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Case report

Topical interferon alpha 2b in the treatment of refractory pseudophakic cystoid macular edema

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ABSTRACT

Purpose: To report the efficacy and safety of interferon alpha 2b in the treatment of pseudophakic cystoid macular edema resistant to conventional therapy.

Observations: A 64-year-old patient presented with pseudophakic cystoid macular edema in her left eye, which developed two months after an uncomplicated cataract surgery and was resistant to multiple topical NSAIDs and multiple intravitreal bevacizumab injections over the course of nine months. She also developed side effects to oral acetazolamide and intravitreal triamcinolone injection; a skin rash and a rise in intraocular pressure (34 mmHg), respectively. She was subsequently started on topical interferon alpha 2b (1 MIU/ml) four times a day nine months after developing pseudophakic cystoid macular edema. Cystoid macular edema improved significantly in four weeks and completely resolved after twelve weeks. Her vision improved from 20/100 before starting treatment to 20/25 twelve weeks after starting treatment. Macular structure and visual acuity were stable throughout a thirty-six weeks follow-up period.

Conclusions: and Importance: This case report displays the potential efficacy and safety of interferon alpha 2b in the treatment of refractory cystoid macular edema after cataract surgery. Ocular surface irritation was the only reported adverse effect of the treatment in our patient, this responded to lubricants.

1. Introduction

Despite the observed decrease in the incidence of complications after cataract surgery due to advanced surgical techniques, post-operative cystoid macular edema remains a substantial cause of decreased visual acuity following cataract surgery.

Based on most research studies, prostaglandins play the most important role in the pathogenesis of cystoid macular edema after cataract surgery.[1] However, lately, the importance of other inflammatory mediators such as vascular endothelial growth factor and other cytokines have been considered.[1]

Topical and oral nonsteroidal anti-inflammatory drugs (NSAIDs),[2] intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections,[3] steroids,[4] and oral acetazolamide[5] have all been used in the treatment of pseudophakic cystoid macular edema with varying results. Subcutaneous interferon alpha has also been used effectively in the treatment of pseudophakic cystoid macular edema.[6]

The safety and efficacy of topical interferon α2b has been demonstrated in the treatment of ocular surface tumors.[7] However, it has not been employed in the treatment of pseudophakic cystoid macular edema.

In this case report, we employed topical interferon α2b in the treatment of refractory pseudophakic cystoid macular edema.

2. Case report

A 64-year-old female had undergone an uncomplicated cataract surgery in her left eye eleven months before presenting to our center. Based on previous reports, she had developed cystoid macular edema 2 months after surgery, and her vision had decreased from 20/25 to 20/100. Topical NSAIDs therapies (ketorolac, diclofenac) and multiple intravitreal bevacizumab injections had proved unsuccessful for nine months. Cystoid macular edema was responsive to intravitreal bevacizumab injections; however, it recurred a few weeks after each injection. She had developed side effects to oral acetazolamide (a skin rash) and intravitreal triamcinolone injection (a rise in intraocular pressure to 34 mmHg was observed one month after injection).

Upon initial presentation to our center, nine months after

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List of abbreviations

NSAIDs	nonsteroidal anti-inflammatory drugs
anti-VEGF	anti-vascular endothelial growth factor
α2b	alpha 2b
IL	interleukin
ml	milliliter
MIU	million international unit

