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Case Report

Intravitreal rituximab for the treatment of a secondary intraocular relapse of a large B-cell lymphoma

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ABSTRACT

Purpose: To report a rare case of secondary intraocular lymphoma treated with intravitreal rituximab, following pars plana vitrectomy.

Observations: A 74-year-old female with history of parotid gland large B-cell lymphoma presented bilateral intraocular recurrence 10 years after the onset of the primary malignancy. Systemic work-up including PET/CT Scan, bone marrow biopsy, brain MRI and CSF analysis were unremarkable, and the patient declined to undergo systemic chemotherapy. Vision loss in her left eye was severe due to significant sub-retinal pigment epithelium (RPE) infiltration involving the macula; this eye was treated with external beam radiation therapy. On the right eye, the relapse manifested with vitreous involvement and fovea-sparing multifocal, sub-RPE infiltration for which the patient received monthly intravitreal rituximab injections, following pars plana vitrectomy. Through the course of therapy, the patient achieved good local control and maintained 20/20 visual acuity on her right eye. Brain magnetic resonance imaging (MRI) surveillance, every 3 months, was performed and revealed a cerebellar recurrence 24 months into the course of therapy.

Conclusions and importance: Our case illustrates how intravitreal immunotherapy with rituximab may provide local control of CD-20 positive secondary intraocular lymphoma; particularly in cases where systemic therapy is not amenable. In our case, a prior vitrectomy, did not appear to interfere with the therapeutic effect of intravitreal rituximab. Close quarterly surveillance with Brain MRI may help disclose central nervous system recurrences in such cases.

1. Introduction

Secondary intraocular lymphoma is a rare manifestation of systemic lymphoma that most commonly presents with uveal infiltration.[1] In contrast, primary intraocular or vitreoretinal lymphoma (PVRL) is generally considered a manifestation of central nervous system (CNS) lymphoma and has most commonly been described in association with vitreoretinal involvement; generally not involving the uvea.[1] There have also been reports of secondary intraocular lymphoma mimicking primary intraocular lymphoma, with vitreoretinal presentations.[2] Intraocular lymphoma may also mimic multiple posterior uveitis entities; therefore, a detailed history, careful review of systems and systemic surveillance are essential tasks for the proper identification of these patients.

In cases of uveal involvement of a secondary lymphoma, systemic chemotherapy plays a significant role in controlling both ocular and systemic aspects of the disease.[2] Furthermore, patients with secondary intraocular lymphoma presenting with manifestations limited to vitreous and subretinal infiltration in the absence of concomitant CNS involvement may benefit from intravitreal chemotherapy to promote local control and preserve baseline visual acuity.[2] We present a rare case of biopsy-confirmed, bilateral secondary intraocular lymphoma, in which intravitreal rituximab served to achieve local control in the eye with macular-sparing vitreoretinal involvement.

2. Case report

A 74-year-old Hispanic female was referred to the Uveitis Service at the University of Puerto Rico School of Medicine due to a presumptive diagnosis of chronic bilateral chorioretinitis of one-year onset that was non-responsive to oral prednisone and intravitreal triamcinolone. On presentation, she complained of progressive painless loss of vision in

