



## Case report

## Cogan syndrome masquerading as corneal ectasia

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## ABSTRACT

**Purpose:** To report a case of Cogan syndrome that presented with the appearance of bilateral asymmetric corneal ectasia on Scheimpflug tomography.

**Methods:** Case Report and Literature Review.

**Results:** A 43-year-old woman previously diagnosed with keratoconjunctivitis sicca and presumed keratoconus presented with seven months of episodic eye pain and progressive bilateral blurry vision with new onset bilateral monocular diplopia. Review of symptoms were significant for tinnitus, vertigo, and sensorineural hearing loss that began many months after her initial presentation for visual symptoms. Scheimpflug tomography showed asymmetric focal steepening on anterior curvature with corresponding focal total corneal thinning, focal posterior elevation, and abnormal ARTMax (205 OD, 103 OS) and BAD-D (2.75 OD, 5.6 OS) values. Clinical examination was notable only for faint anterior corneal stromal inflammation without neovascularization, but there was significant corresponding focal hyperreflectivity on anterior segment optical coherence tomography (OCT) examination with focal epithelial hypertrophy rather than thinning. Given the combined findings of interstitial keratitis and sensorineural hearing loss the patient was diagnosed with Cogan syndrome. She responded well to topical steroids and systemic immunosuppressive therapy, with near resolution of her abnormal topographic and tomographic findings and resolution of monocular diplopia in both eyes.

**Conclusions:** Cogan syndrome should be suspected for any patient with corneal stromal findings and associated with vertigo and/or hearing loss. Anterior segment optical coherence tomography (OCT) can distinguish between ectatic and inflammatory diseases and may help make the appropriate diagnosis in subtle cases.

## 1. Introduction

Cogan Syndrome is a rare autoimmune vasculitis which classically presents with interstitial keratitis, vertigo, and sensorineural hearing loss in young adults. Atypical ophthalmic findings reported include conjunctivitis, uveitis, scleritis and choroiditis.<sup>1</sup> Aggressive immunosuppressive therapy and multi-specialty management of the disease is warranted owing to its systemic manifestations, including vasculitis.<sup>1-3</sup> Despite more than 250 reports on Cogan syndrome in the literature, there is a paucity of data regarding the appearance of corneal topography and tomography in this syndrome.

Herein we present a patient with bilateral interstitial keratitis associated with central corneal thinning that appeared on Scheimpflug tomography as corneal ectasia but who was determined to have Cogan Syndrome, with the diagnosis made using Anterior segment OCT.

## 2. Case report

A 43-year-old female with a history of migraine with aura, hyperlipidemia, and contact lens use initially presented to a different provider with three months of intermittent blurry vision of the left eye, associated with burning pain and redness of both eyes. Her symptoms had persisted despite a contact lens holiday, loteprednol eyedrops, and tobramycin/dexamethasone ointment from her optometrist. Best corrected visual acuity at this visit was 20/20 OD and 20/25 OS with her most recent manifest refraction of  $-3.35 + 0.75 \times 178$  OD and  $-2.75$  sphere OS. She was diagnosed as having keratoconjunctivitis sicca and prescribed conservative therapy with artificial tears.

Three months later, she was referred to the neuro-ophthalmology service due to new onset diplopia. She described worsening vision in both eyes and was found to have bilateral monocular diplopia, worse in the left eye, on examination. Best corrected visual acuity at this visit was 20/25 in both eyes with manifest refractions of  $-3.00 + 1.75 \times 175$  OD

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and -3.00 sphere OS. Her anterior segment slit lamp examination was reportedly unremarkable in both eyes. Scheimpflug corneal tomography (Pentacam HR, Oculus GmbH, Wetzlar, Germany) showed focal corneal steepening with coincident focal total corneal thinning and focal posterior elevation with abnormal findings on the Enhanced Ectasia map in both eyes (Fig. 1). She was then referred to the Cornea Service due to concern for an ectatic process.

The patient was first seen in our clinic 7 months after initial symptom onset. At this time she reported a recent history of hearing loss for which

she had been prescribed a short course of oral steroids, and had recurrent episodes of tinnitus, bilateral hearing loss, progressively worsening headaches, and one hospitalization for extremity numbness and vertigo.

