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Case Report

Alternative Treatment Options to Oral Prednisone in a Patient with Multifocal Choroiditis and Panuveitis

Bahadorani Sepehr*, Johnson Daniel A and Sohn JeongHyeon

Department of Ophthalmology, University of Texas Health Science Center at San Antonio, San Antonio, TX, United States

***Corresponding Author:** Bahadorani Sepehr, Department of Ophthalmology, University of Texas Health Science Center at San Antonio, San Antonio, TX, United States.

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Abstract

Purpose: Multifocal choroiditis and panuveitis (MCP or MFCPU) is a blinding condition that needs immediate ophthalmic and rheumatologic attention. In this study, due to intolerance of oral prednisone as well as increased susceptibility to COVID-19 infection, we have evaluated the efficacy of alternative treatment options in a patient with MCP.

Case Report: Case report of a 32-year-old mono-ocular male with long term history of MCP who has continued to suffer from repeated episodes of uveitis and macular edema. The patient could not tolerate side effects of oral steroids and thus, difluprednate was added as an adjunct therapy to tapering dose of oral prednisone. Changes in best-corrected visual acuity (BCVA), central macular thickness and intraocular pressure following treatment with combination of difluprednate and oral prednisone are reported.

Results: Treatment with topical difluprednate and moderate dose of oral prednisone (0.3 mg/kg/day) has resulted in a rapid and significant reduction in macular edema with associated improvement in BCVA. Difluprednate administration alone, however, was not sufficient to prevent recurrence of macular edema and thus, intravitreal Triesence had to be supplemented for the rescue.

Conclusion: Difluprednate could potentially work as an effective adjunct therapy for treatment of posterior uveitis patients that cannot tolerate high-dose oral steroids. This medication alone, however, may not be sufficient to prevent recurrence of edema in MCP.

Keywords: *Difluprednate; Durezol; Uveitis; Multifocal Choroiditis and Panuveitis; Hypotony; Macular Edema; Triesence; Triamcinolone*

Introduction

Multifocal choroiditis and panuveitis (MCP or MFCPU) is a bilateral condition that presents with focal areas of inflammation in the choroid and deep retina. Over time, these lesions become atrophic and progress into punched-out chorioretinal scars. In the course of the disease, MCP waxes and wanes, but with each recurrence, vision could continue to decline from either recurrent cystoid macular edema or development of choroidal neovascular membranes (CNVMs). In addition, retinal pigment epithelium metaplasia and fibrous scarring could further contribute to the loss of vision [1-3]. Hence, it is essential to control uveitis in these patients and initiate immunomodulatory therapy (IMT) if oral steroids cannot be tapered [4].

In this article, we present a case of a 32-year-old male with 15 years history of MCP that has been treated with oral steroids on multiple occasions. Over the course of time, his multiple episodes of uveitis led to complete loss of vision in one eye and a severe decline of vision

in the other eye (20/200 BCVA) at which time he was referred to our institution. Here we discuss a complicated course of treatment that has warranted testing of alternative options to oral prednisone due to the intolerance of the medication as well as increased risk of coronavirus (COVID-19) infection.

Case Report

A 32-year-old male (134 kg weight) with 15 years history of uveitis is referred to the University Hospital for a second opinion regarding recurrent uveitis. According to the patient's history and medical records, prior laboratory and imaging studies did not reveal a systemic autoimmune condition and he had multiple occasions of uveitis with development of bilateral retinal detachments requiring surgical repair with lensectomy. With every new episode of uveitis flare, he was treated with prednisone and then slowly tapered off the medication. On the first presentation to our retina clinic, the patient exam findings were as follows, with the right eye fundus imaging studies shown in figure 1.

