Providing Inflammatory Control in a Patient With Undifferentiated Unilateral Alternating Posterior Uveitis



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Noninfectious posterior uveitis is a potentially blinding condition that requires vigilant treatment. The following fictitious case study, inspired by a real-life experience, edited for brevity, describes a patient with undifferentiated noninfectious posterior uveitis who presented with unilateral alternating disease. This patient experienced flares in each eye that were initially managed with intravitreal corticosteroid injections, but long-term control was not achieved. Upon receiving a RETISERT (fluocinolone acetonide intravitreal implant) 0.59 mg implant, the patient's disease activity was adequately controlled and IOP was maintained within normal limits through topical IOP-lowering medications.



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Case Report: Unilateral Alternating Posterior Uveitis

BACKGROUND: A 23-year-old female flight attendant presented with headaches and visual loss in her left eye. Her prior medical history included a sport-related knee injury, and she currently manages her pain with ibuprofen 200 mg prn.

DIAGNOSIS: Visual acuity (VA) in the patient's left eye was 20/100, and a slit lamp examination revealed trace flare, stellate keratic precipitates, and an anterior chamber cell score of 2+. VA in her right eye was 20/20 with normal slit lamp examination findings. Dilated fundus examination of the left eye revealed a grade 1 epiretinal membrane (ERM), inflammatory choroidal nodules, retinal pigment epithelium changes, and active retinal venous vasculitis. She did not exhibit morphological hallmarks of well-differentiated noninfectious posterior uveitic conditions such as birdshot chorioretinopathy, multifocal choroiditis, serpiginous choroiditis, multiple evanescent white dot syndrome, or acute posterior placoid pigment epitheliopathy.³ Additionally, the patient did not exhibit any signs of sarcoidosis, multiple sclerosis, or any other systemic inflammatory disease.³ The patient had negative results from extensive uveitis laboratory testing, including fluorescent treponemal antibody absorption, Lyme disease, and tuberculosis tests, minimizing the possibility of infectious uveitis.⁴ Based on these clinical findings, the patient was diagnosed with undifferentiated noninfectious posterior uveitis in her left eye.

Indication

RETISERT® (fluocinolone acetonide intravitreal implant) 0.59 mg is a corticosteroid indicated for the treatment of chronic noninfectious uveitis affecting the posterior segment of the eye.

Important Safety Information

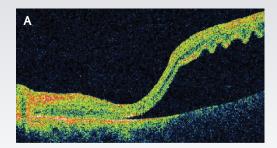
Surgical placement of RETISERT® (fluocinolone acetonide intravitreal implant)
 0.59 mg is contraindicated in active viral, bacterial, mycobacterial or fungal infections of the eye.

Please see additional Important Safety Information throughout and full Prescribing Information for RETISERT® here.

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TREATMENT: The patient was given a posterior sub-tenon's triamcinolone acetonide injection (40 mg) to control her ocular inflammation. One month following the injection, her VA had improved to 20/30, and the number of anterior chamber cells was reduced. In the 2 years following her initial treatment, she received care elsewhere. During this time, VA in her left eye had deteriorated to 20/80, and fluorescein angiography indicated diffuse cystoid macular edema (CME), so she received an intravitreal triamcinolone acetonide injection (4 mg). Approximately 1 year later, she had developed a cataract in her left eye and underwent cataract removal surgery. She began immunomodulatory therapy shortly thereafter. At the end of the 2 years, VA in her left eye was 20/50 with CME and a stable ERM. VA in her right eye was 20/25, but the eye had developed a new ERM.

When the patient returned to me, she presented with mild anterior chamber inflammation and regressed inferior temporal nodules in both eyes. Her right eye had developed a grade 1 cataract and the ERM was non-progressed and mild. Two months later, she developed floaters and active vitritis in the right eye, and her VA had decreased to 20/40. She began a treatment course of topical prednisolone acetate 0.1% QID OU and experienced IOP elevation in both eyes, which was managed with dorzolamide hydrochloride 2%/timolol maleate 0.5% and brimonidine tartrate 0.1% eye drops.



