American Journal of Ophthalmology Case Reports 23 (2021) 101134

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

Posterior cyclodialysis cleft following intravitreal injection

Rachel H. Lee [a], Aubrey R. Tirpack [b], Janet L. Davis [a], Mohamed S. Sayed [a], Vikas Chopra [c], Steven J. Gedde [a,*]

[a] Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, FL, USA
[b] Department of Ophthalmology, Cincinnati Eye Institute, Cincinnati, OH, USA
[c] Department of Ophthalmology, University of California, Los Angeles, Los Angeles, CA, USA

ARTICLE INFO

Keywords:
Complications of intravitreal injections
Hypotony
Cyclodialysis cleft

ABSTRACT

Purpose: To describe an unusual complication of an intravitreal injection.
Observation: Here, we report a case of hypotony following an intravitreal injection due to a posterior cyclodialysis cleft and describe its management and resolution.
Conclusions: Posterior cyclodialysis clefts are a rare cause of hypotony following intravitreal injection. Posterior clefts may not be visualized by conventional gonioscopy. Ultrasound biomicroscopy may be useful in aiding diagnosis.
Importance: This report highlights a rare cause of hypotony following intravitreal injection and illustrates the importance of adjunctive imaging for accurate diagnosis.

1. Introduction

Intravitreal injections (IVIs) are among the most commonly performed ophthalmic procedures worldwide.[1,2] Specifically, IVIs of anti-vascular endothelial growth factors are among mainstay treatments for complications of diabetic retinopathy, retinal vascular occlusions, and age-related macular degeneration.[3–5]

In general, IVIs are well-tolerated. The most common complications of IVIs include subconjunctival hemorrhage, discomfort associated with the injection, cataract, and elevated intraocular pressures. Visually devastating complications including intraocular hemorrhage, retinal detachment, and endophthalmitis are rare.[6–8]

Hypotony following intravitreal injections have been reported infrequently in the literature. Here we describe a case of hypotony after intravitreal injection due to a posterior cyclodialysis cleft.

2. Case report

A 67-year-old phakic male was referred to Bascom Palmer Eye Institute for hypotony of the right eye. The patient's past ophthalmic history was notable for exudative age-related macular degeneration in the right eye, for which he received intravitreal bevacizumab injections. The patient denied a history of trauma. Three days after an IVI of the right eye in the superotemporal quadrant with a 30-gauge needle 4 mm posterior to the limbus, the patient presented to an outside hospital where the on-call ophthalmologist noted hypotony, anterior chamber cell, and vitreous hemorrhage. The ophthalmologist started the patient on prednisolone acetate 1% for presumed iridocyclitis. The patient returned the following day with increased cell and flare, accompanied by headache and low-grade fever for which the ophthalmologist then performed a diagnostic vitreous tap and injection of intravitreal antibiotics with a 25-gauge needle 4 mm posterior to the limbus (1 mg vancomycin, 2.25 mg ceftazidime) for suspected endophthalmitis. Intravitreal cultures showed no growth of causative organisms. Therefore, the patient was placed on difluprednate topical eye drops every 2 h. Over the next month, the patient's best corrected visual acuity in the right eye was reported to remain 20/200, with intraocular pressures ranging from 4 to 14 mm Hg. Attempted tapering of steroids over the course of one month led to recurrent hypotony, for which the patient was referred to Bascom Palmer Eye Institute for further care.

On initial examination, the patient was found to have a best-corrected visual acuity of 20/100 in the right eye and 20/30 in the left eye. Intraocular pressures were 5 mmHg in the right eye and 16 mmHg in the left eye. Slit lamp examination of the right eye was notable for a deep anterior chamber, rare cells, 1+ flare, posterior synechiae and pigment on the anterior lens capsule. Both angles were open to ciliary body in all four quadrants on gonioscopy. Dilated fundoscopic exam of the right eye revealed a resolving inferior vitreous hemorrhage with no

* Corresponding author. Bascom Palmer Eye Institute, 900 NW 17th St. Miami, FL, 33136, USA.
E-mail address: sgedde@med.miami.edu (S.J. Gedde).

