A Case of BDUMP with Unknown Primary Tumor

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Abstract:

Purpose

The purpose of this study is to present the results of the use of intravitreal Aflibercept (Eylea©) in the management of the cystoid macular edema (CME) and subretinal fluid (SRF) associated with a case of bilateral diffuse uveal melanocytic proliferation (BDUMP).

Methods

Color fundus photography, fundus autofluorescence, fluorescein angiography, ocular ultrasonography, and optical coherence tomography were used in the current study to monitor the posterior segment changes. Serial intravitreal Eylea was administered to both eyes every 6-8 weeks.

Patient

We report a case of a 77-year old Caucasian male who presented with bilateral worsening vision over a 6-month period with multiple grey-brown subretinal lesions with associated pigment clumps, choroidal thickening, SRF and CME; features that are consistent with BDUMP. Extensive work-up failed to discover any systemic malignancy 22 months after the initial presentation.

Results

Intravitreal Eylea© led to significant improvement of the CME and SRF. The final visual acuity of the patient stabilized at 20/30 in the right eye (OD, initially 20/30) and 20/60 in the left eye (OS, initially 20/200) after a total of six injections for each eye.

Conclusion

Prompt diagnosis and treatment along with systemic evaluation are key for BDUMP. The reported case is unique for the excellent visual response to intravitreal Eylea therapy.

KeyWords: Aflibercept; Bevacizumab; Bilateral Diffuse Uveal Melanocytic Proliferation

Introduction

Bilateral diffuse uveal melanocytic proliferation (BDUMP) is a rare paraneoplastic ocular syndrome, in which an underlying systemic cancer causes secondary proliferation of benign uveal melanocytes. Clinically, the most common presentation is painless bilateral vision loss. Fundoscopic exam shows diffuse clumping of pigment throughout the retinal pigment epithelium (RPE), lipofuscin deposition and subretinal fluid (SRF). The syndrome unfortunately has a poor prognosis often resulting in severe vision loss[1]. Ocular signs and symptoms may precede manifestation of systemic carcinoma by months, rarely even longer, highlighting the need for an appropriate index of suspicion and prompt evaluation for an undiagnosed cancer[2].

Treatment of BDUMP is challenging. Systemic targeted treatment for the underlying neoplasm is often ineffective and local therapy may be required to treat the exudative retinal detachment. Few cases reports have described targeted ocular therapy [3, 4]. Aflibercept (Eylea; Bayer AG, Leverkusen, Germany) is a recombinant anti-VEGF agent, that has shown efficacy in treating wet AMD and diabetic macular edema[5-7].

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There is little documentation of the response of this condition to anti-vascular endothelial growth factor (VEGF) therapy. Here, we correlate the photographic and SD-OCT findings in a case of a patient with BDUMP.

Case Report

A 77-year-old male presented with a 6-month history of intermittent floaters, photopsia, and decreased vision in both eyes. His past medical history is significant for a surgically treated prostate carcinoma and skin melanoma, both in remission with no evidence of disease. Review of systems was otherwise unremarkable.

On initial presentation, his visual acuity was 20/30 OD, 20/200 OS without evidence of intraocular inflammation of the anterior or posterior segments. Both eyes demonstrated multiple and diffuse areas of pigment clumping and orange lipofuscin deposition through the RPE. Fundus autofluorescence pictures showed a mixed pattern of hyper and hypo-autofluorescence correlating to areas of lipofuscin deposition. Fluorescein angiography (FA) demonstrated multifocal lesions with early hypofluorescence and late hyperfluorescence. B-scan ultrasonography revealed multifocal areas of choroidal thickening (Figure 1).

OCT demonstrated significant subfoveal fluid and CME in the left eye as well as disruption of the ellipsoid zone, and patchy thickening of the RPE in both eyes, corresponding to the plaque-like areas of lipofuscin on the fundus photographs and the areas of window defects on FA (Figure 1).

Systemic imaging surveillance for a recurrence of his previous cancers, or a new systemic cancer including MRI brain/orbit, CT chest/abdomen/pelvis, PET CT scan, colonoscopy and skin examination were unrevealing. Uveitis workup including chest x-ray, ESR, ANA, ACE, VDRL, Lyme titer, PPD test, ANCA, toxoplasmosis, and toxocariasis testing were all negative.

Due to decreased visual acuity and the presence of SRF in the left eye, the decision was made to give an intravitreal injection of anti-VEGF therapy.

He was treated initially with 3 injections of avastin with minimal response in terms of vision function or anatomic changes on OCT, therefore the decision was made give an intravitreal injection of Eylea®. At the 2-month follow-up, the patient’s vision improved to 20/60 OS with stable vision at 20/30 OD. Serial imaging with OCT showed regression of the SRF and sub-RPE material, improved visualization of the choriocapillaris, and mild but stable atrophy of the RPE (Figure 2).

Subsequent continued surveillance for an occult malignancy causing this paraneoplastic syndrome has been unremarkable. At 22 months after diagnosis, the patient continues to show response to Eylea® (total 6 injections) and has not yet been diagnosed with any active systemic cancer on screening with whole body PET scan under the care of a systemic oncologist. His last recorded visual acuity is 20/30 OD and 20/60 OS.

Figure Legend:

Figure 1: Fundus photographs, autofluorescence, and B-scans of both eyes. Color fundus photograph of the right eye (A) and left eye (D) showing multiple oval and rounded subretinal patches corresponding to RPE mottling changes reflected by areas of hyper- and hypo-autofluorescence (B, E). B-scan ultrasonography reveals increased choroidal thickness in both eyes.

Figure 2: Optical coherence tomography (OCT) of both eyes before and after Eylea treatment. OCT macular scans of both eyes showing decreased subretinal plaques (B, D) and resolution of the subretinal fluid (B) at the end of the serial Eylea injections.
Discussion

The five cardinal signs of BDUMP originally described by Gass et al. [1] are: (1) multifocal, round subretinal patches, (2) associated hyperfluorescence during the early phases of angiography; (3) multiple, elevated, pigmented and non-pigmented uveal melanocytic lesions; (4) exudative retinal detachment; and (5) rapid progression of cataract.

In nearly half of the cases, there is a history or known diagnosis of non-ocular malignancy at the time of diagnosis of BDUMP[8]. In our patient, all oncology work-up came back negative. The patient was referred to an oncologist for regular follow-up with PET-CT scans and at 22 months follow-up, a systemic malignancy has not yet been found.

Auto-fluorescence, FA, and OCT imaging contribute greatly to the diagnosis of BDUMP. Alternating patches of RPE destruction and irregular thickening of RPE associated with overlying pockets of SRF can be monitored on OCT, including improvement with therapy [9].

Treatment of BDUMP is usually directed towards the primary cancer, however these patients sometimes go undiagnosed, despite appropriate work-up, for years [1]. The excellent response of our case to anti-VEGF therapy suggests a role of VEGF in the pathogenesis of the SRF and need for targeted ocular therapy. This has also been suggested in limited case reports in the literature [10]. Our case responded particularly well to the off-label use of intravitreal Eylea® which suggests that this and other anti-VEGF agents may aid in the resolution of SRF in BDUMP patients. Further elucidation of the mechanisms of development of SRF in BDUMP, including the immunologic mechanisms of tumor control, may aid in better understanding of how to best treat these eyes.

Declarations

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No conflicting relationship exists for any author.

Summary Statement

This case report discusses the off-label use of intravitreal injection of Aflibercept in the management of a case of bilateral diffuse uveal melanocytic proliferation.

References


