American Journal of Ophthalmology Case Reports 15 (2019) 100482

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.elsevier.com/locate/ajoc

Case report

Ciliochoroidal effusion syndrome with central serous-like chorioretinopathy and secondary angle closure following exogenous testosterone use

Daniel Brill, Desiree Albert, Taylor Fields, Shravani Mikkilineni, David Crandall, Hua Gao*

Henry Ford Health System, Department of Ophthalmology, Detroit, MI, USA

ARTICLE INFO

Keywords:
Central serous chorioretinopathy
Ciliochoroidal effusion syndrome
Secondary angle closure glaucoma
Testosterone
Ultrasound biomicroscopy

ABSTRACT

Purpose: To report a unique presentation of ciliochoroidal effusion syndrome with central serous-like chorioretinopathy and secondary angle closure following exogenous testosterone use.

Observations: A 37 year-old man presented with a two week history of blurred vision, elevated intraocular pressure, and myopic shift in his right eye. Gonioscopy showed angle closure. After YAG iridotomy, ultrasound biomicroscopy (UBM) showed ciliochoroidal effusion and anterior rotation of the ciliary processes. Subsequent color fundus photography, enhanced depth imaging optical coherence tomography (EDI-OCT) and near-infrared reduced-illuminance autofluorescence imaging (NIR-RAFI) showed macular striae, choroidal folds, and increased choroidal thickness without presence of subretinal fluid (SRF) or pigment epithelial detachment (PED). Further questioning revealed the patient was using dermal testosterone gel for six months for treatment of hypogonadism. The patient stopped using the testosterone gel, and his visual acuity and intraocular pressure significantly improved six weeks later. Follow-up UBM showed significant improvement of the ciliochoroidal effusion, and repeat multimodal images demonstrated resolution of the macular striae and choroidal folds, and slightly improved choroidal thickness.

Conclusions and importance: Our patient demonstrates a rare case of ciliochoroidal effusion, central serous-like chorioretinopathy, and secondary angle closure that dramatically improved with cessation of testosterone. We believe that this unique clinical constellation is the first to be reported associated with exogenous testosterone use.

1. Introduction

Several drug classes are known to induce angle closure glaucoma, including adrenergic agonists, anticholinergics, anticoagulants, antihistamines, cholinergics, selective serotonin reuptake inhibitors, sulfonamide derivatives, tetrahydrocannabinol, and tricyclic/tetracyclic antidepressants.[1] Sulfonamides are associated with inducing ciliochoroidal effusion syndrome via choroidal effusion and ciliary body edema.[1,2] This may result in a secondary anterior displacement of the lens-iris diaphragm with acute angle closure, myopic shift, and macular striae.[1,2]

Exogenous steroid use is known to cause or exacerbate open angle glaucoma through decreased uveoscleral outflow.[3] While elevated serum glucocorticoid levels are also known to be associated with central serous chorioretinopathy (CSCR),[4–7] there is not evidence of an association between exogenous steroid use and ciliochoroidal effusion.[8]

Here we describe a unique case of ciliochoroidal effusion, central serous-like chorioretinopathy, and secondary angle closure glaucoma associated with exogenous testosterone use, all of which significantly improved with drug cessation.

2. Case report

A 37 year-old male presented to the glaucoma clinic with a two-week history of blurred vision in his right eye. He had no past ocular diagnoses or surgeries. He was not using any ocular medications or refractive correction. He reported no significant medical problems.

On exam, his uncorrected visual acuity was 20/400 in the right eye and 20/20 in the left. Manifest refraction corrected his right eye to 20/20 with −3.50 sphere. His intraocular pressure (IOP) was 30 mmHg in the right eye and 18 mmHg in the left. He had peripheral iridocorneal touch in the right eye. On gonioscopy of the right eye, there were no visible angle structures, and he was open to bare trabecular meshwork OS. The patient was diagnosed with acute angle closure glaucoma and sudden myopic shift in the right eye, and shallow anterior chamber in the left eye. YAG laser peripheral iridotomy was performed in the right

* Corresponding author. Henry Ford Health System, Department of Ophthalmology, 2799 West Grand Boulevard, Detroit, MI, 48202, USA.
E-mail address: hgao1@hfhs.org (H. Gao).

https://doi.org/10.1016/j.ajoc.2019.100482
Received 25 July 2018; Received in revised form 30 May 2019; Accepted 30 May 2019
Available online 05 June 2019
2451-9936/ © 2019 The Authors. 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/).