On examination, the patient's best corrected visual acuity was 20/40 in both eyes with manifest refractions of -3.00 + 1.75 x 174 OD and -3.25 Sphere OS. Slit lamp exam was notable for subtle focal anterior stromal inflammation in both eyes, without corneal neovascularization in either eye (Fig. 2). Scheimpflug tomography demonstrated irregular anterior curvature in both eyes, with focal steepening associated with

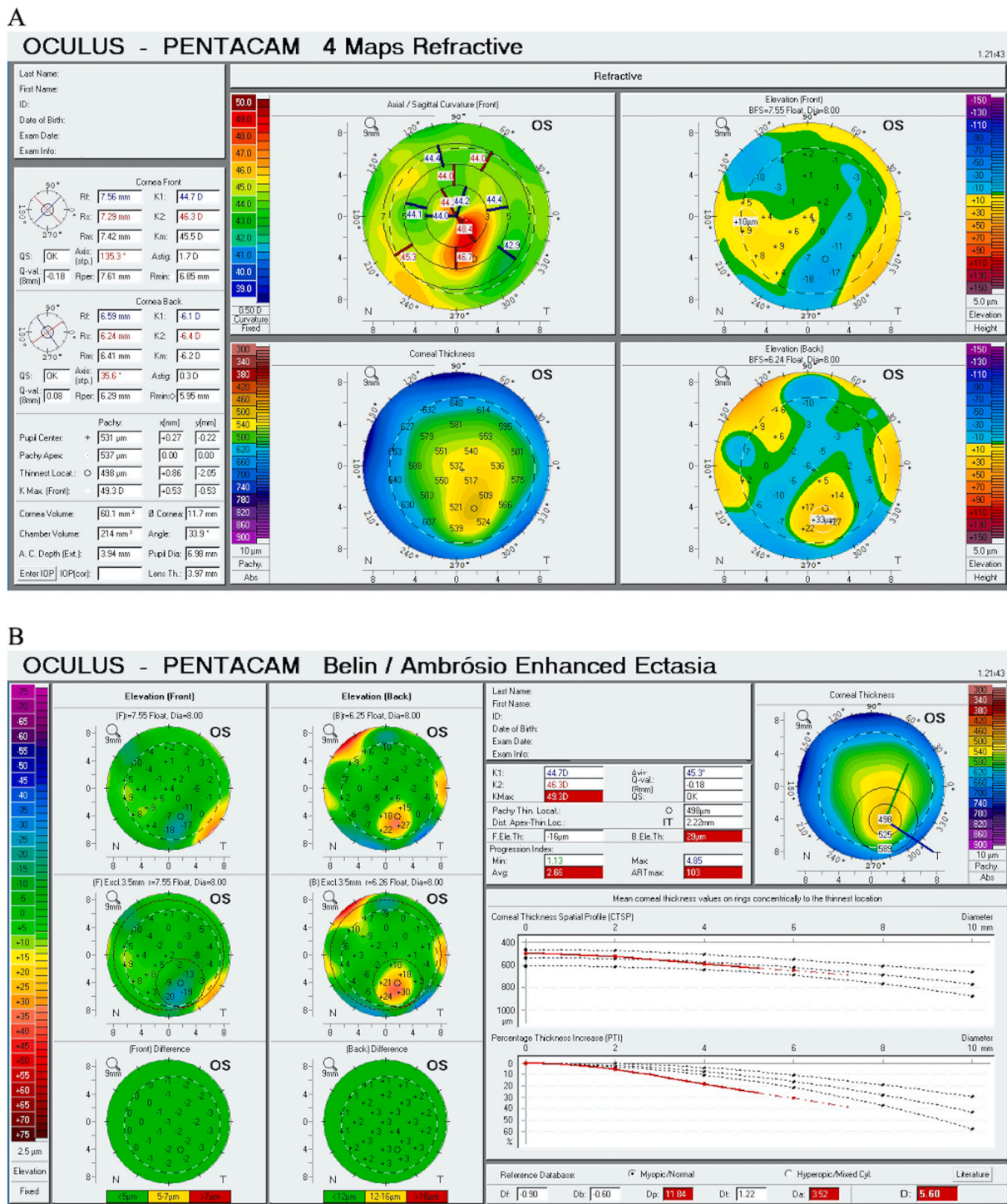


Fig. 1. Scheimpflug tomography of the left eye at initial imaging. The four map refractive view (A) shows focal corneal steepening on anterior curvature, with coincident central corneal thinning and focal posterior elevation. The enhanced ectasia map (B) shows multiple abnormalities, including ART Max (103) and BAD-D (5.6) metrics. There were similar but less dramatic findings in the right eye (not shown).