https://doi.org/10.1016/j.ajoc.2021.101134
Received 27 February 2021; Received in revised form 2 May 2021; Accepted 27 May 2021
Available online 10 June 2021
2451-9936/© 2021 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

evidence of retinal tears or detachment and a cup-to-disc ratio of 0.45. Ocular coherence tomography (OCT) imaging of the optic nerve revealed slight disc edema; OCT imaging of the macula confirmed retino-choroidal folds (Fig. 1). Examination of the left eye was unremarkable. A cyclodialysis cleft was suspected but not visualized on careful gonioscopy; therefore, high-frequency ultrasound biomicroscopy (UBM) was obtained. UBM was notable for a posterior cyclodialysis cleft in the right eye, with direct communication between the posterior chamber and suprachoroidal space with suprachoroidal fluid in the superotemporal quadrant from approximately 9:30 to 10 o'clock (Fig. 2A and B).

It was unclear whether the cleft and ciliary body detachment were solely responsible for his hypotony. The patient was started on oral prednisone 60 mg daily and acyclovir 800 mg twice daily, to empirically treat inflammation as a possible etiology of hypotony, in addition to atropine three times daily. Bevacizumab injections were suspended. After one month, the patient returned to the clinic with a best-corrected visual acuity of 20/200, intraocular pressure of 7 mm Hg in the right eye and rare pigmented cells in the anterior chamber on slit lamp examination. After failing to improve on oral agents, the patient was consented for pneumatic retinopexy with cryotherapy with the hope of achieving cleft closure. Oral prednisone and acyclovir were discontinued.

Five weeks later, prior to scheduled surgery, the patient presented to the emergency room with severe right eye pain and nausea. Best-corrected visual acuity was 20/150 in the right eye, and the IOP in the right eye measured 60 mmHg. Exam was notable for a deep and quiet anterior chamber, posterior synechiae and moderate posterior subcapsular cataract, and hazy view to the posterior pole. UBM showed closure of the posterior cyclodialysis cleft and reattachment of the ciliary body (Fig. 2C and D). Intraocular pressures were reduced with topical ocular antihypertensive medications.

Within one week, the patient was weaned off all IOP lowering medications, and the IOPs remained stable between 8 and 22 mmHg for the following three months. The patient eventually underwent cataract surgery followed by pars plana vitrectomy with epiretinal membrane peel. At his most recent postoperative visit, the patient had a best-corrected visual acuity of 20/30 with an intraocular pressure of 14 mmHg on no medications in the right eye. His macular degeneration has remained stable, without recurrence of macular folds on subsequent exams and OCTs.

3. Discussion

Overall complication rates after intravitreal injections are low. According to prior studies, the overall rates of serious adverse ocular complications–including cataract, vitreous hemorrhage following IVI, and reduction in best-corrected visual acuity–following intravitreal injections are under 10%.[7,9,10] Hypotony following IVI is even more rare; here we report the first case of a posterior cleft following intravitreal injection.

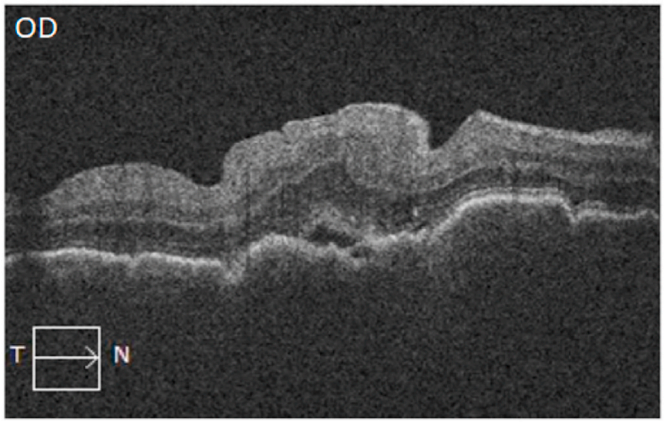

Fig. 1. Ocular coherence tomography (Zeiss, Jena, Germany) showing hypotony maculopathy of the right eye.

We surmise that in this patient, the needle track and physical injection of the IVI agent was likely sufficient to cause a ciliary body detachment. Expert consensus guidelines recommend that intravitreal injections should be administered 3.5–4 mm posterior to the limbus,[1] through the pars plana to avoid the lens, ciliary body, and retina. Anterior injection could plausibly damage the ciliary body and result in vitreous hemorrhage. Shallow or early injection might cause fluid dissection along the needle track, creating a communication between the posterior chamber and suprachoroidal space and rupturing the ciliary body. The resulting ciliary body detachment could lead to hypotony due to a posterior uveal cleft. Due to its location, posterior clefts may not be visible by conventional gonioscopy. In this patient, adjunct UBM imaging was useful in identifying the posterior cyclodialysis cleft and making the correct diagnosis.

