American Journal of Ophthalmology Case Reports 37 (2025) 102240

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

Persistent bilateral sclerouveitis following bimatoprost implantation and removal☆

Cheng Jiao [a,b], Ganesh Prabakaran [a], Thomas Berk [c], Homaira Ayesha Hossain [c], Sruthi Arepalli [c,*]

[a] Medical College of Georgia, Augusta University, Augusta, GA, USA
[b] University of North Carolina, Chapel Hill, NC, USA
[c] Emory Eye Center, Emory University, Atlanta, GA, USA

ARTICLE INFO

Keywords:
Bimatoprost implant
Prostaglandin
Sclerouveitis

ABSTRACT

Purpose: To report a case of persistent bilateral sclerouveitis following bilateral bimatoprost implantation (Durysta) that required implant removal and oral steroid course.

Observation: A 75-year-old Caucasian male with no prior ocular inflammation experienced bilateral sclerouveitis post bilateral bimatoprost implantation. Despite implant removal from both eyes, the ocular inflammation persisted, showing cystoid macular edema in both eyes and exudative retinal detachment in the right. A comprehensive assessment revealed no clear etiology and no definitive systematic inflammatory syndrome. The ocular inflammation was unresponsive to topical steroids and only receded following weeks-long course of oral steroids. Eventually, the patient required immunosuppression due to recurrence of the inflammation.

Conclusion and importance: The persistence and severity of this inflammatory response to bimatoprost implants, despite its removal, highlight the importance of considering patient-specific risk factors and tailoring management accordingly. Clinicians should be prepared for possible severe reactions requiring intervention.

1. Introduction

The bimatoprost implant (Durysta; Allergan, Inc.) is an intracameral device for patients with open-angle glaucoma that releases a prostaglandin analogue (PGA) over four to six months.[1] Notable adverse reactions include conjunctival hyperemia and corneal endothelial cell loss, but no reports have documented sclerouveitis following implantation.[2,3] This report presents an unique case of bilateral sclerouveitis following bilateral bimatoprost implantation with inflammation persisting post-removal.

2. Case report

A 75-year-old Caucasian male with no prior history of ocular inflammation presented with bilateral sclerouveitis. He had undergone simultaneous, bimatoprost implantation elsewhere in both eyes (OU) for a diagnosis of primary open angle glaucoma and developed uveitis OU 1 week after implantation. He subsequently underwent implant removal after five months in the right eye (OD) and eight months in the left eye (OS) after his inflammation failed to resolve with topical prednisolone acetate. After removal, the patient continued to have persistent inflammation for nine months in the right eye and six months in the left eye while on topical steroids. He was referred to our center for a second opinion. Medical history was significant for hypertension and diabetes, while ocular history included selective laser trabeculoplasty (SLT) and uncomplicated cataract surgery OU four years prior.

On presentation, his vision was 20/150 OD and 20/60 OS, with intraocular pressure (IOP) measuring 14 OU. Slit lamp examination was significant for 2+ scleral injection and tenderness to palpation OU. Both intraocular lenses were well positioned, and there was trace anterior chamber cell OU, with trace vitreous cell OD and 1+ vitreous cell OS. Fundoscopic examination revealed enlarged cup to disc ratio (0.5) OU and cystoid macular edema (CME) OU. Further, a small exudative retinal detachment was noted in the temporal periphery OD, thought to be

☆ Claims of Priority: After conducting a literature review on October 9th, 2024 utilizing PubMed and Google Scholar using the key words (bimatoprost implant and sclerouveitis), we did not find any prior reports of sclerouveitis in the setting of this medication.

* Corresponding author. Emory Eye Center, Emory University, 1365B Clifton Road, N.E., Suite 2400, Atlanta, GA, 30307, USA.
E-mail address: sruthiarepalli@gmail.com (S. Arepalli).

https://doi.org/10.1016/j.ajoc.2024.102240
Received 26 June 2024; Received in revised form 10 December 2024; Accepted 17 December 2024
Available online 19 December 2024

secondary to the underlying scleral inflammation, and a small peripheral chorioretinal scar was noted OS without overlying inflammation. Ultrasonography revealed choroidal thickening with a small peripheral exudative retinal detachment with no breaks OD, and choroidal thickening with slight fluid in the subtenon space OS. Ultrasound biomicroscopy confirmed no retained lens fragments, lens tilt, or remaining bimatoprost implant OU. Fluorescein angiography confirmed disc and macular leakage. (Fig. 1A and 1B).