developing cystoid macular edema, her vision was 20/100 in the left eye. The anterior and posterior segment exams were completely normal. Intraocular pressure was within the normal range. Optical coherence tomography (retinal thickening and cystic hyporeflective areas) and fluorescein angiography (perifoveal leakage and optic disc staining) both confirmed cystoid macular edema. Fluorescein angiography did not appreciate disc leakage, large vessels leakage, or staining. Ultrasound biomicroscopy was obtained to locate the lens haptics position. The results revealed lens in capsular bag and no contact between the lens haptics and the iris (Fig. 1). Various laboratory tests associated with infectious and non-infectious uveitis were performed and all results were within the normal limit, negative, or non-reactive. The patient was reluctant to continue intravitreal anti-VEGF therapy and was seeking another method of treatment. After a discussion regarding the treatment options, the patient agreed to initiate experimental topical interferon α2b therapy four times a day (1 MIU/ml). Topical drops were prepared by our compounding pharmacy by adding two milliliters of distilled water to one milliliter of interferon α2b three MIU (3 MIU/ml vial). Four weeks after initiating treatment, optical coherence tomography showed significant decrease in foveal thickness and cystic spaces. Treatment was continued for twelve weeks using the same protocol, after which we confirmed the stability of the macular structure and began tapering the treatment dose every eight weeks by one drop. At her last visit, she was using one drop a day. The only reported side effect was ocular surface irritation, which improved with the use of lubricants (artificial tears).

We have planned to continue one drop a day for eight weeks and then one drop every other day for another eight weeks before ceasing treatment (Table 1). The optical coherence tomography obtained at her last visit did not demonstrate any cystoid macular edema, and vision in the left eye was 20/25. Fig. 2 demonstrates the changes in central macular optical coherence tomography from the first visit (before starting treatment) to the last visit (thirty-six months after starting treatment).

3. Discussion

To our best knowledge, this is the first case report in which topical interferon α2b was employed in the treatment of refractory cystoid macular edema after cataract surgery. Interferon α2b acts against various biologic targets such as VEGF, interleukin-8 (IL-8), IL-10, TGF-β, and TNF-α.[8] It has been shown that interferon alpha improves the barrier effect of retinal vessel endothelial cells in the retina,[9] and can also penetrate the sclera despite having a large molecular structure.[10] Systemic adverse effects such as flu-like symptoms (90%), leukopenia (30%), alopecia (10%), depression (8%), gastrointestinal disturbances (> 1%), and increased liver enzymes (< 1%) have been previously reported with systemic interferon alpha employment.[11–14]

Based on its anti-inflammatory, anti-proliferative, and anti-angiogenic effects, systemic and subtenon interferon alpha has been employed in the treatment of a wide range of posterior segment problems with an inflammatory component such as: diabetic macular edema, age related macular degeneration, posterior uveitis, uveitic cystoid macular edema, and Irvine-Gass syndrome.[6,9,15–17] The fact that a good response is observed in inactive uveitis with cystoid macular edema and pseudophakic cystoid macular edema supports the mechanism of stabilization of the blood-retina barrier by interferon alpha.[6,9]

Topical interferon α2b has been employed in the treatment of different types of ocular surface tumors, and its safety and efficacy have been shown in multiple studies.[7,18–20] The major side effects reported are irritant conjunctivitis and keratitis which are treated with lubricants without treatment discontinuation.[7,18–20] None of the adverse effects of systemic administration of interferon alpha has been reported with topical treatment.[7,18–20]

In our patient, standard treatment modalities failed. We started our patient on topical interferon α2b based on the efficacy and safety profiles of this treatment in ocular surface tumors. The only concern was that of adequate penetration to the posterior vitreous and retina via topical administration. Lincoff et al. demonstrated high concentration of interferon alpha in the choroid after retrobulbar injection.[10] Moreover, the efficacy of interferon α2b via subtenon administration has been demonstrated in the treatment of diabetic macular edema[15] which may also indicate good penetration of the sclera despite its high molecular weight. However, animal studies are needed to investigate the pharmacokinetic and pharmacodynamic properties of topical interferon α2b. Our patient responded to the proposed experimental treatment after 4 weeks which may indicate reasonable penetration to the posterior vitreous and retina. The temporal relationship between the use of topical interferon α2b and the resolution of chronic cystoid macular edema (unresponsive cystoid macular edema for nine months) points to the efficacy of this treatment and not spontaneous resolution. As efficacy was shown in the initial trial period, we continued the treatment, tapering the treatment dose every eight weeks by one drop. Surface irritation was the only reported side effect in our patient; it was treated successfully with lubricants.