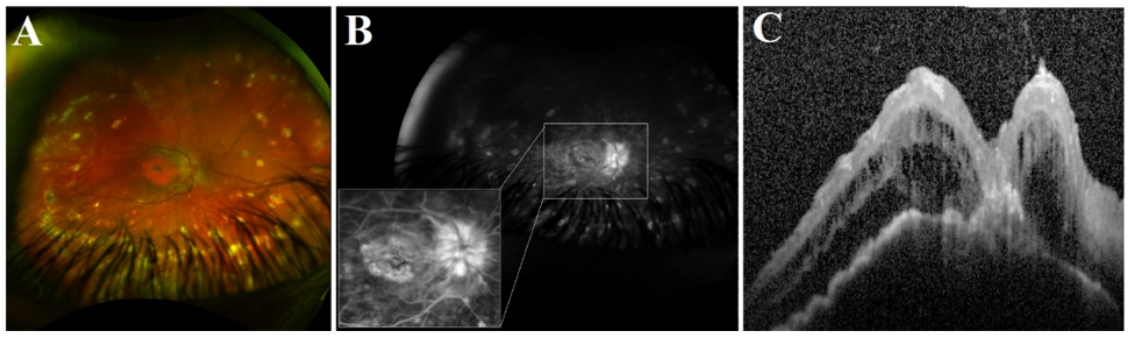

Figure 1: *Fundus wide-field imaging (Optos, Dunfermline, UK) reveals punched out lesions along with macular pigmentary dropout (Panel A). Fluorescein angiography using Optos machine reveals optic disc hyperfluorescence, window defect in the macular area, and staining of peripheral punched out lesions (Panel B). Spectral-domain optical coherence tomography (Spectralis OCT, Heidelberg Engineering, Franklin, USA) reveals spongiform edema with areas of hyper-reflectivity near the RPE layers (Panel C).*

Left eye - Visual acuity of no light perception (NLP) with intraocular pressure of 11 mmHg; slit lamp exam revealed aphakia with aniridia and band keratopathy. Despite a limited view due to the corneal finding, the anterior chamber appeared quiet and the fundus exam showed silicone oil and bands of fibrous tissues.

Right eye - Visual acuity of 20/250 with intraocular pressure of 5 mmHg; aphakia with inferior keratic precipitates, 2+ anterior chamber cells and ½+ cells in anterior vitreous; pale nerve with macular pigmentary changes and punched out lesions in the periphery.

For this latest episode of uveitis flare which has started a month prior to presentation to our clinic, the patient was started on oral prednisone by an ophthalmologist in Mexico and then completely tapered off. The patient, however, was maintained on 4-times a day prednisolone acetate eye drops and daily atropine. After completing the imaging studies as illustrated in figure 1, tentative diagnosis of multifocal choroiditis and panuveitis has been made with a plan to repeat the lab and imaging studies (due to the remote history of testing), increase the frequency of prednisolone acetate to every hour while awake and then treat the patient with two rounds of bevacizumab once uveitis has improved. Patient had prior treatments with bevacizumab in the past for CNVM. In particular, given the extent of retinal pigment epithelium (RPE) changes and macular edema, it was difficult to differentiate the cause of macular thickening from inflammation

or CNVM on either fluorescein or OCT angiography (data not shown). Hence, it was decided to treat the patient with two round of bevacizumab and pending the degree of improvement, decide on whether to continue anti-VEGF (vascular endothelial growth factor) treatment or to switch to steroid therapy for posterior edema. The patient is also referred to a rheumatologist for evaluation for immunomodulatory therapy. In the follow up, the degree of anterior chamber cells was reduced to ½+ cells with negative imaging and lab test results (Syphilis, Brucella, Tuberculosis, Angiotensin Converting Enzyme, Lysozyme, Lyme, HLA-B27, HLA-B5701, Toxocara, Toxoplasma, Urinalysis). However, bevacizumab injections did not show any improvement in macular edema and after two months of follow up, the patient has developed recurrence of intraocular inflammation with 4+ anterior chamber cells and worsening of macular edema, as illustrated in figure 2, Panel A. The patient's vision reduced to 20/800 and intraocular pressure reduced to 4 mmHg. At this point, oral prednisone 60 mg a day was restarted and prednisolone acetate switched to topical difluprednate, 6 times a day. However, one week later, due to headaches and difficulty with sleep, the prednisone was reduced to 40 mg a day and difluprednate frequency increased to 8 times a day. With this new regimen, the side effects of oral steroid subsided and the patient had a swift resolution of anterior uveitis with significant improvement in macular edema to almost full resolution (Figure 2, Panel B) within 2 weeks of treatment. The best-corrected visual acuity also improved to 20/150 and the patient remained stable until seen by the rheumatology team, at which time, due to the rapid spread of COVID-19 and increased susceptibility of infection, oral prednisone is discontinued and administration of immunomodulatory therapy (IMT) is postponed. Hence, the ophthalmology team has decided to increase the frequency of topical difluprednate eye drops to every one hour while awake. In a two weeks follow up visit, the edema has started to recur, at which time intravitreal injection of 0.1 ml Triesence (40 mg/ml triamcinolone acetonide) has resulted in a robust rescue of macular edema. The patient has continued to receive the monthly maintenance dose of intravitreal Triesence to prevent recurrence of edema until IMT is initiated.