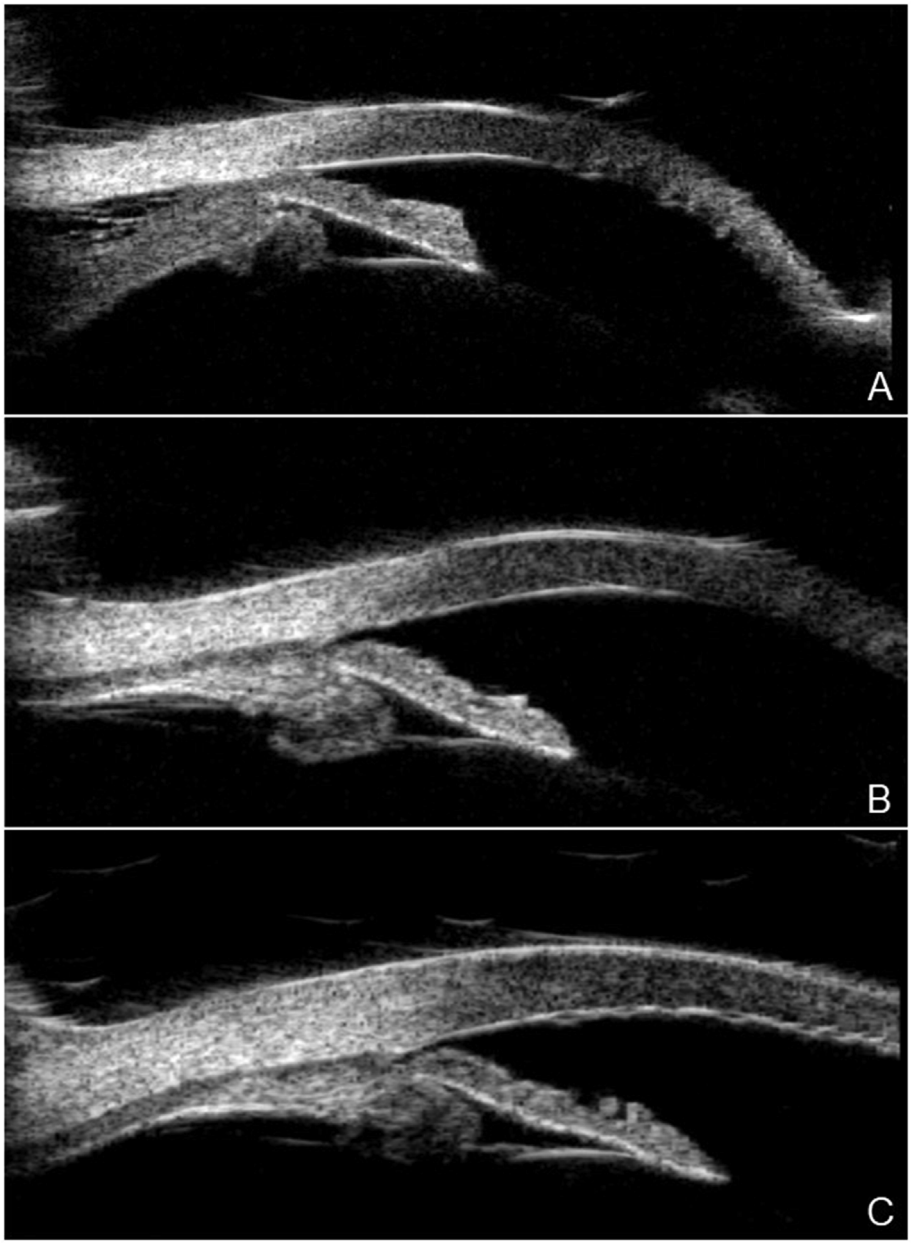

Fig. 1. Ultrasound biomicroscopy. **1A**.Right eye before cessation of testosterone showing large ciliochoroidal effusion. **1B.** Left eye before cessation of testosterone showing minimal ciliochoroidal effusion. **1C.** Right eye six weeks after cessation of testosterone showing resolution of ciliochoroidal effusion.

eye to remove any component of pupillary block. Patient was started on bimatoprost and timolol.