Given the small chorioretinal scar in the left eye, an aqueous chamber tap was performed in the left eye and returned negative for Herpes simplex virus, varicella-zoster virus, cytomegalovirus, and toxoplasmosis. Further laboratory results were negative for QuantiFERON-TB Gold (tuberculosis), rapid plasma reagin, syphilis IgM/IgG, double-stranded DNA, anti-cyclic citrullinated peptide, angiotensin-converting enzyme, antineutrophil cytoplasmic antibodies, toxoplasmosis antibodies, and human leukocyte antigen B27 (HLA-B27). Pertinent positive findings included bibasilar patchy opacities inconsistent with sarcoidosis on chest X-ray, and an elevated rheumatoid factor to 6.7. The patient was evaluated with rheumatology and found to have no signs of systemic inflammation and no signs of rheumatoid arthritis. The patient was treated with difluprednate four times a day OU for four weeks with no effect, and transitioned to oral steroids (60 miligrams, (mg) which led to marked improvement within two weeks at this dosage, and achieved resolution of the intraocular inflammation and CME OU, as well the exudative detachment OD at four weeks. After the taper of oral steroids was completed at a rate of 10 mg every week, the patient developed recurrent CME OU without any other signs of intraocular inflammation that responded to topical prednisolone acetate four times a day OU. However, during his follow-up, the patient developed a steroid-dependent IOP of 41 mm of mercury (mmHg) in the right eye and 42 mmHg in the left eye while on topical steroid therapy that required dorzolamide, timolol, and rhopressa. Despite topical therapy, the IOP remained elevated, and eventually, an Ahmed glaucoma shunt was implanted OU. Given his recurrent ocular inflammation and CME, as well as his steroid responsive IOP rises, a transition to immunomodulatory therapy was recommended. The patient was started on mycophenolate mofetil, 1 g, twice a day, and tapered off topical steroids after 1 month of initiating immunosuppression without recurrence of inflammation or CME his remaining follow up period of six months.

3. Discussion

Here, we present an unique case of bilateral sclerouveitis following bimatoprost implantation. While prostaglandin exposure has been previously associated with uveitis, its occurrence is quite rare. The severity and persistence of the uveitis in this instance necessitated the removal of the PGA implant and the use of oral steroids.

The bimatoprost implant (Durysta) uses a preloaded single-use applicator to facilitate intracameral injection.[4] Once implanted, it is positioned in the inferior iridocorneal angle, offering continuous PGA release to the iris-ciliary body.[5] There are two main mechanisms through which the implant lowers IOP. Firstly, the outflow of aqueous humor through the uveoscleral and trabecular routes is increased.[6] Secondly, the drug decreases episcleral venous pressure, further facilitating outflow.[7]

A prior meta-analysis of topical prostaglandin use showed a mere 0.22 % incidence of inflammation.[6] It is noteworthy that PGA use has been associated with a higher incidence of CME and uveitis in patients with a history of recent ocular surgery, aphakia or pseudophakia, or a history of uveitis.[6] The median time of uveitis onset was 6 days after PGA application.[6] Topical bimatoprost has previously been implicated as a potential trigger for both non-granulomatous and granulomatous anterior uveitis, as well as choroidal detachment.[8–10] In such cases, discontinuation of the bimatoprost, coupled with administration of topical or systemic steroids, led to complete resolution of the inflammation over several weeks.[8–10]

Data from the Phase III trials of the bimatoprost implant revealed a higher incidence of inflammatory adverse events in the treatment group. These primarily included anterior chamber cell (2.3 %) and iritis (3.4 %). However, these cases were mild and temporary. None warranted implant removal.[2] The leading cause for implant removal was other adverse events such as corneal edema or corneal endothelial cell loss, seen in a minority of participants (2.9 %). One post-trial report has described a case of bilateral CME following implantation.[11] While the inflammation resisted treatment with topical non-steroidal anti-inflammatory drops, two months of topical steroids alone cleared the ocular inflammation without necessitating implant removal or more aggressive systemic therapies.[11] In contrast, our case developed persistent inflammation for nine months OD and six months OS while on