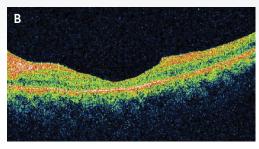
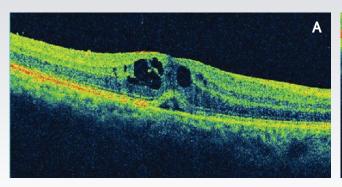


Figure 1. OCT images of retinal detachment in the left eye (A), which was resolved after 2 weeks of oral prednisone 60 mg QD and prednisolone acetate 0.1% QID treatment (B).

Six months later, VA in her left eye had declined to 20/100, and the ERM had worsened. She underwent a pars plana vitrectomy procedure for removal of the ERM and internal limiting membranes. She was also given an intravitreal triamcinolone (8 mg) injection in her left eye. Approximately 1 month following the surgical procedure, the patient returned with a large inferior retinal detachment with no visible breaks in her left eye and shifting fluid (Figure 1). She was placed on oral prednisone 60 mg QD and continued with topical prednisolone acetate 0.1% QID. Within 2 weeks, all subretinal fluid was resolved, vision was 20/80, and her central foveal thickness was $163 \, \mu m$.

Shortly after the retinal detachment in her left eye, she experienced an inflammatory flare in her right eye (Figure 2). She was given an intravitreal injection of triamcinolone acetonide (4 mg), and her symptoms resolved in approximately 1 week. Throughout the following year, her left eye remained stable, while her right eye continued to display signs of active uveitic activity, which we managed with intravitreal injections of triamcinolone acetonide (4 mg) every 6 months (Figure 3). She also underwent cataract removal surgery in her right eye during this time. The ERM in her right eye subsequently worsened; and, she underwent a pars plana vitrectomy with removal of the ERM and internal limiting membranes.



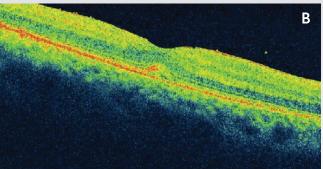


Figure 2. OCT images of the first flare in the right eye (A). Subretinal fluid was resolved with an intravitreal injection of triamcinolone acetonide (4 mg) (B).

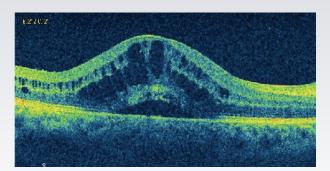


Figure 3. Recurrent flares in the right eye resulted in subretinal fluid, seen here on OCT, that was managed with an intravitreal injection of triamcinolone acetonide (4 mg).

PATIENT FOLLOW-UP: In the immediate post-implantation period, the patient experienced a temporary decrease in VA.

Oral prednisone, immunomodulatory therapy, and topical prednisolone acetate were steadily tapered over 3 months following RETISERT implantation. One year after RETISERT therapy, her right eye was quiescent and remained quiescent for a total of 8 years (Figure 4). In clinical trials, 37% of RETISERT-implanted eyes required surgical intervention to manage elevated IOP and approximately 77% of RETISERT-implanted eyes required topical IOP-lowering medications. The patient experienced elevated IOP (26 mm Hg) that was managed with brimonidine tartrate 0.25%/timolol maleate 0.5%. Eight years following implantation, the RETISERT implant dissociated from the anchoring strut and required surgical removal. The dissociation of the drug pellet from

WHY RETISERT? Although the patient's left eye was stable, she had lost vision due to under-treated uveitis flare ups. She had received five intravitreal triamcinolone injections in her right eye, in addition to immunomodulatory therapy, but she was still experiencing inflammatory flares regularly. As a corticosteroid implant indicated for the treatment of chronic noninfectious uveitis affecting the posterior segment of the eye, RETISERT is a viable alternative for patients with noninfectious posterior uveitis who are unresponsive to corticosteroid injections or immunomodulatory therapy. ^{5,6}
The patient was counseled on the risks and benefits of RETISERT, including cataract development and IOP elevation, and she elected to receive a RETISERT implant in her right eye. Since the patient was bilaterally pseudophakic at the time of RETISERT implantation, she was not at risk for RETISERT-induced cataract formation.