The patient was seen for follow-up examination two days later. His right eye uncorrected visual acuity improved to 20/200 and IOP improved to 19 mmHg. Topical atropine 1% was started to shift the lens-iris diaphragm posteriorly for treatment of any component of posterior pushing.

At one week, the patient's right eye manifest refraction decreased to −2.00 sphere. His IOP was 22 mmHg. Gonioscopy showed no angle structures temporally and superiorly and bare trabecular meshwork nasally and inferiorly. UBM 360° radial scans showed slit-like and closed angles, 360° of ciliochoroidal effusion, and anterior rotation of the ciliary processes (Fig. 1A). In the left eye, UBM showed slit-like to narrow angles, anterior rotation of the ciliary body, and anterior bowing of the peripheral iris with trace ciliochoroidal effusion (Fig. 1B).

At 10 weeks, the patient was referred to retina clinic. His uncorrected visual acuity improved to 20/50 in the right eye. His IOP was 20 mmHg. Dilated fundus exam showed macular striae extending across the fovea in the right eye, and no such striae were noted in the left eye (Fig. 2A). The macular striae were most notable with NIR-RAFI (Fig. 2B). EDI-OCT images of the macula showed significantly increased choroidal thickness in both eyes, right eye greater than the left, and choroidal folds in the right eye (Fig. 2C). Fluorescein angiogram showed no evidence of any leakage, and fundus autofluorescence imaging showed trace irregularity right eye, and normal left eye (Fig. 2D). There was no SRF or PED present.

Thorough medical history revealed the patient was taking a topical testosterone gel, AndroGel™ (AbbVie Inc., North Chicago, Illinois), for the last 6 months for treatment of hypogonadism. The patient was advised to decrease the dosage of his testosterone, but the patient decided to stop taking it after this visit.

At 16 weeks (six weeks after cessation of testosterone), the patient's uncorrected visual acuity improved to 20/20 and IOP was 24 mmHg.

