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Improvement of pseudophakic cystoid macular edema with subconjunctival injections of interferon α2b:a case report

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ABSTRACT

Purpose: To report a patient with resistant cystoid macular edema after an uneventful phacoemulsification cataract surgery who responded to subconjunctival interferon α2b injections.
Observations: This report describes a 60-year-old male patient with pseudophakic cystoid macular edema that was unresponsive to multiple courses of topical non-steroidal anti-inflammatory drugs and steroids during the follow-up period. Weekly subconjunctival interferon α2b (5 MIU/ml) was administered four times. Cystoid macular edema completely resolved after the 4th injection.During a six-month follow-up period, cystoid macular edema did not recur. No adverse local and systemic side effects were observed.
Conclusions and importance: Weekly subconjunctival interferon α2b injections might be a safe and effective treatment modality in the treatment of stubborn pseudophakic cystoid macular edema to conventional treatment.

1. Background

Advanced surgical techniques in cataract surgery with phacoemulsification have considerably decreased the risk of complications. Topical corticosteroids, and/or topical non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used to prevent and reduce inflammatory responses after cataract surgery which might become complicated by Cystoid macular edema (CME).

CME is of the major causes of decreased vision following cataract surgery even after an uneventful one. Angiographic and clinical pseudophakic CME (PCME) have been reported to occur in about 20% and 1–2% of cataract surgeries respectively.[1,2]

CME might resolve spontaneously without any intervention in nearly 90% of cases; however, a small number of cases might experience permanent visual loss.[1]Considering the fact that cataract surgery is one of the most common surgical procedures in ophthalmology, it draws a special attention to investigate new treatment modalities in resistant cases to conventional therapies.[1]A variety of topical, local and systemic therapies including topical and local corticosteroids, topical and oral NSAIDs, and systemic carbonic anhydrase inhibitors (CAIs) alone or in combination have been employed in the treatment of pseudophakic CME (PCME) with different success rates.[1–3]

Interferon is a glycoprotein hormone (multifunctional protein) with cytokine-like effects that stimulates anti-inflammatory effects under different conditions including hypoxia. In addition, interferon has anti-proliferative, immunomodulatory and anti-angiogenic properties.[4]

At cellular level, interferon attenuates neuronal injury by reducing apoptosis when it attaches to a receptor on the cell membrane. Interferon begins a cascade of molecular signaling that interrupts the apoptotic molecular signaling inside cells, reduces inflammation and protects the cells from any injury secondary to hypoxemia, ischemia, and edema.[5]

In this case report, a patient with resistant PCME following an uncomplicated cataract surgery who was successfully treated with weekly subconjunctival interferon α2b injections is presented. To the best of our knowledge, this is the first case of employing subconjunctival interferon α2b injections in the treatment of PCME.

2. Case presentation

A 60-year-old man with an unremarkable past medical and ocular history presented to our clinic with decreased vision in his left eye one month after cataract surgery.He had undergone cataract surgery five months before his first presentation to us. Based on patient's medical records after surgery, he had developed CME one month after his uneventful cataract surgery. CME in left eye had not responded to multiple

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courses of treatment with topical NSAIDS (diclofenac)and corticosteroids (betamethasone) over a period of 4 months before his first visit with us.

On ocular examination, best corrected visual acuity (BCVA) in the left eye was 20/50 with no improvement with pinhole. Refraction of the left eye was +0.25D. The BCVA in right eye was 20/20.

The intraocular pressure (IOP) in both eyes was 15 mmHg. Slit lamp examination of the left eye showed a normal anterior segment. There was no inflammation in anterior chamber (cell and flare) and anterior vitreous (cell). Posterior chamber intraocular lens (PCIOL) was centered in the bag and no white plaques were observed inside the capsular bag after full pupillary dilation. Posterior segment examination revealed clear view with no vitreous haze, normal optic disc, normal retina and retinal vasculature, and thickening of central macula with blunted light reflex.The anterior and posterior segment examination were normal in the other eye. Macular optical coherence tomography (OCT) was performed, using Spectralis OCT (Heidelberg Engineering, Vista, California, USA).

Macular OCT also depicted increased macular thickness and cystic spaces (Fig. 1A). The treatment options and their risks and benefits of each treatment option including subtenon and intravitreal corticosteroid injections were discussed with the patient. Moreover, the experimental subconjucnctival interferon α2b injection therapy with its risks and benefits were discussed with the patient as well. He decided to proceed with the experimental treatment. The informed consent was obtained with a complete explanation of the procedure, including possible side effects and complications. Subsequently, all medications including topical NSAIDS and corticosteroids were discontinued and interferon α2b, 5 million International Units (5 MIU/ml vial, Pooyesh Darou, Tehran,Iran), was injected subconjunctivally in his left eye.