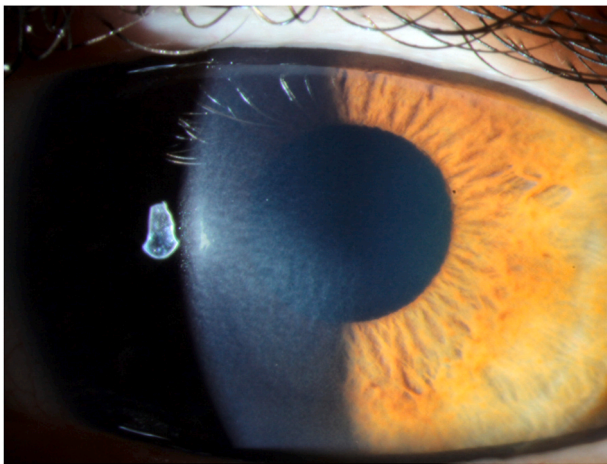


Fig. 2. Slit lamp photograph of the left eye at initial presentation. Anterior corneal stromal inflammation is subtle but visible focally paracentrally. There were similar but less dramatic findings in the right eye (not shown).

focal corneal thinning. Anterior segment optical coherence tomography (OCT) (Avanti, Optovue, Inc., Fremont, CA, USA) revealed well demarcated hyperreflectivity of the anterior two thirds of the corneal stroma in both eyes, with focal total thinning in conjunction with overlying focal epithelial thickening in both eyes (Fig. 3) coincident with and adjacent to the region of maximal steepening seen on Scheimpflug imaging.

While the patient’s symptoms and findings on Scheimpflug tomography was suspicious for an ectatic disease process, her overall clinical presentation was inconsistent with keratoconus, due to the presence of focal epithelial hypertrophy rather than thinning coincident with and directly adjacent to the area of maximal steepening directly overlying the region of focal corneal thinning. This indicated compensatory epithelial remodeling (thickening) due to stromal tissue loss causing a trough-like appearance in the anterior stroma (Fig. 3) rather than an ectatic corneal disease process with forward protrusion of the corneal stroma. Additionally, the findings on slit lamp examination combined with focal hyperreflectivity seen on OCT indicated an inflammatory process was occurring. She was therefore diagnosed as having bilateral interstitial keratitis with suspicion for Cogan syndrome given her recent vestibuloauditory symptoms.

The patient was started on topical prednisolone acetate 1% drops four times per day in the left eye along with oral acyclovir 400 mg taken