Although the posterior cyclodialysis cleft was small in size, there were several indications that the cleft caused the patient's persistent hypotony. First, maximum conservative therapy with oral prednisone for one-month duration failed to resolve the patient's choroidal effusions and persistent hypotony. Thus, although a uveitic etiology could have contributed to his initial presentation—with a history of fevers accompanied by anterior chamber reaction—it was likely not the sole cause of his hypotony. Furthermore, the patient developed sudden, marked IOP elevation characteristic of spontaneous closure of a cyclodialysis cleft, and repeat UBM scan confirmed cleft closure. Additionally, anterior chamber inflammation ultimately resolved following cleft closure, suggesting that the presence of cyclodialysis cleft and ciliary body injury may have exacerbated or contributed to the presence of anterior chamber inflammatory response. Taken together, these series of events present compelling evidence that the cleft was sufficient to cause chronic hypotony recalcitrant to medical therapy; and that cleft closure allowed for resolution of symptoms.

Pasadhika et al. described a posterior uveal cleft following an insertion of a fluocinolone acetonide implant. The patient was noted to have separation of the uveal tissue at the pars plana, allowing communication between the vitreous cavity and suprachoroidal space. After pars plana vitrectomy, removal of the implant, and cryotherapy at the site of the posterior cleft, intraocular pressure normalized.[11] Similar to our patient, this report describes a cleft involving posterior uveal structures that allowed a communication between the suprachoroidal space and the vitreous cavity in that case, and the posterior chamber in ours. In the absence of an intraocular implant, the posterior cleft in our patient was able to close with medical management only. It is unknown if the proposed surgical procedure would have been able to close the cleft, as it was modeled after techniques that have been used to successfully close anterior clefts.

Hypotony following intravitreal injections are rare. One group reported a wound leak following an IVI with a 30-gauge needle, associated with a Seidel positive test and bleb formation. The group reported that the leak had closed after three days and the patient's vision and intraocular pressure returned to baseline.[12] Another group reported a Seidel positive IVI injection site in a patient who had pars plana vitrectomy and pan-retinal photocoagulation for vitreous hemorrhage due to proliferative diabetic retinopathy nine months prior. Exploratory surgery revealed a punctiform scleral wound without vitreous incarceration, requiring surgical closure.[13] Similarly, another patient with a history of pars plana vitrectomy for vitreous opacities developed hypotony and choroidal detachment following IVI with a 30-gauge needle. Surgical exploration revealed patent scleral wound, requiring surgical closure.[14] In each of these prior reports, the authors suggest that these presentations were related to primary failure of the sclerotomy sites to close. Unlike these prior reports, our patient had no evidence of a patent sclerotomy visible on clinical exam, nor on UBM imaging.