4. Conclusions

This case report points to the potential efficacy and safety of topical interferon α2b in the treatment of refractory pseudophakic cystoid macular edema. Further potent and randomized control studies are

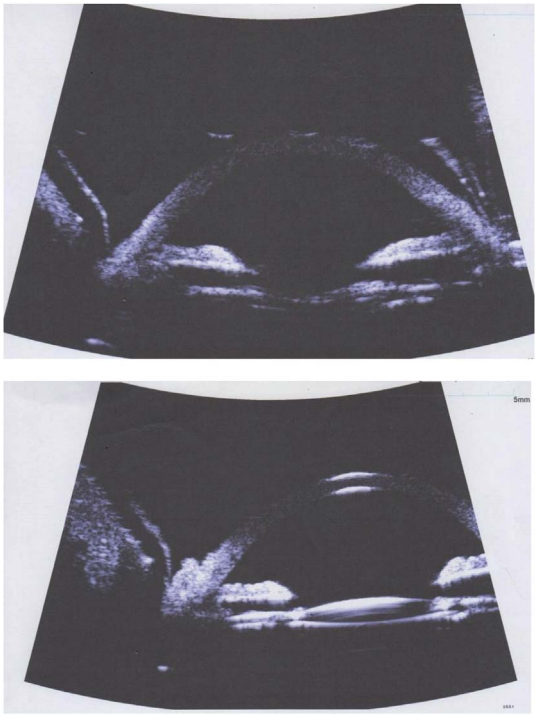

Fig. 1. Ultrasound biomicroscopy of the study eye, which shows intracapsular intraocular lens implantation with good centration and no contact between the intraocular lens haptics and iris.

Table 1
Treatment schedule.

Treatment Schedule	Duration of Treatment
Four times a day	Twelve weeks as there was an improvement after one month of experimental treatment
Three times a day	Eight weeks
Two times a day	Eight weeks
One time a day	Eight weeks
One time every other day	Eight weeks

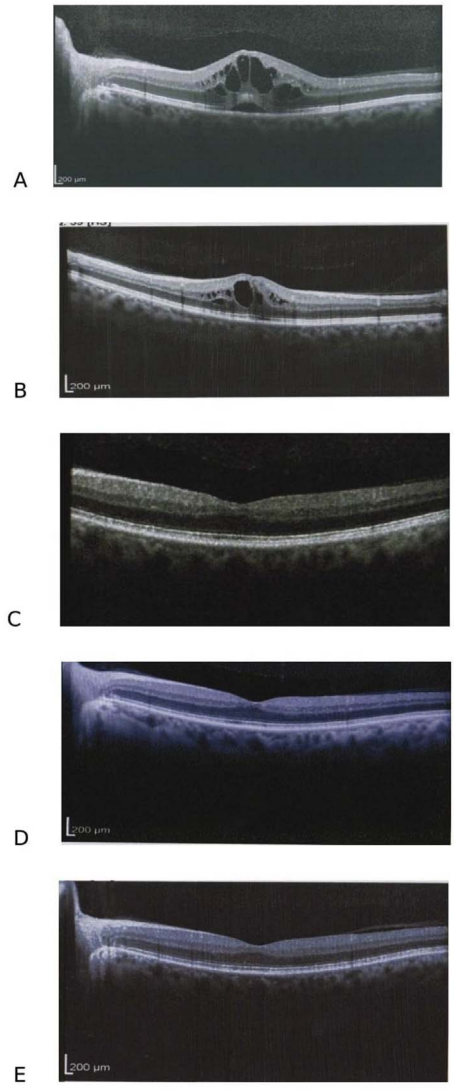

Fig. 2. Changes in central macular optical coherence tomography (A) before starting treatment, (B) four weeks after starting treatment, (C) twelve weeks after starting treatment, (D) twenty-four weeks after starting treatment, and (F) thirty-six weeks after starting treatment.

required to prove our findings.

Patient consent

The written informed consent was given by the patient for publishing the data and left eye images.

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