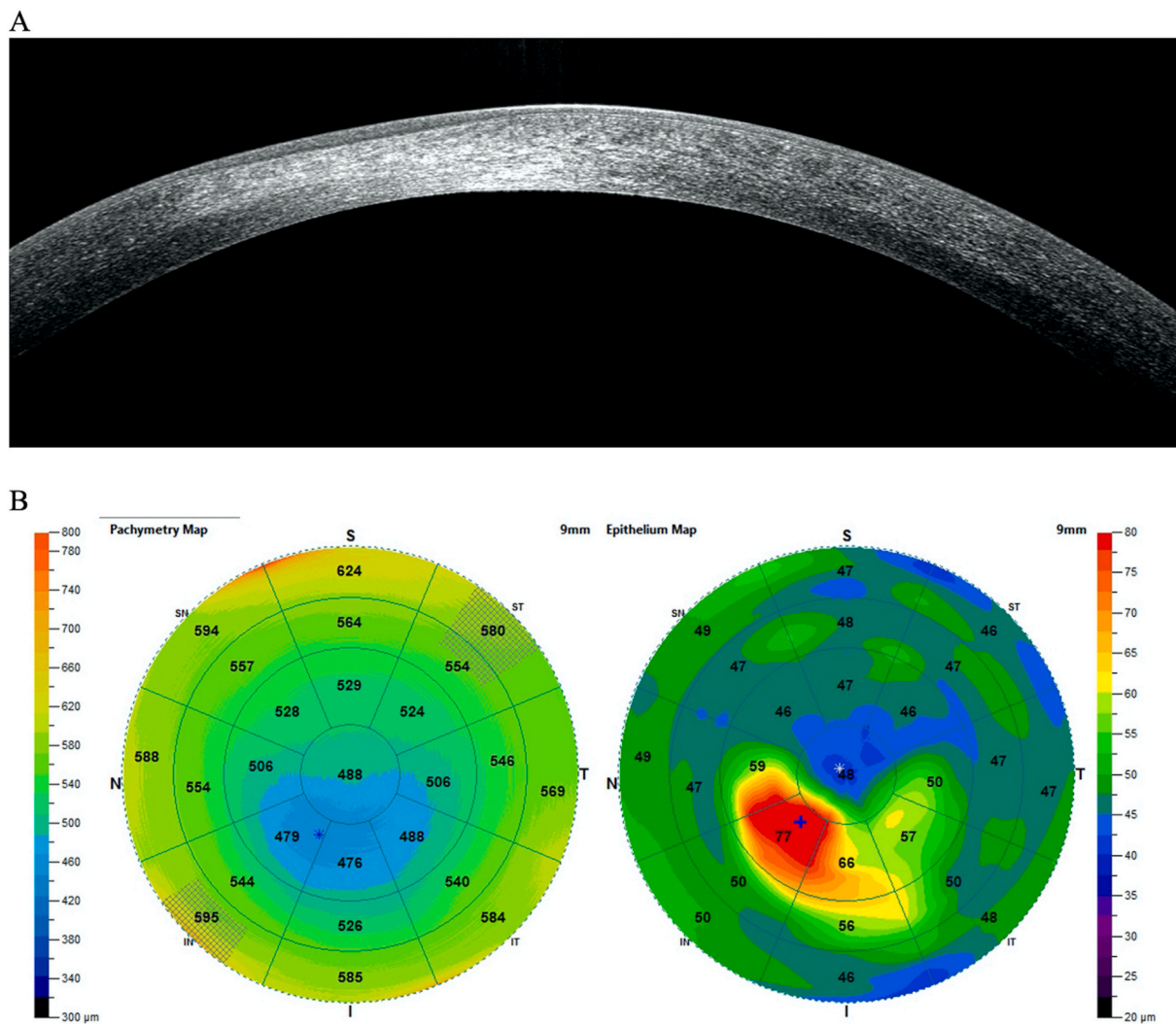


Fig. 3. Anterior segment OCT image of the left eye. In cross-section (A) there is focal corneal stromal thinning with overlying focal epithelial thickening and focal hyperreflectivity is visible in the anterior two thirds of the corneal stroma. In image B, total thickness is focally thinned; however, there is compensatory focal epithelial hypertrophy rather than thinning in this region.

two times daily. Laboratory workup initiated by the patient’s rheumatologist was negative for infectious etiologies including tuberculosis, hepatitis, syphilis, Lyme disease, and herpes simplex virus (IgG), and antiviral therapy was subsequently stopped. She was found to have elevated inflammatory markers (WBC 13.74, ESR 31, CRP 2.7). Testing for ANCA, ANA, and rheumatoid factor were negative. MRI Brain with and without contrast demonstrated signal changes involving the right frontal subcortical white matter, thought to be nonspecific. Audiogram was positive for sensorineural hearing loss. She was diagnosed with having Cogan Syndrome and started on oral prednisone (60 mg daily) and azathioprine (50 mg twice daily) by her rheumatologist.

The patient remained on a prolonged taper of prednisolone acetate 1% drops and oral prednisone. She did not tolerate azathioprine and was initiated on oral methotrexate by her rheumatologist. At six months follow up, the patient achieved best corrected vision of 20/16 in the

right eye ( $-3.00 + 0.50 \times 010$ ) and 20/25 in the left eye ( $-3.25 + 0.50 \times 114$ ). Corneal stromal haze was undetectable on slit lamp exam in either eye. Anterior segment OCT revealed near resolution of the anterior corneal stromal hyperreflectivity, as well as improvement in corneal thinning and overlying epithelial hypertrophy, in both eyes (Fig. 4). Scheimpflug tomography exhibited only mild residual curvature irregularity in both eyes (Fig. 5).