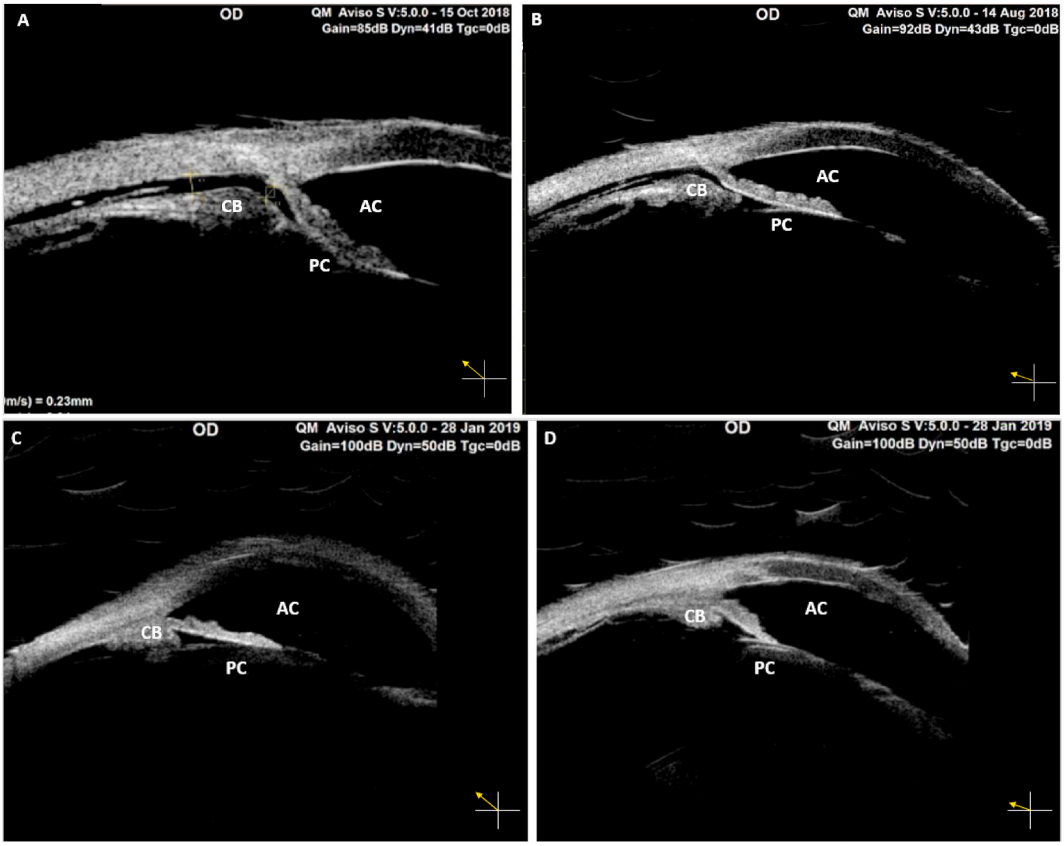

Fig. 2. Ultrasound biomicroscopy (Aviso S, Quantel Medical, Paris, France) showing cyclodialysis cleft connecting the posterior chamber to the suprachoroidal space (**Panel A-B).** Repeat ultrasound biomicroscopy showed closure of the cleft (**Panel C-D)**. AC- anterior chamber; PC-posterior chamber; CB- ciliary body.

Iatrogenic cyclodialysis cleft following ophthalmic surgery occurs infrequently, and has been previously reported following cataract surgery, incisional glaucoma surgery, and other intraocular procedures. Prior case reports have described probable cyclodialysis cleft following trabeculectomy, as well as cyclodialysis clefts following ab-interno trabeculotomy, goniotomy, surgical insertion of a gancyclovir implant, and seemingly uncomplicated cataract surgery.[15-22] The authors from these reports suggest that the presence of cyclodialysis cleft in their patients were likely the result of procedure technique, of improperly positioned intraocular equipment, or re-opening of a cleft following distant trauma.

4. Conclusions

In conclusion, hypotony following IVI is an uncommon event. During intravitreal injection, incomplete penetration into the vitreous cavity, early injection, or continued injection on needle withdrawal could lead to a posterior cyclodialysis cleft. Ultrasound biomicroscopy may be a useful adjunct to identify clefts not visible on direct gonioscopy and should be considered for all patients with hypotony of unknown etiology. Close observation in the short- to intermediate-term of posterior cyclodialysis clefts may be appropriate, given the possibility of spontaneous closure.

Patient consent

Consent to publish this case report has been obtained from the patient in writing.

Disclosures

The authors declare no funding or grant support.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

CRediT authorship contribution statement

Rachel H. Lee: Data curation, Writing – original draft, Writing – review & editing. **Aubrey R. Tirpack:** Validation, Writing – review & editing. **Janet L. Davis:** Conceptualization, Validation, Writing – review & editing. **Mohamed S. Sayed:** Conceptualization, Writing – review & editing. **Vikas Chopra:** Conceptualization, Validation, Writing – review & editing. **Steven J. Gedde:** Conceptualization, Validation, Writing – review & editing, Supervision.

Declaration of competing interest

The following authors have no relevant financial disclosures: RL, AT, JD, MS, VC, SG.

Acknowledgements

None.

