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Case Reports

Cystoid macular edema associated with acitretin

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Summary

Cystoid macular edema represents a "final common pathway" response of the retina to a variety of insults. It has been reported in association with vascular problems, inflammatory conditions, inherited diseases, tractional problems, intraocular surgery and medications. We report a case of cystoid macular edema associated with acitretin in a 65-year-old woman and document its resolution with optical coherence tomography (OCT).

Introduction

Acitretin is an oral retinoid, increasingly used in the treatment of psoarisis and chemopreventive therapy for some cutaneous malignancies. It is a known teratogen and has been reported to cause a myriad of systemic side effects, including pancreatitis, hepatotoxicity, and mucocutaneous pathology.[1] Retinoids have also been linked to intracranial hypertension. Acitretin activates all three retinoic acid receptor subtypes (alpha, beta, and gamma).[2] These nuclear hormone receptors affect cellular differentiation, proliferation, and inflammation.[1] Retinoids are actively metabolized in the photoreceptor outer segments, Müller cells, and the retinal pigment epithelium (RPE). Ocular dryness and irritation are the most common ophthalmic side effects of retinoid use.[1] Nyctalopia has also been described, and reduced retinal function on electroretinography has been documented.[3]

Case Report

A 65-year-old woman presented at Royston Centre, Napier, New Zealand, with a 3-month history of progressive blurring of central vision in both eyes. Her medical history was remarkable for stable, chronic lymphocytic leukemia, without ocular involvement or clinical need for treatment, and previous lower limb melanoma excision. Fifteen months before presenting, her dermatologist had prescribed acitretin 20 mg daily for severe warts on both hands that had not responded to conventional treatment. Her other medications included a proton pump inhibitor for dyspepsia and an oral nonsteroidal anti-inflammatory drug (NSAID) for osteoarthritis. Ophthalmic history was unremarkable.

On ophthalmological examination, her best-corrected visual acuity was 6/18 in each eye. It was noted to be 6/7.5 in both eyes 4 months previously by her optometrist. The intraocular pressure (IOP) in each eye was 12 mm Hg. Anterior segment examination was normal. On fundus examination, bilateral epiretinal membranes and white drusenoid deposits were seen in the maculae, with central macular neuroretinal edema. Optical coherence tomography (OCT) and fundus fluorescein angiography demonstrated cystoid macular edema (Figures 1 and 2A). A diagnosis of acitretin-associated maculopathy was made. Acitretin was discontinued, and she was started on 1.0% prednisolone acetate eyedrops and topical 0.5% ketorolac trometamol 4 times daily in both eyes.

Two months later, her best-corrected visual acuity had improved to 6/12 in the right and 6/9 in the left eye. OCT revealed increased foveal edema on the right and improved appearance on the left (Figure 2). The IOP was 23 mm Hg in the right eye and 24 mm Hg in the left eye. Oral acetazolamide 250 mg twice daily was added to the treatment regimen, which was decreased to once per day after 2 weeks because upper limb paraesthesia had developed. With this treatment regimen, a gradual improvement of the macular edema and visual acuity was observed through her 6-month follow-up (Figure

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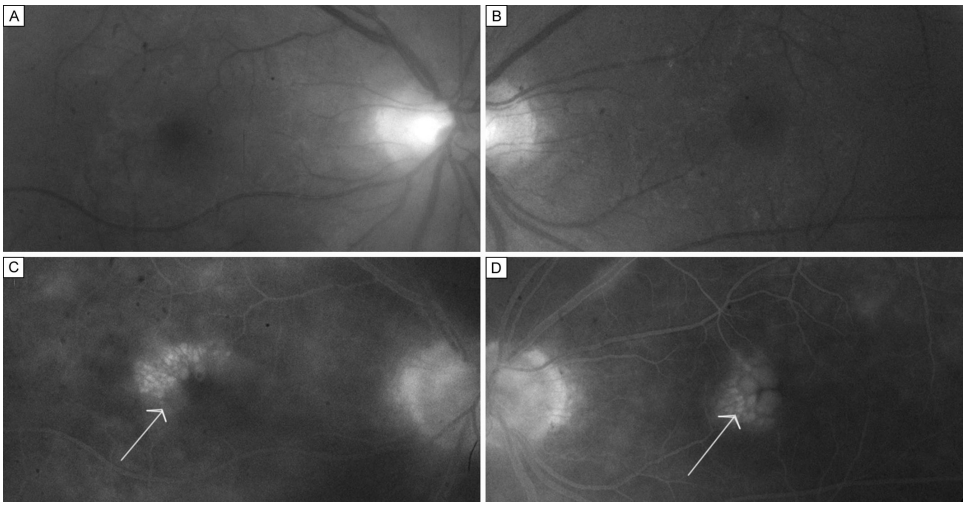

Figure 1. Right (A) and left (B) red-free photographs and right (C) and left (D) fundus fluorescein angiogram late-frame images showing cystoid macular edema. Diffuse hyperfloursecence is seen at the level of the retinal pigment epithelium involving the macula.

