular lymphoma that masquerades as AMD.

In 2016, Komatsu *et al*.[9] reported a case of primary intraocular lymphoma (PIOL), in which vitelliform maculopathy was accompanied with vitreous organization and sub-RPE infiltration in the peripheral retina. Pang *et al*.[4] pointed out the importance of vitelliform maculopathy as a preceding lesion in PIOL in three cases. In all cases, subretinal materials were transient and preceded diagnosis of PVRL, suggesting a paraneoplastic process, though the possibility of lymphoma cells presented as subretinal debris cannot be excluded.[4]

In a case series described by Keino *et al*.,[10] spectral-domain OCT (SD-OCT) images revealed hyperreflective nodules or bands above or at the level of the RPE and separation of RPE from Bruch's membrane in near one-fourth of cases. However, their most common SD-OCT finding was attenuation of the ellipsoid zone that was seen in nearly one-half of the cases. We showed that the large solid sub-RPE infiltrations may decrease spontaneously over time and lead to small PEDs with attenuated ellipsoid zone.

In summary, PVRL/PCNSL can present as multiple confluent drusenoid PEDs with sub-RPE materials that can regress spontaneously within 3–6 months, leaving small solitary PEDs. PVRL/PCNSL may mimic AMD, but a significantly waxing and waning course may help make correct diagnosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Reddy SV, Huckfeldt RM. Masquerades of Age-Related Macular Degeneration. Focal Points 2018, Module 8: 1-18. Available from: https://store.aao.org/focal-points-2018-module-masquerades-of-age-related-macular-degeneration.html. [Last accessed 01 Dec 2019].
2. Mochizuki M, Singh AD. Epidemiology and clinical features of intraocular lymphoma. Ocul Immunol Inflamm 2009;17:69-72.
3. Riemens A, Bromberg J, Touitou V, Sobolewska B, Missotten T, Baarsma S, *et al*. Treatment strategies in primary vitreoretinal lymphoma: A 17-center European collaborative study. JAMA Ophthalmol 2015;133:191-7.
4. Pang CE, Shields CL, Jumper JM, Yannuzzi LA. Paraneoplastic cloudy vitelliform submaculopathy in primary vitreoretinal lymphoma. Am J Ophthalmol 2014;158:1253-6100.
5. Sagoo MS, Mehta H, Swampillai AJ, Cohen VM, Amin SZ, Plowman PN, *et al*. Primary intraocular lymphoma. Surv Ophthalmol 2014;59:503-16.
6. Zhou M, Xu G. Recent progress in the diagnosis and treatment of primary vitreoretinal lymphoma. Taiwan J Ophthalmol 2016;6:170-6.
7. Kase S, Namba K, Jin XH, Kubota KC, Ishida S. Spontaneous regression of intraocular lymphoma. Ophthalmology 2012;119:1083-4.
8. Miserocchi E, Modorati G, De Benedetto U, Colucci A, Bandello F. Birdshot retinochoroidopathy masquerading as intraocular lymphoma. Ocul Immunol Inflamm 2012;20:306-8.
9. Komatsu K, Sakai T, Kaburaki T, Tsuji H, Tsuneoka H. Atypical presentation of primary intraocular lymphoma. BMC Ophthalmol 2016;16:171.
10. Keino H, Okada AA, Watanabe T, Echizen N, Inoue M, Takayama N, *et al*. Spectral-domain Optical Coherence Tomography Patterns in Intraocular Lymphoma. Ocul Immunol Inflamm 2016;24:268-73.