### 3. Discussion

Cogan Syndrome is a disease of uncertain etiology that causes inflammatory ocular and vestibuloauditory symptoms, which can be concurrent or separated by years. Ocular presentation is most commonly a bilateral interstitial keratitis manifesting as ocular irritation, photophobia, and blurred vision,<sup>3</sup> while atypical ocular presentations include

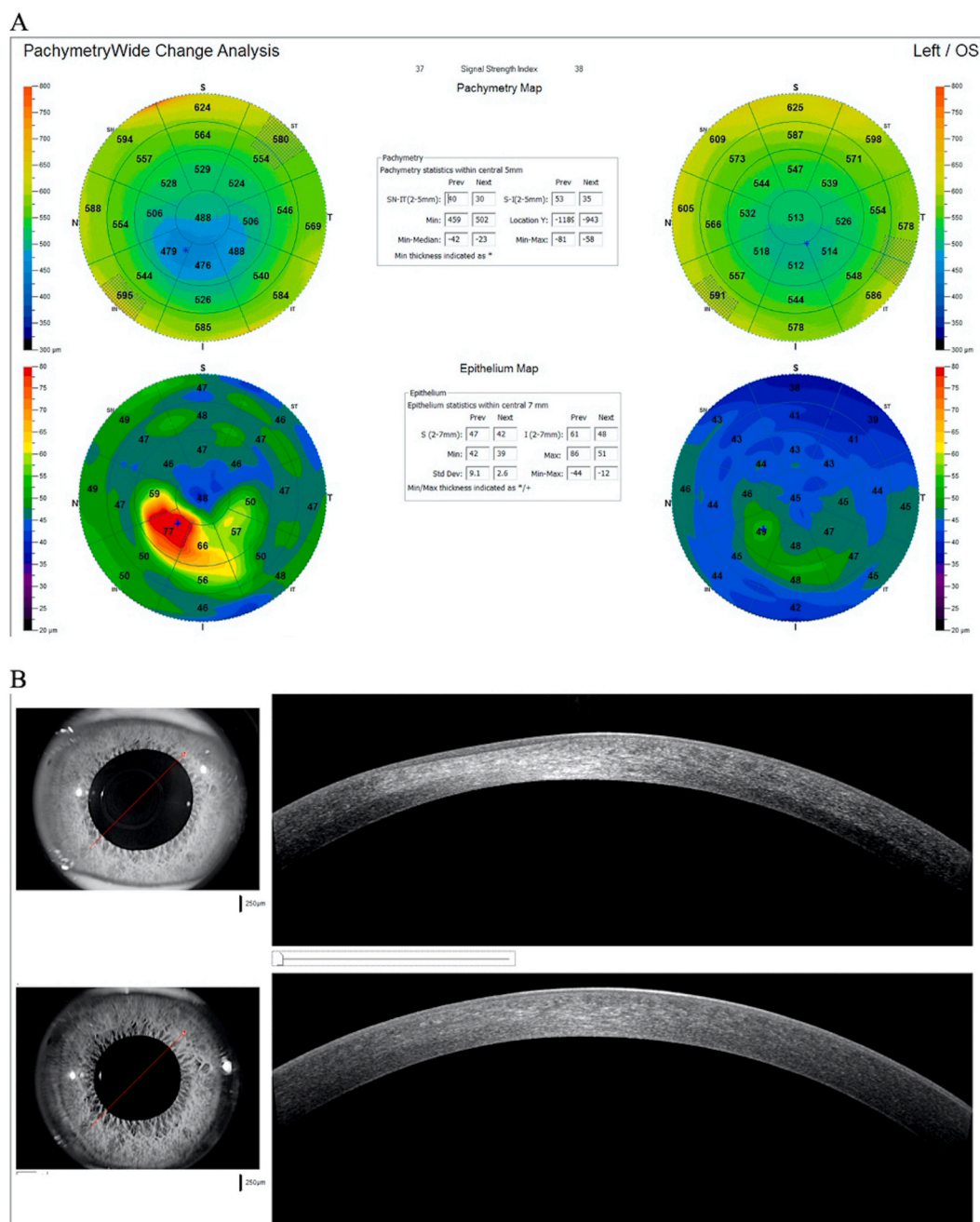
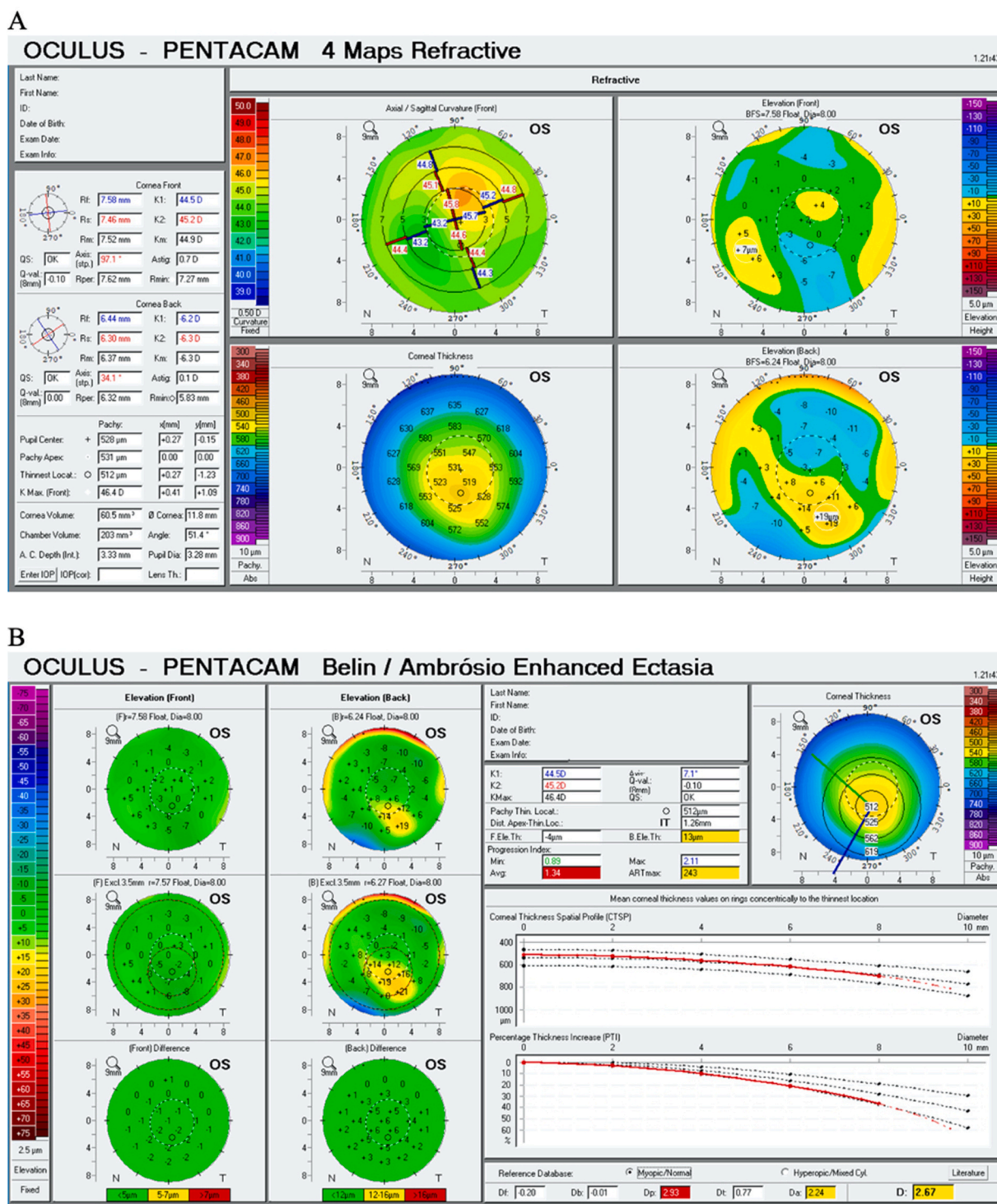


