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Unilateral progressive keratoconus associated with ipsilateral craniofacial fibrous dysplasia treated with corneal cross-linking

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ABSTRACT

Purpose: The purpose of this study is to describe a case of unilateral keratoconus associated with ipsilateral craniofacial fibrous dysplasia and its subsequent management with corneal collagen cross-linking.

Observations: This is an interventional case report of a 16-year-old male with a history of polyostotic fibrous dysplasia of the left frontal bone and orbital roof status post partial resection six years prior who presented to the pediatric ophthalmology clinic with progressively blurry vision in the left eye. Refraction in this eye revealed an increase in cylinder by > 3D from his last refraction two years prior. Pentacam corneal tomography confirmed the diagnosis of keratoconus in the left eye. The patient underwent corneal collagen cross-linking in the affected eye. Postoperatively, he experienced marked improvement in corrected visual acuity with scleral contact lenses and maintained stable astigmatism and keratometry values on Pentacam corneal tomography at his most recent visit 12 months postoperatively.

Conclusions: While it is otherwise felt to be a bilateral disease, unilateral keratoconus may present in the context of ipsilateral orbital pathology. Corneal collagen cross-linking may be used to successfully prevent keratoconus progression in the setting of stable orbital pathology.

1. Introduction

Keratoconus is an ectactic corneal disease characterized by progressive stromal thinning, irregular astigmatism, and decreased visual acuity. The prevalence and incidence rates of keratoconus have been estimated to be between 0.2 and 4790 per 100,000 persons and 1.5 and 25 cases per 100,000 persons/year respectively with some variations in regard to ethnicity and geography.[1] Keratoconus is widely considered a bilateral disease, and that while it may present asymmetrically, it will eventually involve the fellow eye if observed for long enough.[2,3] However some case reports have described stable unilateral keratoconus, suggesting the presence of a subset of true unilateral disease that warrants further research.[3,4] It has been hypothesized that secondarily induced ectasia may be caused by a purely mechanical process, such as eye rubbing in a predisposed cornea, which may cause unilateral disease.[2,4]

There are a few published case reports of orbital tumors associated with ipsilateral, unilateral keratoconus.[5–7] However, these previously reported cases do not describe the use of corneal collagen cross-linking in the affected eye. In this report, we describe a case of unilateral keratoconus associated with ipsilateral polyostotic fibrous dysplasia of the left frontal bone and orbital roof that underwent successful stabilization of keratoconus progression after corneal collagen cross-linking.

2. Case report

A 16-year-old male presented to the pediatric ophthalmology clinic with progressive vision loss in the left eye for the past year. He denied any history of eye rubbing, allergies, atopy, connective tissue disorders or a family history of keratoconus. His past medical history was significant for craniofacial polyostotic fibrous dysplasia involving the left frontal bone and orbital roof for which he was status post partial resection six years prior to his presentation. A computerized tomography (CT) scan taken three months prior to his presentation showed mild progression of disease within the left hemimandible, the left sphenoid, and the frontal bones. As there was concern for the development of comprehensive optic neuropathy from tumor growth that would require repeat orbital surgery, an urgent eye examination was performed.

Ophthalmologic examination was significant for an uncorrected Snellen visual acuity of 20/15 in the right eye versus 20/100, improving