We prescribed 500 mg of oral acetaminophen before and every 6 hours for 24 h after injection as prophylaxis against flu-like syndrome.

After 1 week, there was no change in visual acuity and the second injection was performed. On the third-week follow-up visit, a dramatic improvement in the shape and contour of the left eye macula was observed. Macular thickness decreased to 406 μm from the baseline with a thickness of 483μm. Moreover, BCVA significantly improved from 20/50 to 20/30 (Fig. 1B). Based on the dramatic response after 2 injections, we continued weekly injections for two more injections. At five-week follow-up visit, one week after the 4th injection, CME resolved completely. At his last follow-up visit, six months after the first injection, the macular OCT demonstrated stable thickness and contour with no cystic spaces. Moreover, BCVA was 20/25 in his left eye with no change in refraction from initial presentation to our clinic (Fig. 2).

3. Discussion and conclusions

3.1. Therapeutic regimens for treatment of CME have been widely studied.[6–8]

However, subconjunctival interferon α2b has never been employed in the treatment of PCME. This study is the first report of employing subconjunctival interferon α2b in the treatment of PCME.

Interferon α mechanisms of action for the treatment of CME are not completely known; however, subcutaneous interferon α has been employed in treatment of posterior segment inflammation including inflammatory CME and this might be related to its anti-inflammatory and anti-angiogenic effects.[5–8]

The occurrence of PCME is assumed to be secondary to an increase in vascular permeability following release of inflammatory mediators such as prostaglandins. There is a higher tendency for developing CME in patients with ocular inflammation after an intraocular operation.[9]

In a case series, Butler et al., demonstrated the effectiveness of subcutaneous interferon α2b injection in the treatment of four patients with

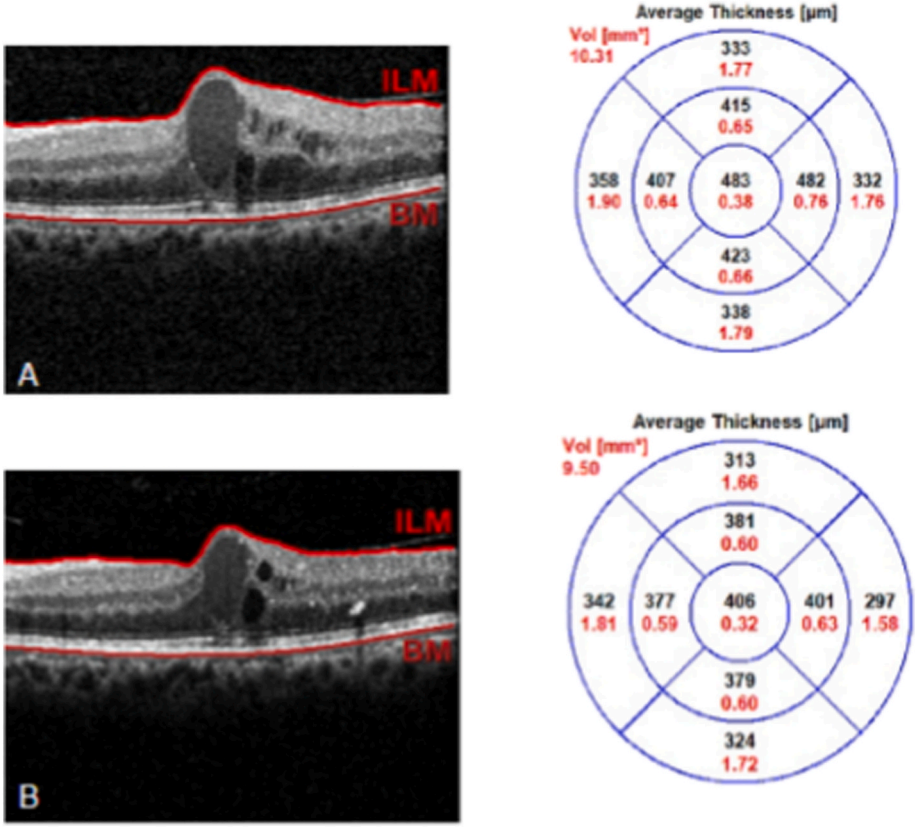

Fig. 1. A Macular OCT showing post cataract surgery cystoid macular edema with central thickness of 483μm. **B.** Macular OCT one week after second subconjunctival injection of interferon α2b showing significant decrease in central thickness to 406μm.

