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Authors

Bever, Gregory J
Kim, Dan J
Afshar, Armin R
et al.

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THERAPEUTIC VITRECTOMY AS AN ADJUNCT TREATMENT TO SYSTEMIC CHEMOTHERAPY FOR INTRAOCULAR LYMPHOMA

Gregory J. Bever, MD[*], **Dan J. Kim, BS**[*], **Armin R. Afshar, MD, MBA**[*], **James L. Rubenstein, MD, PhD**[†], **Bertil E. Damato, MD, PhD**[*]

[*]Ocular Oncology Service, Department of Ophthalmology, University of California San Francisco, San Francisco, California

[†]Division of Hematology/Oncology, Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, California

Abstract

Purpose—To report the outcome of a previously vitrectomized eye having less lymphoma disease burden compared with the contralateral nonvitrectomized eye over the course of 3.5 years while on systemic chemotherapy.

Methods—Case report.

Results—A 51-year-old man with vitreoretinal lymphoma with central nervous system involvement underwent vitrectomy in his left eye. Over the following 3.5 years on systemic chemotherapy, the left eye had less lymphoma disease burden compared with the contralateral nonvitrectomized right eye.

Conclusion—Therapeutic vitrectomy may be a useful adjunct to systemic chemotherapy in vitreoretinal lymphoma, particularly in cases of vitreous predominant disease manifestation.

Keywords

chemotherapy; intraocular lymphoma; vitrectomy

Vitreoretinal lymphoma is most commonly a diffuse large B-cell lymphoma, although can rarely be of T-cell origin.[1] Clinically, the disease often presents with vitreous haze and/or orange-yellow sub–retinal pigment epithelium deposits.[1] Most patients develop central nervous system lymphoma, which can manifest before, after, or simultaneously with the ocular disease.

Many treatment modalities have been used over the years. In the 1950s, patients were most often treated with enucleation.[2] In the 1970s, radiotherapy became the mainstay of treatment.[3] Later, various forms of methotrexate-based systemic chemotherapy were used

Reprint requests: Gregory J. Bever, MD, Ocular Oncology Service, Department of Ophthalmology, University of California San Francisco, 8 Koret Way, San Francisco, CA 94143; greg.bever@ucsf.edu.

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with improvement in outcomes over radiotherapy alone.[4] Next, intravitreal chemotherapy regimens were added to the treatment armamentarium.[5]

Here, we report a case of vitreoretinal lymphoma where vitrectomy in one eye proved, serendipitously, to be therapeutic when followed over time on a systemic chemotherapy regimen.

Case Report

A 51-year-old man presented to his local ophthalmologist in June 2011 with bilateral uveitis. In August 2012, a vitreous biopsy of the left eye was performed by an outside ophthalmologist. The results were inconclusive for lymphoma. The patient subsequently developed a retinal detachment, which was initially treated with pneumatic retinopexy, and then, developed a macula-on redetachment inferiorly. This was, subsequently, repaired through combined pars plana vitrectomy and scleral buckle in December 2012. The patient also underwent left eye cataract extraction with intraocular lens implantation in May 2013.

The patient presented to UCSF in May 2013 for evaluation after developing weakness and memory loss. Brain magnetic resonance imaging at that time showed multifocal homogenously enhancing lesions surrounding the ventricles and involving the corpus callosum. In early June 2013, ophthalmic examination showed the right eye to have a visual acuity of 20/25 with vitreous infiltrates allowing only a hazy view of the fundus. The left eye had a visual acuity of 20/200, a clear vitreous, a swollen optic disk, and indentation by a circumferential buckle with laser scars. Later in June 2013, a brain biopsy confirmed diffuse large B-cell lymphoma and the patient began systemic treatment with high-dose methotrexate, temozolomide, and rituximab.

When referred to the ocular oncology service at UCSF, in August 2013, the right eye had visual acuity of 20/20, with 3–4+ anterior vitreous cells and a clear view of the fundus, which was normal. The left eye had visual acuity of 20/100, corrected to 20/50, 1–2+ cells, and an epiretinal membrane at the macula.