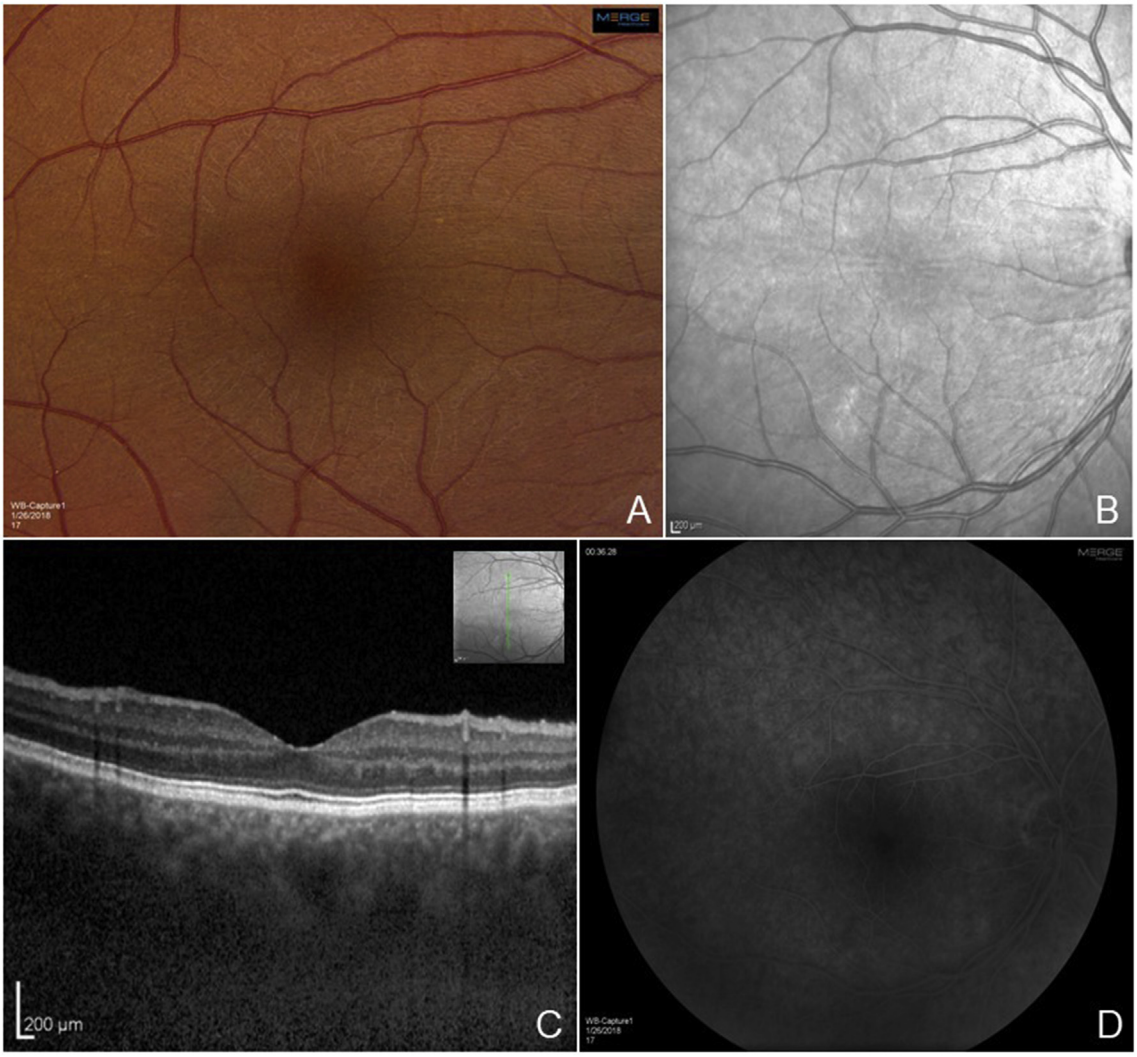

Fig. 2. Right eye before cessation of testosterone. **2A.** Fundus photograph showing macular striae. **2B.** NIR-RAFI highlighting choroidal folds. **2C.** OCT showing choroidal folds, and increased choroidal thickness. **2D.** FA late stage showing no leakage.

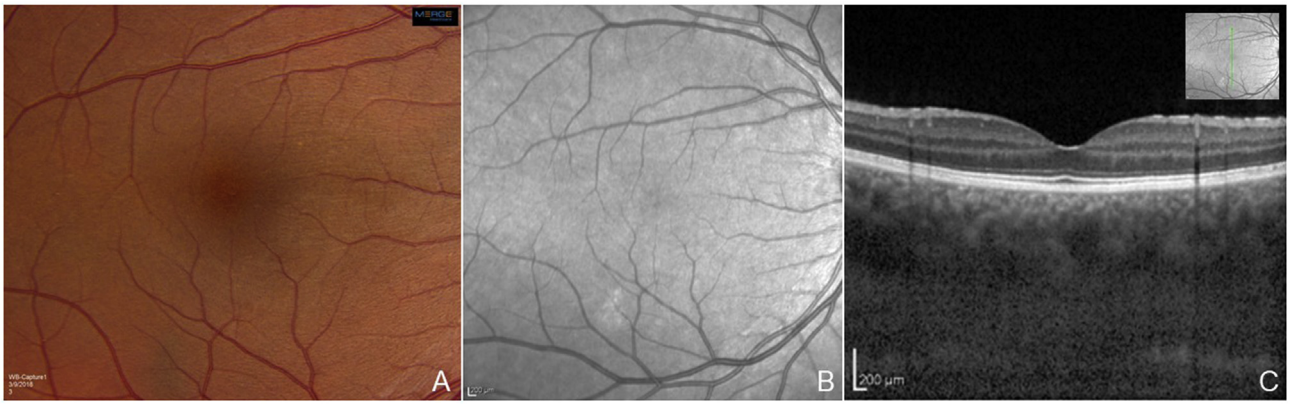

Fig. 3. Right eye at six weeks after cessation of testosterone. **3A.** Fundus photograph showing completely resolved macular striae. **3B.** NIR-RAFI highlighting completely resolved choroidal folds. **3C.** EDI-OCT showing resolved choroidal folds and slightly improved choroidal thickness.