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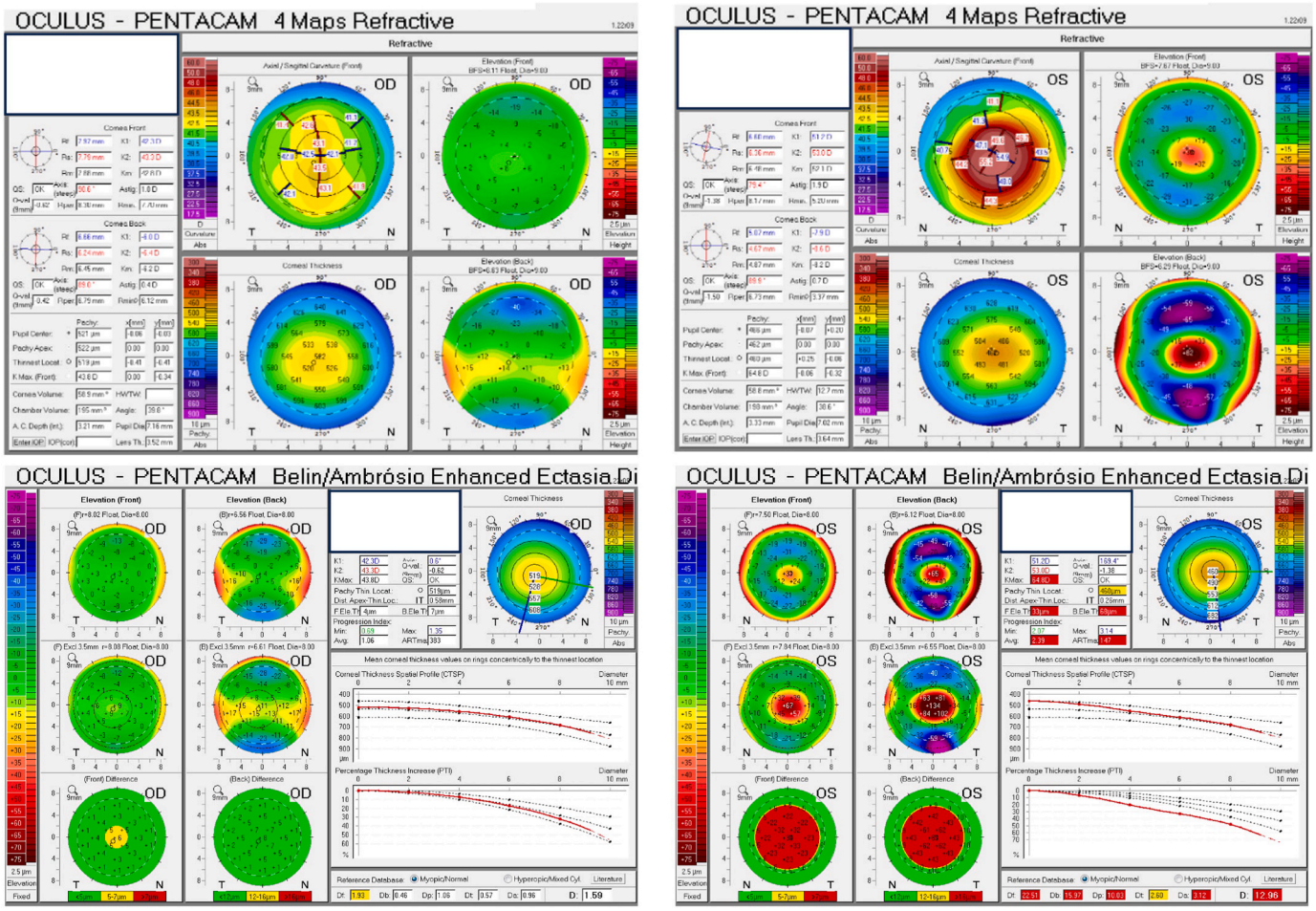

Fig. 1. Pentacam corneal tomography of both eyes. The left eye reveals signs of advanced keratoconus, notably with significant inferior paracentral steepening anteriorly and posteriorly, a steep keratometry value of 53 diopters, thinning in the areas of steepening on pachymetry maps with a steep percentage thickness increase (PTI) progression curve, abnormal keratoconus index (KI) of 1.19, and markedly abnormal Belin/Ambrósio Enhanced Ectasia Display maps. The right eye is largely within normal limits.