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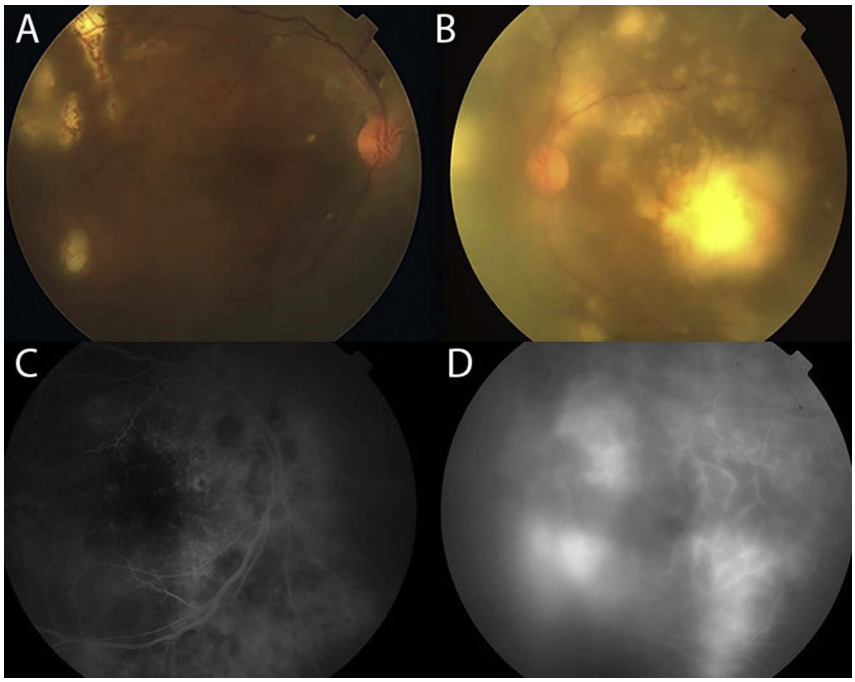

Fig. 1. Findings upon initial presentation. A. Color fundus photograph of the right posterior pole reveals mild vitreous infiltration and subretinal lesions sparing the fovea. B. Color fundus photograph of the left posterior pole reveals a denser vitreous and multifocal uveal infiltration. Fluorescein angiography of the posterior pole displays corresponding hypofluorescent areas and perivascular hyperfluorescence, on the right and left eye, C and D, respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

her left eye for one year and recent floaters in her right eye. She denied photophobia, redness, pain, flashes, or history of ocular trauma. The review of systems was unremarkable. Ten years before presentation she had been treated outside our institution for a left parotid gland large B-cell lymphoma with combined chemotherapy and external beam radiation therapy. Further details of her previous treatment regimen were unknown as her medical records were unavailable. She suffered type 2 diabetes mellitus, arterial hypertension, and had undergone bilateral cataract surgeries. Visual acuity was 20/40 OD and CF 3 FT OS. Anterior segment exam was unremarkable. The right eye had mild vitreous cells and multifocal subretinal and sub-RPE white-creamy infiltrates sparing the fovea (Fig. 1A). The left eye had dense vitreous infiltration and severe multifocal chorioretinal lesions with foveal involvement and a large elevated lesion in the temporal equatorial retina (Fig. 1B). Fluorescein angiography displayed hypofluorescent foci corresponding to the subretinal lesions on both eyes and late perivascular hyperfluorescence on the left eye (Fig. 1C and D).

Infectious and inflammatory disease work-up including RPR, FTA-ABS, HIV, Lyme antibody, chest X-Ray, Angiotensin Converting Enzyme, Lysozyme, and PPD was unremarkable. Brain and orbit magnetic resonance imaging (MRI) disclosed no further orbital or CNS infiltration. Whole body PET/CT scan, lumbar puncture and bone marrow biopsy did not show any systemic lesions.

A diagnostic pars plana vitrectomy of the left eye confirmed the diagnosis of diffuse large B-cell lymphoma. Immunohistochemistry markers correlated with the patient's primary parotid lymphoma, including positivity for BCL-2 and CD-20 markers (Table 1). Therapeutic options, including systemic chemotherapy, were carefully discussed with the patient and her family, yet the patient emphatically declined systemic chemotherapy despite our team's recommendations.

She received external beam radiotherapy of the left eye with a total dose of 45 Gy in 25 fractions. Vitrectomy of the right eye further confirmed the presence of secondary intraocular lymphoma. The right eye was treated with monthly intravitreal rituximab (1mg/0.1 ml). After twelve consecutive monthly intravitreal injections, the patient had maintained a visual acuity of 20/20 with regression of her subretinal lesions and no ocular complications; at this junction, she decided to continue with monthly intravitreal rituximab injections outside our institution. Close systemic surveillance which included quarterly brain MRI unveiled cerebellar involvement twenty-four months after the initial presentation, despite the patient being asymptomatic.