Repeat UBM in both eyes showed continued anterior bowing of the peripheral iris with slit-like angles and anteriorly rotated ciliary processes, and nearly resolved ciliochoroidal effusion in the right eye (Fig. 1C). Repeat color fundus photographs, NIR-RAFI, and OCT showed near complete resolution of macular striae and choroidal folds (Fig. 3A–C). Final exam at 20 weeks was stable.

3. Discussion

Our patient demonstrates a rare case of bilateral ciliochoroidal effusion syndrome demonstrated by UBM after exogenous testosterone use. AndroGel™ is a hydroalcoholic gel containing testosterone and inactive components carbomer 980, ethanol 67%, isopropyl myristate,

purified water, and sodium hydroxide.[9] Reviewing the AndroGel™ package insert does not reveal components previously associated with angle closure or ciliochoroidal effusion.[9] AndroGel™ can be prescribed for primary or secondary hypogonadism.[9]

As we have no prior ophthalmologic exams or imaging prior to initial presentation, it is possible that the patient may have had preexisting narrow angles or plateau iris configuration despite his relatively emmetropic eyes. Mydriatic agents, such as sympathomimetics and anticholinergics, can lead to angle closure via pupillary dilation in eyes with originally narrow angles. However, these preexisting conditions do not explain why he developed bilateral ciliochoroidal effusions that dramatically improved after cessation of testosterone therapy.

Our patient's asymmetric exam findings are unexpected, but not uncommon. Bilateral pathology affecting the eyes can be asymmetrical. The findings of trace ciliochoroidal effusion and narrow angle in his left eye are supportive of an asymmetric systemic process. Without initiating topical therapy and cessation of testosterone use, we believe this eye would have been eventually involved as well.

After YAG iridotomy, our patient's manifest refraction and intraocular pressure did improve. Of note, the patient was also given intraocular pressure lowering therapy and atropine. We believe these agents, rather than YAG iridotomy, improved his ciliochoroidal effusion syndrome, as there was no component of pupillary block on UBM and significant ciliochoroidal effusion remained 10 weeks after YAG iridotomy. Furthermore, the patient's ciliochoroidal effusion and symptoms nearly resolved 6 weeks after cessation of exogenous testosterone.

Cannabis and sulfonamide derivatives have been reported to cause ciliochoroidal effusion syndrome. As with our patient, drug induced cilichoroidal effusion resulted in anterior displacement of the lens-iris diaphragm and anterior rotation of the ciliary body, causing angle closure. Thus, we believe this is the first reported case of testosterone associated angle closure glaucoma.[2,10] Fortunately, our patient's myopic shift, intraocular pressure, macular striae, and choroidal folds drastically improved after cessation of testosterone.

The exact mechanism by which elevated testosterone causes CSCR is not fully understood, but there is a generally accepted pathogenesis theory by J. Donald Gass.[11,12] There is laboratory evidence of human retinal pigment epithelium (RPE) having androgen receptors and messenger RNA for 5α-reductase, which can convert testosterone to dihydrotestosterone, a more potent form of testosterone.[13,14] Testosterone is a vasoactive hormone, which causes vasodilation and may increase the permeability of the choriocapillaris.[15–18] Subsequent choroidal thickening may damage the RPE, resulting in subretinal fluid (SRF) and pigment epithelial detachment (PED).[11,19,20]

While our patient does not have SRF or PED indicative of classical CSCR, this case may demonstrate a central serous-like chorioretinopathy. Our patient presented with choroidal folds and increased choroidal thickness, but without SRF and PED or leakage on fluorescence angiogram. These findings may support Gass' stepwise pathogenesis theory of CSCR.[11,12] Specifically, CSCR secondary to testosterone occurs via its vasodilatory properties causing increased choroidal permeability and secondary RPE damage.[15–18] Afterwards, SRF and PED may occur, which fortunately never developed in our patient.

As with other associations of drug induced ciliochoroidal effusion syndrome, exogenous testosterone should be stopped immediately. In patients without hyperopia, cycloplegic agents may reduce intraocular pressure via their ability to retract the ciliary processes and deepen the anterior chamber. Intraocular pressure lowering eye drops and peripheral iridoplasty may be effective. Although the exact mechanism of our patient's angle closure is unknown, we believe exogenous testosterone should be added to the possible causative agents of cilichoroidal effusion syndrome.