In November 2013 (Figure 1A), the right eye had a visual acuity of 20/15 with 2–3+ anterior vitreous cells and a clear view of the fundus. The left eye had a visual acuity of 20/50 +2 with 1+ anterior vitreous cells and a clear view of the fundus. Optical coherence tomography showed a small amount of fovea-involving cystoid macular edema in the left eye.

In January 2014, the patient underwent consolidation systemic chemotherapy with etoposide and cytarabine. At that time, the cystoid macular edema in the left eye resolved without topical or intravitreal therapy. In April 2014, maintenance therapy with lenalidomide 5 mg/day was started. By June 2014, the patient had developed a trace nuclear subcapsular cataract (NSC) and posterior subcapsular cataract (PSC) in the right eye. In September 2014, the lenalidomide dose was increased to 10 mg/day because the vitreous infiltrate in the right eye had worsened, reducing the visual acuity to 20/25. The vitreous haze in the right eye persisted, but the vision improved to 20/20. The left eye remained unchanged, with a clear vitreous.

In early March 2015 (Figure 1B), the right eye had a visual acuity of 20/20 with 3+ anterior vitreous cell and appreciable vitreous haze. The right eye had a stable trace NSC and PSC. The left eye had a visual acuity correctable to 20/60− with no anterior vitreous cell and a clear view of fundus. Optical coherence tomography of the left eye showed a lamellar hole. Because of the right eye vitreous involvement, the patient received an additional dose of rituximab in later March 2015.

In September 2015 (Figure 1C), the right eye had a visual acuity of 20/15− and 3+ anterior vitreous cell, appreciable vitreous haze, and a stable trace NSC and PSC. The left eye had a visual acuity correctable to 20/30− with no anterior vitreous cell or haze.

In March 2016, the lenalidomide dose was increased further to 20 mg/day because visual acuity in the right eye had deteriorated to 20/25. This improved the visual acuity until October 2016, when the vitreous haze increased. In January 2017 (Figure 1D), the vitreous haze in the right eye was considerable, whereas the left eye remained without any vitreal involvement.

The patient was reluctant to undergo radiotherapy or to receive intravitreal injections. Therapeutic vitrectomy was, therefore, performed in the right eye in March 2017. One month postoperatively, the right eye had a visual acuity correctable to 20/30 with a stable trace NSC and PSC, a clear vitreous, and a normal fundus. The left eye was unchanged without evidence of vitreous infiltration. Five months postoperatively, the right eye had a visual acuity correctable to 20/30− with an increased cataract (now 1+ PSC and 2+ NSC), a clear vitreous, and a normal fundus. The left eye was still unchanged without evidence of vitreous infiltration.

The patient did not experience recurrence of central nervous system lymphoma disease at any point after initial presentation.

Discussion

This case is an example of a previously vitrectomized eye having less lymphoma disease burden compared with the contralateral nonvitrectomized eye over the course of 3.5 years while on systemic chemotherapy.

To the best of our knowledge, there has only been one previous report of therapeutic vitrectomy in the treatment of vitreoretinal lymphoma.[6] In that case, the patient was treated with systemic chemotherapy (methotrexate, pro-carbazine, vincristine, and intraventricular methotrexate) and whole-brain radiotherapy (eyes were not involved in the radiation field). The patient's right eye responded well to this treatment, but the left eye had persistent vitreous disease that was initially responsive to intravitreal methotrexate. The left eye eventually failed intravitreal chemotherapy and, thus, a complete vitrectomy was performed. The authors make a point to differentiate this from the typically performed diagnostic vitrectomy where a smaller amount of vitreous is removed. In that reported case, the left eye had a good outcome (in terms of examination and visual acuity) over the course of 2 years.