Fig. 4. Anterior segment OCT showing (A) change in total pachymetry and epithelial remodeling of the left eye at four months after initiation of topical ophthalmic steroids. Image B shows the improvement in corneal stromal hyper-reflectivity and focal thinning.



**Fig. 5.** Scheimpflug tomography of the left eye four months after initiating topical steroid therapy. The four map refractive view (A) shows that the focal corneal steepening has essentially resolved, with mild residual irregular astigmatism, reduced focal thinning, and reduced focal elevations. The enhanced ectasia map (B) shows improved ART Max and BAD-D scores. There were similar improvements in the right eye (not shown).

conjunctivitis, uveitis, episcleritis, scleritis, and retinal vasculitis.<sup>2</sup> Due to the systemic nature of the disease, referral to otolaryngology and rheumatology is imperative given risk for severe sensorineural hearing loss (50–90%) and systemic vasculitis (10–80%), including aortitis if left untreated.<sup>2,4,5</sup> Topical corticosteroids are utilized for ocular inflammation, and oral corticosteroids are recommended for severe ocular inflammation, vestibuloauditory symptoms, and systemic vasculitis.<sup>2</sup> While permanent vision loss is less common, profound and chronic

sensorineural hearing loss has been noted in roughly half of patients.<sup>3</sup>