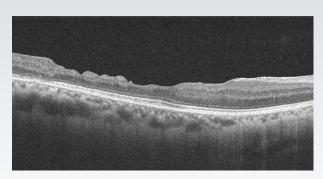


Figure 4. OCT image of the right eye 1 year following RETISERT implantation. There is no evidence of subretinal fluid, and uveitis activity is quiescent.

the anchoring strut has been previously described and was attributed to an adhesive process used in older implants, but this has since been modified in newer implants. RETISERT is designed to release fluocinolone acetonide at a steady state over approximately 30 months. RETISERT may be replaced upon depletion of fluocinolone acetonide as evidenced by recurrence of uveitis. However, in her most recent visit both of her eyes continued to remain quiescent, and IOP was maintained within normal limits so reimplantation was not performed. Fifteen months after pellet removal, the patient retained 20/25 VA and complete quiescence of her posterior uveitis.

Important Safety Information (cont'd)

hemorrhage, vitreous loss, and wound dehiscence.

- Based on clinical trials with RETISERT®, during the 3-year post-implantation period, nearly all phakic eyes are expected to develop cataracts and require cataract surgery.
- As with any surgical procedure, there is risk involved. Potential complications accompanying intraocular surgery to place RETISERT® into the vitreous cavity may include, but are not limited to, the following: cataract formation, choroidal detachment, endophthalmitis, hypotony, increased intraocular pressure, exacerbation of intraocular inflammation, retinal detachment, vitreous

Please see additional Important Safety Information throughout and full Prescribing Information for RETISERT® here.

Conclusions

Noninfectious posterior uveitis is a condition that requires long-term management.⁸ Intravitreal corticosteroid injections are often used to manage intraocular inflammation, but may not provide adequate control in some situations. This case study describes a patient who presented with unilateral alternating disease and received multiple corticosteroid injections, but continued to experience inflammatory flares. After 5 years of multiple therapies, the patient was able to achieve adequate inflammatory control with a RETISERT implant.

Important Safety Information (cont'd)

- Following implantation of RETISERT®, nearly all patients will experience an immediate and temporary decrease in visual acuity in the implanted eye which lasts for approximately one to four weeks post-operatively.
- Use of corticosteroids may result in elevated IOP and/or glaucoma. Based on clinical trials with RETISERT®, within 3 years post-implantation, approximately 77% of patients will require IOP lowering medications to control intraocular pressure and 37% of patients will require filtering procedures to control intraocular pressure.
- Patients should be advised to have ophthalmologic follow-up examinations of both eyes at appropriate intervals following implantation
 of RETISERT®. Physicians should periodically monitor the integrity of the implant by visual inspection.
- Ocular administration of corticosteroids has been associated with delayed wound healing and perforation of the globe where there is thinning of the sclera.
- The most frequently reported ocular adverse events in clinical trials with RETISERT® occurring in 50-90% of patients included: cataract, increased intraocular pressure, procedural complications and eye pain. The most common non-ocular event reported was headache (33%).

Please see additional Important Safety Information throughout and full Prescribing Information for RETISERT® here.

References: 1. Dick AD, Tundia N, Sorg R, et al. Risk of ocular complications in patients with noninfectious intermediate uveitis, posterior uveitis, or panuveitis. Ophthalmology. 2016;123(3):655-662. 2. Thorne JE, Suhler E, Skup M, et al. Prevalence of noninfectious uveitis in the United States: a claims-based analysis. JAMA Ophthalmol. 2016;134(11): 1237-1245. 3. Jabs DA, Busingye J. Approach to the diagnosis of the uveitides. Am J Ophthalmol. 2013;156(2):228-236. 4. Lin P. Infectious uveitis. Curr Ophthalmol Rep. 2015;3(3):170-183. 5. RETISERT [prescribing information]. Bausch & Lomb Incorporated. 6. Haghjou N, Soheilian M, Abdekhodaie MJ. Sustained release intraocular drug delivery devices for treatment of uveitis. J Ophthalmic Vis Res. 2011;6(4):317-329. 7. Akduman L, Cetin EN, Levy J, et al. Spontaneous dissociation and dislocation of Retisert pellet. Ocul Immunol Inflamm. 2013;21(1):87-89. 8. McCluskey PJ, Towler HM, Lightman S. Management of chronic uveitis. BMJ. 2000;320(7234):555-558.

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