Table 1
Comparison between immunohistochemistry (IHC) panel of left eye vitreous biopsy specimen and original panel of primary parotid gland tumor, showing similar IHC profile.

Left eye vitreous biopsy	Left parotid gland biopsy
Bcl-2: POSITIVE	Bcl-2: POSITIVE
Bcl-6: WEAKLY POSITIVE	Bcl-6: POSITIVE
CD 20: POSITIVE	CD 20: POSITIVE
CD 79a: POSITIVE	CD 79a: POSITIVE
Ki67: POSITIVE IN MOST NEOPLASTIC CELLS	Ki67: POSITIVE IN MOST NEOPLASTIC CELLS
CD 43: POSITIVE	CD 43: NEGATIVE
CD 5: NEGATIVE	CD 5: NEGATIVE
CD 38: NEGATIVE	
CD 44: NEGATIVE	
Epstein-Barr Virus: NEGATIVE	
LAMBDA: NEGATIVE	
KAPPA: NEGATIVE	

3. Discussion

Our rare case of bilateral secondary intraocular lymphoma features an uncommon clinical presentation of systemic lymphoma. The right eye had limited vitreous and subretinal involvement, resembling more the classic clinical findings found in primary vitreoretinal lymphoma (PVRL). Due to the lack of active systemic involvement on presentation, the patient decided to forgo systemic chemotherapy with high-dose methotrexate. We then refocused our first-line treatment strategy using two different approaches for local control in each eye, while limiting ocular side effects in order to preserve functional vision in her right eye.

Given the particular vitreoretinal manifestation in the right eye, we decided to use local intravitreal therapy with rituximab, rather than methotrexate, due to its specific affinity for a CD-20 + lymphoma. It has been reported that ocular tissues do not express CD-20 receptors and thus would be spared with rituximab.[3] Local immunotherapy therefore enabled the patient to achieve local control and maintain excellent visual function. It is noteworthy, that the dose of 1mg/0.1 ml of rituximab was able to convey a positive therapeutic effect, despite being used in a fully vitrectomized eye.

As systemic chemotherapy was not pursued, the full extent of the ocular response in the right eye can be exclusively accredited to local measures, which also included pars plana vitrectomy. The role of pars plana vitrectomy in the management of intraocular lymphoma is mostly diagnostic in the absence of CNS involvement. However, vitrectomy has been proposed to provide a transient therapeutic benefit in these cases.[4,5] Although the effectivity of vitrectomy as a debulking procedure for lymphoma is beyond the scale of this article, our case may suggest that pars plana vitrectomy helps stabilize the posterior segment in cases of secondary intraocular lymphoma.

Neuroimaging surveillance allowed for the identification of CNS involvement in our patient two years after presentation. This is particularly important, given the correlation of CNS involvement with a high mortality in cases of intraocular lymphoma.[1] In a retrospective study of cases of secondary lymphoma mimicking primary vitreoretinal lymphoma, two out of three cases developed CNS involvement and ultimately died.[2] Thus, although systemic lymphoma is a different entity than PVRL or primary CNS lymphoma, including neuroimaging, as part of our systemic surveillance protocol for our patient, identified CNS involvement in the absence of any neurological symptoms.

4. Conclusions

Intravitreal rituximab may help achieve local control of CD-20 positive secondary intraocular lymphoma, especially in instances where systemic chemotherapy is not a viable option. In our case, a complete pars plana vitrectomy did not seem to interfere with the positive therapeutic effects of rituximab. Close systemic surveillance, including neuroimaging, should be pursued in these patients.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Conflicts of interest

The following authors have no financial disclosures: JE, SL, NP, MS, RV and AL.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ajoc.2018.01.032.

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