Our patient’s diagnosis of stromal keratitis was assisted by anterior segment OCT, which showed focal epithelial hypertrophy overlying stromal thinning in addition to stromal hyperreflectivity that was subtle and previously missed by multiple practitioners on slit lamp examination. The measurement of regional corneal epithelial thickness and characterization of its behavior in response to changes in corneal architecture are increasingly drawing interest in clinical practice.<sup>6–9</sup>

Corneal epithelial thickness mapping has emerged as a valuable tool for a wide variety of applications, including screening and diagnosis of corneal ectatic processes, refractive surgery screening, and identification of underlying irregular stromal curvature, as in this case. Various remodeling patterns have been identified that help distinguish between ectatic and non-ectatic corneal conditions.<sup>7-9</sup> Epithelial remodeling is driven by underlying changes in stromal curvature, typically in an attempt to maintain a smooth, optical surface. Thus, a relatively uniform epithelial pattern is indicative of a normal, underlying stromal curvature and an irregular epithelial pattern typically implies underlying abnormalities in the curvature of the stroma. While much of the focus of epithelial remodeling highlights the focal thinning that occurs overlying ectatic corneas, the epithelium will also thicken significantly to fill in troughs in advanced ectasias and other non-ectatic conditions,<sup>9</sup> such is in this case.

The pattern of focal epithelial hypertrophy coincident with the region of maximal corneal steepening was opposite to the pattern anticipated in an ectatic cornea, which would instead be expected to have a pattern of thinner epithelium overlying the region of corneal steepening with a surrounding annulus of epithelial thickening.<sup>6-9</sup> In this case the epithelial remodeling seems to have overcompensated for the focal loss of stromal tissue given the focal increase in anterior corneal curvature initially present that resolved as corneal inflammation subsided. Since detailed corneal imaging was not available prior to our first consultation with the patient, we cannot comment on the temporal relationship between epithelial remodeling and corneal steepening in this case. The pronounced epithelial thickening to fill in the trough created by the focal stromal tissue loss was, however, not unique; we have seen and described this phenomenon in advanced keratoconic corneas as well.<sup>7</sup>

While corneal ectasias have traditionally been thought to be non-inflammatory, recent reports suggest this is incorrect.<sup>10-13</sup> A variety of inflammatory pathways appear to be involved in the ectatic process. In keratoconus, elevated levels of pro-inflammatory cytokines (such as IL-1 $\alpha$  and TNF- $\alpha$ ), activation of proteases including matrix metalloproteinases, and decreased activity of protease inhibitors have been demonstrated.<sup>10-13</sup> This in combination with a decrease in antioxidant and anti-inflammatory molecules (such as glutathione, lactoferrin, and IL-10) is thought to contribute to oxidative stress and keratocyte apoptosis.<sup>13</sup>

Progressive corneal ectasia has been reported in a 27 year old male patient with recurrent interstitial keratitis from HSV, with disease progressing to severe thinning, scarring that required corneal transplantation for visual rehabilitation.<sup>14</sup> In contrast to our patient, their patient had physical findings of an ectatic process, including Vogt's striae, Fleischer Ring and paracentral thinning seen at the slit lamp that progressed despite therapy. Given that patient's younger age, it is difficult to confirm all of the manifestations were due to interstitial keratitis without a concurrent diagnosis of keratoconus. In contrast, our patient's tomographic findings reversed with topical and systemic anti-inflammatory therapy.

In summary, this case highlights the importance of anterior segment OCT evaluation, including epithelial thickness maps, in the management of suspected corneal ectasias. Cogan syndrome can prove challenging to diagnose based on clinical findings alone; in these cases we recommend the use of both Scheimpflug corneal tomography and anterior segment OCT imaging to differentiate corneal ectasias from other inflammatory corneal disorders.

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## Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

## Research ethics

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

## Authorship

All listed authors meet the ICMJE criteria. We attest that all authors contributed significantly to the creation of this manuscript, each having fulfilled criteria as established by the ICMJE.

We confirm that the manuscript has been read and approved by all named authors.

We confirm that the order of authors listed in the manuscript has been approved by all named authors.

## Declaration of competing interest

The authors have no conflicts of interest to disclose regarding the publication of this manuscript.

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