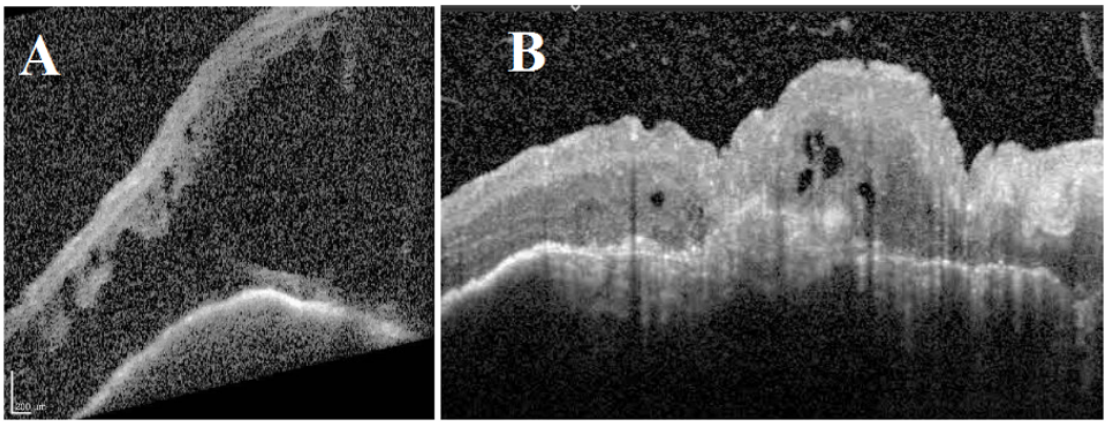

Figure 2: *Spectral-domain optical coherence tomography (Spectralis OCT, Heidelberg Engineering, Franklin, USA) shows significant improvement in edema from (panel A) to (panel B) upon initiating topical difluprednate with moderate dose of oral prednisone (40 mg per day).*

Discussion

Treatment of multifocal choroiditis and panuveitis (MCP or MFCPU) could involve topical, periocular, or systemic corticosteroids. In addition, patients with chronic disease may benefit from IMT medications that allow long term control at lower doses of oral steroid [1-4]. This case report is of particular interest considering the mono-ocular status of the patient and the need for a fast and effective therapy to help reduce macular edema before any further damage developed. In this patient, the treatment course was complicated by intolerable

side effects of high dose oral prednisone as well as risk of enhanced susceptibility to COVID-19 infection from systemic immunosuppression. Hence, alternative treatments to oral prednisone needed to be explored. Given the absence of lens capsule and prior history of vitrectomy, dexamethasone intravitreal implant (OZURDEX; Allergan, Inc., Irvine, CA) was not recommended owing to the risk of pellet migration to the anterior chamber [5]. Furthermore, the risk of scleral leakage and worsening of hypotony also remained [6]. Thus, our adjunct treatment options included either intravitreal or subtenon triamcinolone versus topical difluprednate.

For this patient, we elected to use topical difluprednate as an adjunct therapy since the patient was monocular and there would be no risk of exogenous endophthalmitis or recurrent retinal detachment as would occur with an intraocular injection. Furthermore, Kakimoto., *et al.* (2018) demonstrated that topical difluprednate is more effective than subtenon injection of triamcinolone in reducing vitreous inflammatory cytokines in a rabbit model of uveitis [7]. Our results demonstrate that an adjunct therapy of difluprednate with moderate dose of oral prednisone (0.3 mg/kg/day) is highly effective in resolution of inflammation for our MCP patient. Nevertheless, edema has recurred upon discontinuation of oral prednisone despite hourly administration of difluprednate, indicating that difluprednate alone may not be sufficient for treatment of macular edema in MCP. Supplementation with intravitreal Triesence, however, has resulted in a robust and prominent resolution of macular edema.

Conclusion

Difluprednate can be administered as an adjunct therapy in patients with posterior uveitis that cannot tolerate high dose of oral prednisone. In the absence of other systemic or intravitreal therapies, however, difluprednate alone may not be sufficient to prevent recurrence of macular edema.

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