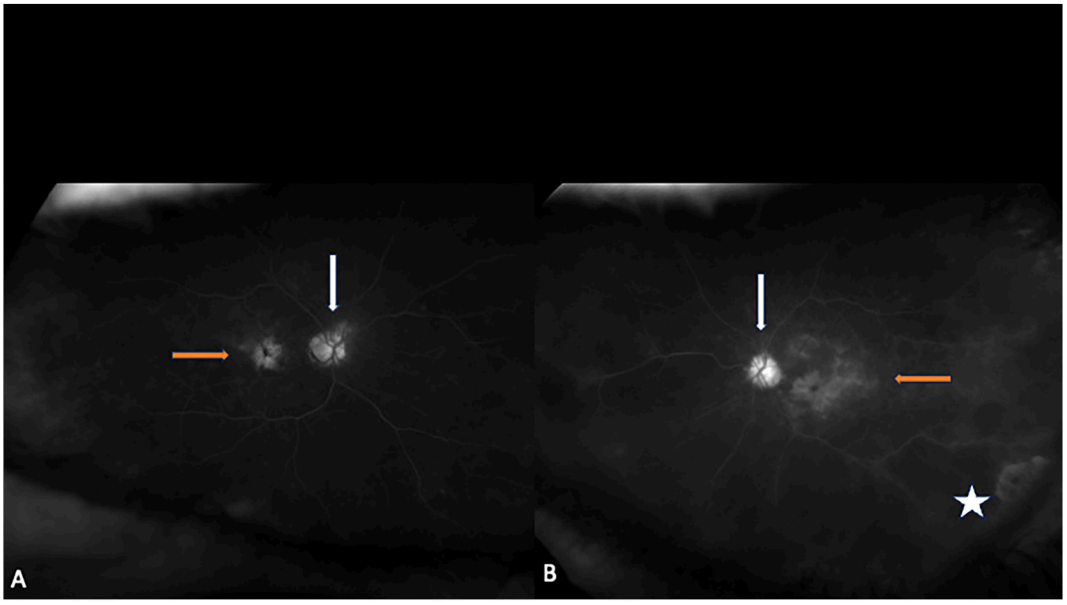

Fig. 1. A 75 year old Caucasian male with bilateral sclerouveitis following bilateral bimatoprost implantation. Late phase fluorescein angiography on presentation confirming disc leakage (white arrow) and macular leakage (orange arrow) right (A) and left eye (OS) (B), with staining of the peripheral chorioretinal scar OS (star). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

topical steroids, and eventually required oral prednisone to achieve quiescence.

Multiple rationales for uveitis following bimatoprost implantation exist. It has been proposed that prostaglandins prompt ocular inflammation by compromising the blood-aqueous barrier. Specifically, PGAs activate prostaglandin F receptors, leading to the release of PGE_2 inflammatory cytokines.[12] Additionally, this can then induce matrix metalloproteinases enzymes, which degrade various components of the extracellular matrix including Type 1 collagen. A subsequent rise in the permeability of the ciliary epithelium can cause an increased leakage of protein into the aqueous humor, intensifying the intraocular inflammatory response.[13] Both these mechanisms in concert potentiate a uveitic response. In the specific context of our patient, he had undergone prior SLT, disrupting the trabecular meshwork. This disruption may have also led to increased permeability and sensitivity to the bimatoprost, exacerbating the effects. Compared to topical bimatoprost administration, the bimatoprost implant's concentration is vastly higher (4.400-fold) at the iris-ciliary body, theoretically elevating the risk of uveitis further.[5]

4. Conclusion

Our report highlights the novel findings of a patient developing bilateral sclerouveitis after bimatoprost implant with persistent inflammation. The severity observed suggests that in certain scenarios, removal of the implant and/or treatment with oral steroids and possibly even immunomodulatory therapy may be necessary. In the future, clinicians should remain vigilant to patient's history and potential risk factors which may amplify inflammatory susceptibility with bimatoprost implant.