Our case had longer follow-up, showing a lack of vitreous burden in the left eye compared with the right eye over the course of 3.5 years. Both the case reported here, and the previously reported case has the important distinction of having undergone a complete vitrectomy, rather than just a diagnostic vitrectomy. It is possible that complete removal of the vitreous eliminates all the scaffolding available for lymphoma cells to accumulate within the vitreous cavity. This notion of needing “complete” vitrectomy may explain why such a sustained reduction in vitreous haze in the vitrectomized eye as compared to the fellow eye has not been previously reported in the many cases where patients with vitreoretinal lymphoma have had a unilateral diagnostic vitrectomy.

It is possible that the left eye simply had less lymphoma disease burden and this observation may have occurred without vitrectomy. Arguing against this notion is the June 2013 examination, which showed the left eye having optic nerve swelling, whereas the right eye was considerably more quiet.

It is unclear whether this same phenomenon would have been observed without concurrent systemic chemotherapy. It is possible that debulking with vitrectomy allows systemic chemotherapy to better penetrate the vitreous cavity, thereby decreasing the disease burden. Alternatively, removal of the vitreous scaffold may have allowed the lymphoma cells to leave the vitreous cavity more easily. Further study is needed to know what role systemic chemotherapy plays in this observation.

In this case, the right eye eventually underwent therapeutic complete vitrectomy to relieve the vitreous involvement that was not responding to systemic chemotherapy. Moving forward, this case adds further evidence that lymphomatous vitreous infiltration unresponsive to systemic therapy may be amenable to therapeutic vitrectomy.

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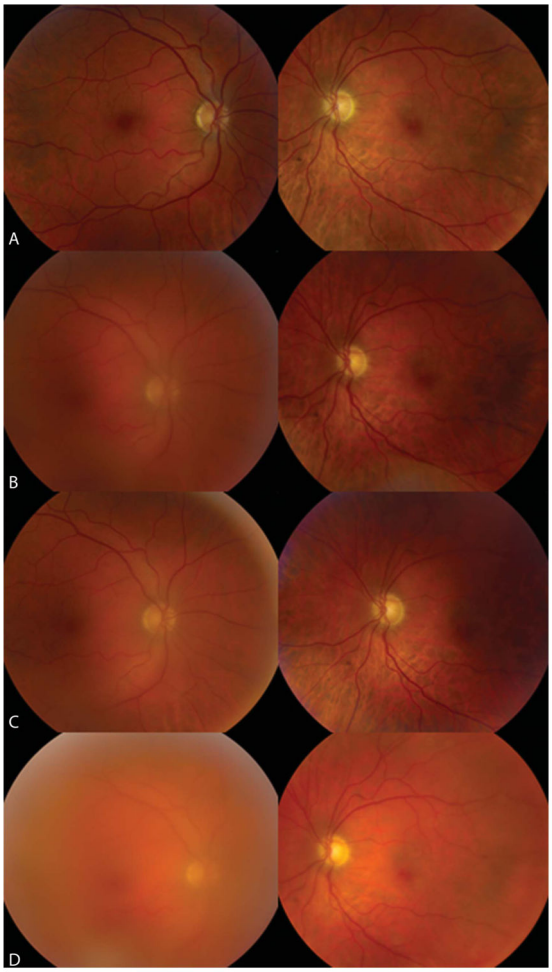

Fig. 1.

Fundus photographs showing the nonvitrectomized right eye and previously vitrectomized left eye throughout a 3.5-year course of systemic chemotherapy for central nervous system/retinal lymphoma. **A.** Right and left eyes in November 2013, a few months after starting systemic chemotherapy. Neither eye shows vitreous or retinal involvement. **B.** In March 2015, the right eye developed vitreal involvement, despite continued systemic chemotherapy, whereas the left eye remained free of disease. **C.** Despite additional salvage rituximab therapy, in September 2015, the right eye continued to show vitreal involvement, whereas the left eye was quiet. **D.** In January 2017, the vitreal involvement continued to worsen in the right eye, whereas the left eye was still without vitreal or retinal involvement on systemic chemotherapy.