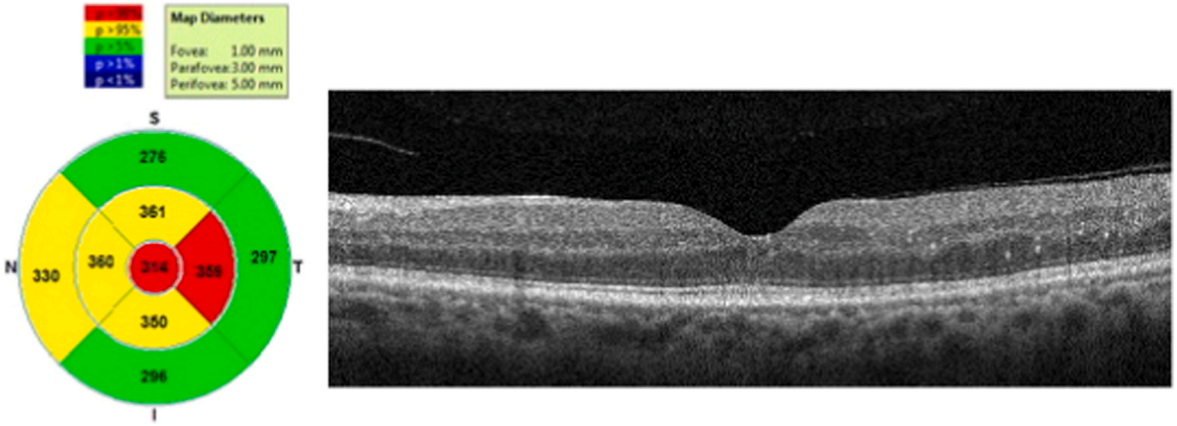

Fig. 2. Macular OCT 6 months after last subconjunctival injection of interferon α2b showing 314μm central thickness.

refractory CME secondary to uveitis.[6]

Deuter et al. also reported the advantages of subcutaneous interferon α2a injection in treatment of patients with chronic Irvine-Gass syndrome.[7] Interferon α2a improves PCME by stabilization of the of the blood-retina barrier and decreasing in vascular permeability.[7]

The efficacy and safety of topical interferon α2b in the treatment of PCME has been studied. Maleki et al. study showed the significant improvement in BCVA and CME in four weeks and complete resolution of CME three months after topical administration of interferon α2b four times a day (1 MIU/ml).[8]

Kawali et al. documented the efficacy of topical interferon in PCME. They noted dramatic improvement within 1–2 weeks in most of their cases, with complete resolution of PCME in five cases within 1–2 months.[10]

There are some advantages for subconjunctival interferon α2b injection over topical drops including faster action and no need for compounded drops. Moreover, it may potentially increase the patient compliance.[11] This treatment also avoids complications associated with periocular and intravitreal corticosteroid injections including steroid-induced ocular hypertension and glaucoma.[11]Therefore, subconjunctival interferon may be considered as a reasonable treatment option for the treatment of CME.

The most common adverse effect of subconjunctival interferon injection is developing a flu-like syndrome that may persist up to two days after injection. Oral acetaminophen can dampen the severity of this adverse event.[11]

Follicular conjunctivitis and subconjunctival hemorrhage are the other complications associated with subconjunctival interferon injection.[11]

Previous studies have shown the safety of interferon α2b weekly subconjunctival injections with different doses of 1, 3, 5 and 10 MIU/ml in the treatment of ocular surface squamous neoplasia.[12]

We decided to use once a week injection of interferon based on previous reports regarding the safety and effectiveness of weekly subconjunctival injections of interferon α2b in treatment of OSSN.[11,12]

In present study, no side effects were observed aside from the inconvenience of the multiple subconjunctival injections and mild chemosis after injections that resolved spontaneously in one or two days. Our patient stopped all other ocular medications including topical NSAIDS and topical corticosteroids concomitant with subconjunctival interferon injections. Although we prescribed a short course of acetaminophen for the patient to prevent interferon induced flue-like syndrome, however as previous treatments with NSAIDS and steroids were unsuccessful, we attribute the resolution of CME to the effect of subconjunctival interferon.We may consider the subconjunctival interferon α2a injection as a minimally-invasive alternative option when conventional treatments fail. However, further investigation and long-term observation of a larger number of patients will be required to fully assess the safety and efficacy of different doses of subconjunctival interferon α2b in PCME.

In conclusion, the outcome of our case suggests subconjunctival interferon injection as an effective and safe treatment modality for post cataract surgery CME.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publishing the information and images.

Availability of data and materials

Not applicable.

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None.

Authors' contributions

All authors listed have contributed sufficiently to the project to be included as authors. H.A was responsible for the design and interpretation of the clinical information. A.E and R.P were responsible for the acquisition of data as well as the drafting the paper and substantial revisions of the manuscript. All authors read and approved the final version of the manuscript.

Declaration of competing interest

Each author warrants that he or she has no commercial associations that might pose a conflict of interest in connection with the submitted article. None of the authors have a proprietary interest.

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Not applicable.

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