CRediT authorship contribution statement

Cheng Jiao: Writing – original draft. **Ganesh Prabakaran:** Writing – review & editing, Investigation. **Thomas Berk:** Methodology, Writing – review & editing. **Homaira Ayesha Hossain:** Writing – review & editing. **Sruthi Arepalli:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Data curation, Conceptualization.

Patient consent

Consent to publish this case report was obtained. The report does not contain any personal information that could lead to the identification of the patient.

Funding

No funding or grant support

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

None.

References

1. Durysta (bimatoprost implant). Package insert. *Allergan*. 2021.
2. Bacharach J, Tatham A, Ferguson G, et al. Phase 3, randomized, 20-month study of the efficacy and safety of bimatoprost implant in patients with open-angle glaucoma and ocular hypertension (ARTEMIS 2). *Drugs*. Nov 2021;81(17):2017–2033. https://doi.org/10.1007/s40265-021-01624-9.
3. Weinreb RN, Bacharach J, Brubaker JW, et al. Bimatoprost implant biodegradation in the phase 3, randomized, 20-month ARTEMIS studies. *J Ocul Pharmacol Therapeut*. Jan-Feb 2023;39(1):55–62. https://doi.org/10.1089/jop.2022.0137.
4. Kesav NP, Young CEC, Ertel MK, Seibold LK, Kahook MY. Sustained-release drug delivery systems for the treatment of glaucoma. *Int J Ophthalmol*. 2021;14(1):148–159. https://doi.org/10.18240/ijo.2021.01.21.
5. Seal JR, Robinson MR, Burke J, Bejanian M, Coote M, Attar M. Intracameral sustained-release bimatoprost implant delivers bimatoprost to target tissues with reduced drug exposure to off-target tissues. *J Ocul Pharmacol Therapeut*. Jan/Feb 2019;35(1):50–57. https://doi.org/10.1089/jop.2018.0067.
6. Hu J, Vu JT, Hong B, Gottlieb C. Uveitis and cystoid macular oedema secondary to topical prostaglandin analogue use in ocular hypertension and open angle glaucoma. *Br J Ophthalmol*. Aug 2020;104(8):1040–1044. https://doi.org/10.1136/bjophthalmol-2019-315280.
7. Lee SS, Robinson MR, Weinreb RN. Episcleral venous pressure and the ocular hypotensive effects of topical and intracameral prostaglandin analogs. *J Glaucoma*. Sep 2019;28(9):846–857. https://doi.org/10.1097/IJG.0000000000001307.
8. Parentin F. Granulomatous anterior uveitis associated with bimatoprost: a case report. *Ocul Immunol Inflamm*. Mar 2003;11(1):67–71. https://doi.org/10.1076/ocii.11.1.67.15580.
9. Packer M, Fine IH, Hoffman RS. Bilateral nongranulomatous anterior uveitis associated with bimatoprost. *J Cataract Refract Surg*. Nov 2003;29(11):2242–2243. https://doi.org/10.1016/s0886-3350(03)00470-x.
10. Massimo L, Micelli Ferrari L, Nikolopoulou Gisotti E, et al. Granulomatous uveitis and choroidal detachment in a patient after topical treatment with Bimatoprost: a case report. *Eur J Ophthalmol*. May 2022;32(3):NP19–NP22. https://doi.org/10.1177/1120672121990573.
11. Patel SH, Badar A, Bakhsh S, Jusufbegovic D. Bilateral cystoid macular edema following bimatoprost implants. *Retin Cases Brief Rep*. Aug 25 2022. https://doi.org/10.1097/ICB.0000000000001346.
12. Tsuge K, Inazumi T, Shimamoto A, Sugimoto Y. Molecular mechanisms underlying prostaglandin E2-exacerbated inflammation and immune diseases. *Int Immunol*. Aug 23 2019;31(9):597–606. https://doi.org/10.1093/intimm/dxz021.
13. Lopilly Park HY, Kim JH, Lee KM, Park CK. Effect of prostaglandin analogues on tear proteomics and expression of cytokines and matrix metalloproteinases in the conjunctiva and cornea. *Exp Eye Res*. Jan 2012;94(1):13–21. https://doi.org/10.1016/j.exer.2011.10.017.