References

1. Avery RL, Bakri SJ, Blumenkranz MS, et al. Intravitreal injection technique and monitoring: updated guidelines from an expert panel. *Retina*. 2014;34(suppl 12): S1–S8, 12.
2. Grzybowski A, Told R, Sacu S, et al. Update on intravitreal injections: euretina expert consensus recommendations. *Ophthalmologica*. 2018;239:181–193, 2018.
3. Wong TY, Liew G, Mitchell P. Clinical update: new treatments for age-related macular degeneration. *Lancet*. 2007;370(9583):204–206.

4. Nicholson BP, Schachat AP. A review of clinical trials ofanti-VEGF agents for diabetic retinopathy. *Graefes Arch Clin Exp Ophthalmol*. 2010;248(7):915–930.
5. Wong TY, Scott IU. Clinical practice. Retinal-vein occlusion. *N Engl J Med*. 2010;363 (22):2135–2144.
6. Falavarjani KG, Nguyen QD. Adverse events and complications associated with intravitreal injection of anti-VEGF agents: a review of literature. *Eye*. 2013;27: 787–794.
7. Ramos MS, Xu LT, Singuri S, et al. Patient-reported complications after intravitreal injection and their predictive factors. *Ophthalmol Retina*. 2020. https://doi.org/10.1016/j.oret.2020.09.024. In press.
8. Shikari H, Silva PS, Sun JK. Complications of intravitreal injections in patients with diabetes. *Semin Ophthalmol*. 2014;29:276–289.
9. Nguyen QD, Brown DM, Marcus DM, et al. Ranibizumab for diabetic macular edema: results from 2 phase III randomized trials: RISE and RIDE. *Ophthalmology*. 2012;119, 789-80.
10. Heier JS, Brown DM, Chong V, et al. Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. *Ophthalmology*. 2012;119:2537–2548.
11. Pasadhika S, Smith JR, Flaxel CJ. Posterior uveal cleft and hypotony complicating insertion of a fluocinolone acetonide implant. *Retin Cases Brief Rep*. 2010;4:137–139.
12. Wickremasinghe SS, Michalova K, Guymer RH, Harper CA. Wound leak after intravitreal injection of bevacizumab. *Retin Cases Brief Rep*. 2008;2(3):245–246. https://doi.org/10.1097/ICB.0b013e3181652477.
13. Gambrelle J, Kodjikian L, Abi-Ayad N, et al. Béance persistante de la sclérotomie après injection intravitréenne de triamcinolone à l'aide d'une aiguille de 30-gauges [Persistent unsealed sclerotomy after intravitreal injection of triamcinolone acetonide with a 30-gauge needle]. *J Fr Ophtalmol*. 2006;29(9):e22.
14. Rodrigues EB, Meyer CH, Schmidt JC, et al. Unsealed sclerotomy after intravitreal injection with a 30-gauge needle. *Retina*. 2004;24:810–812.
15. Martinez-Bello C, Capreans C, Sanchez-Salorio M. Ultrasound biomicroscopy in the diagnosis of supraciliochoroidal fluid after trabeculectomy. *AJO (Am J Ophthalmol)*. 1999;128:372–375.
16. Berk TA, An JA, Ahmed IIK. Inadvertent cyclodialysis cleft and hypotony following ab-interno trabeculotomy using the trabectome device requiring surgical repair. *J Glaucoma*. 2017;26:742–746.
17. Gentile RC, Lewis JM, Puklin JE. Cyclodialysis complicating intravitreal ganciclovir implantation. *Arch Ophthalmol*. 1997;115(9):1204–1205.
18. Mushtaq B, Chiang MY, Kumar V, et al. Phacoemulsification, persistent hypotony, and cyclodialysis clefts. *J Cataract Refract Surg*. 2005;31:1428–1432.
19. Shue A, Levine RM, Gallousis GM, et al. Cyclodialysis cleft associated with kahook dual blade goniotomy. *J Curr Glaucoma Pract*. 2019;13:74–76.
20. Portney DS, Michelson SJ, Besirli CG, et al. Cryotherapy for the management of refractory hypotony secondary to post-goniotomy cyclodialysis cleft. *Am J Ophthalmol Case Rep*. 2020;20:100876.
21. Tanito M, Sugihara K, Tsutsui A, et al. Midterm results of microhook ab interno trabeculotomy in initial 560 eyes with glaucoma. *J Clin Med*. 2021;10:814.
22. Ioannidis A, Barton K. Cyclodialysis cleft: causes and repair. *Curr Opin Ophthalmol*. 2010;21:150.