Patient consent

Consent to publish case details was obtained from our patient.

Conflicts of interest

None of the authors have any financial disclosures.

Funding

No funding or grant support received.

Authorship

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

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ajoc.2019.100482.

References

1. Tripathi RC, Tripathi BJ, Haggerty C. Drug-induced glaucomas: mechanism and management. *Drug Saf.* 2003;26:749–767.
2. Abtahi MA, Abtahi SH, Fazel F, et al. Topiramate and the vision: a systematic review. *Clin Ophthalmol.* 2012;6:117–131.
3. Ritch R. Pathophysiology of glaucoma in uveitis. *Trans Ophthalmol Soc U K.* 1981;101(Pt 3):321–324.
4. Bouzas EA, Karadimas P, Pournaras CJ. Central serous chorioretinopathy and glucocorticoids. *Surv Ophthalmol.* 2002;47:431–448.
5. Carvalho-Recchia CA, Yannuzzi LA, Negrao S, et al. Corticosteroids and central serous chorioretinopathy. *Ophthalmology.* 2002;109:1834–1837.
6. Garg SP, Dada T, Talwar D, Biswas NR. Endogenous cortisol profile in patients with central serous chorioretinopathy. *Br J Ophthalmol.* 1997;81:962–964.
7. Karadimas P, Bouzas EA. Glucocorticoid use represents a risk factor for central serous chorioretinopathy: a prospective, case-control study. *Graefes Arch Clin Exp Ophthalmol.* 2004;242:800–802.
8. Razeghinejad MRMJ, Katz LJ. Iatrogenic glaucoma secondary to medications. *Am J Med.* 2011;124:20–25.
9. *Androgel (Testosterone Gel) [package Insert]*. North Chicago, Illinois: AbbVie Inc.; 2013.
10. Hanna R, Tiosano B, Dbayat N, Gaton D. Unilateral angle-closure glaucoma with ciliochoroidal effusion after the consumption of cannabis: a case report. *Case Rep Ophthalmol.* 2014;5:439–443.
11. Nudleman E, Witmer MT, Kiss S, Williams GA, Wolfe JD. Central serous chorioretinopathy in patients receiving exogenous testosterone therapy. *Retina.* 2014;34:2128–2132.
12. Hussain DGJ. Idiopathic central serous chorioretinopathy. *Indian J Ophthalmol.* 1998;46:131–137.
13. Wickham LA, Gao J, Toda I, Rocha EM, Ono M, Sullivan DA. Identification of androgen, estrogen and progesterone receptor mRNAs in the eye. *Acta Ophthalmol Scand.* 2000;78:146–153.
14. Rocha EM, Wickham LA, da Silveira LA, et al. Identification of androgen receptor protein and 5 alpha-reductase mRNA in human ocular tissues. *Br J Ophthalmol.* 2000;84:76–84.
15. Yildiz O, Seyrek M. Vasodilating mechanisms of testosterone. *Exp Clin Endocrinol Diabetes.* 2007;115:1–6 official journal, German Society of Endocrinology [and] German Diabetes Association.
16. Kim YT, Kang SW, Bai KH. Choroidal thickness in both eyes of patients with unilaterally active central serous chorioretinopathy. *Eye.* 2011;25:1635–1640.
17. Iliescu R, Reckelhoff JF. Testosterone and vascular reactivity. *Clin Sci.* 2006;111:251–252 London, England : 1979.
18. Hougaku H, Fleg JL, Najjar SS, et al. Relationship between androgenic hormones and arterial stiffness, based on longitudinal hormone measurements. *Am J Physiol Endocrinol Metab.* 2006;290:E234–E242.
19. Kitaya N, Nagaoka T, Hikichi T, et al. Features of abnormal choroidal circulation in central serous chorioretinopathy. *Br J Ophthalmol.* 2003;87:709–712.
20. Ciloglu E, Unal F, Dogan NC. The relationship between the central serous chorioretinopathy, choroidal thickness, and serum hormone levels. *Graefes Arch Clin Exp Ophthalmol.* 2018;256:1111–1116.