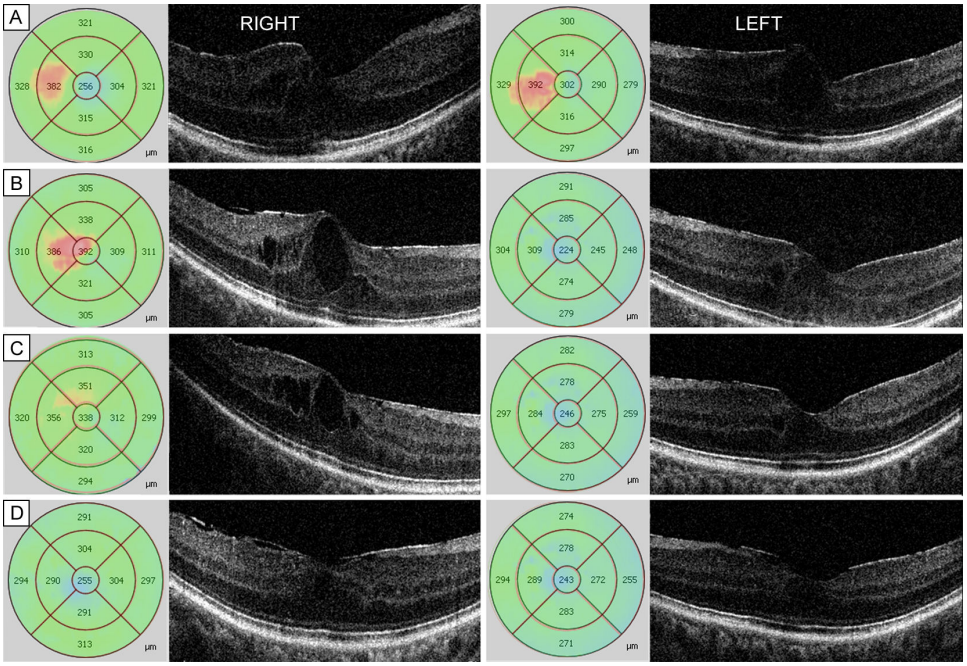

Figure 2. Right and left serial optical coherence tomography data at presentation (A), 2 months (B), 5 months (C), and 6 months (D). Macular thickness profiles (in micrometers) are shown beside the cross-sectional foveal images.

2B–D), with best-corrected vision of 6/9 in the right and 6/6 in the left eye. OCT of both eyes showed resolution of the cystoid macular edema despite bilateral epiretinal membranes and drusen. Her medications were stopped.

Discussion

Acitretin-associated maculopathy has previously been reported in a 32-year-old man who presented with a 3-day history of blurred vision in both eyes.[4] Results of OCT and fundus fluorescein angiography suggested bilateral cystoid macular edema, which resolved completely with oral acetazolamide 250 mg twice a day for 3 days. In our case, the cystoid macular edema subsided

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only after several months. In total, the patient maintained a regimen of 1.0% prednisolone acetate 4 times daily and 0.5% ketorolac trometamol 4 times daily for 6 months. Oral acetazolamide was commenced 2 months after the start of topical treatment at 250 mg twice daily for the initial 2 weeks and continued at once daily. The rise in the IOP of both eyes most likely represents a steroid response. We considered oral acetazolamide as our second-line agent due to its side effects profile. All therapy was stopped after 6 months, with resolution of the cystoid macular edema.

Acitretin was the most likely cause of cystoid macular edema in our patient. Although she had a history of chronic lymphocytic lymphoma, there were no clinical signs of anterior segment inflammation, retinitis, or choroiditis. Retinoids are involved in the formation and accumulation of lipofuscin in the RPE and RPE lipofuscin fluorophores form as a byproduct of the retinoid visual cycle.[5] Additionally, the 9-cis retinoid isoform has been shown to be capable of inducing dose-dependent vascular endothelial apoptosis in vivo, in the absence of an intact RPE monolayer.[6] It is possible that accumulation of retinoid metabolism byproducts at the RPE contributes to the development of cystoid macular edema in a susceptible individual. This may help explain why our 65-year-old patient with drusen responded to treatment more slowly than did the 32-year-old previously reported.[4]

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