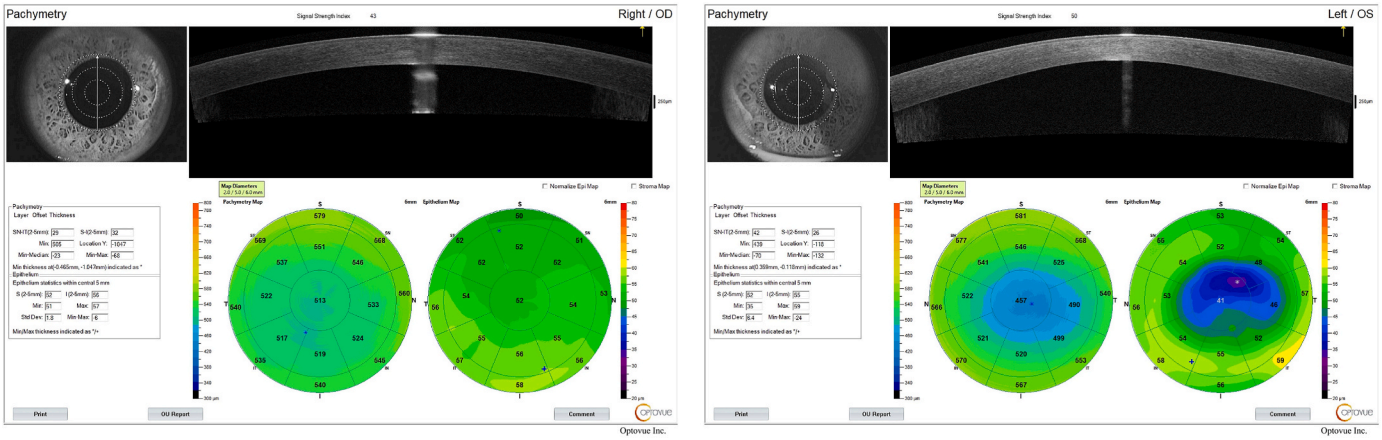

Fig. 2. Optovue optical coherence tomography of both eyes. The right eye shows normal total corneal thickness and epithelial thickness. The left eye however shows signs of advanced keratoconus, notably with thinner pachymetry (central corneal thickness 467 compared to 513 in the right eye) and apical epithelial thinning (corneal thickness of 41 μm and below, as seen with the blue and purple colors). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

to 20/70 with pinhole in the left eye. This represented a significant decline from his last eye examination two years prior, when uncorrected visual acuity was 20/15 in the right eye and 20/20- in the left eye in the setting of a minimal hyperopic spherical error found on cycloplegic retinoscopy. Intraocular pressures were normal, there was no relative afferent pupillary defect, and visual fields to confrontation were full. Slit lamp examination was significant for mild proptosis and hypoglobus of the left eye and a noticeable conical shape to the left cornea without

scarring or Vogt striae. Dilated funduscopic examination was within normal limits, notably without optic nerve pallor or edema. Cycloplegic retinoscopy revealed a markedly scissored retinoscopic reflex and a >3D increase in cylindrical error in the left eye from the last refraction two years prior. Pentacam corneal tomography showed signs of advanced keratoconus, including significant inferior paracentral steepening with associated thinning, steep keratometry, abnormal keratoconus index, and markedly abnormal Belin/Ambrósio Enhanced Ectasia Display maps in the left eye only (Fig. 1). Optovue-OCT epithelial thickness maps also showed epithelial thinning over the apex of the cornea characteristic of keratoconus (Fig. 2). However these findings were not seen in the contralateral eye.

As the patient's decreased vision was concluded to be secondary to keratoconus rather than optic nerve compromise, the neurosurgical team deferred repeat surgical intervention and elected to observe closely with serial neuroimaging. To prevent further progression of ectasia, the patient underwent uncomplicated corneal collagen crosslinking in the left eye using the epithelium-off Dresden protocol. Three months post-operatively, his visual acuity improved to 20/20 in the left eye with a scleral contact lens, and 12 months postoperatively, repeat Pentacam imaging demonstrated stable astigmatism, keratometry, and corneal morphology from that seen preoperatively without any evidence of further disease progression.

3. Discussion

Keratoconus has been associated with environmental factors such as atopy, allergic eye disease, and eczema, which are felt to contribute to disease progression through mechanical pressure on the globe from eye rubbing. Keratoconus is largely considered to be a bilateral process, however unilateral disease has also been described in association with direct mechanical pressure exerted on the globe by an ipsilateral orbital process, such as orbital cavernous hemangioma, orbital dermoid cyst, or fibrous dysplasia.[5–7] It is important to note, however, that even without these comorbidities, patients may present with what appears to be unilateral keratoconus due to behavioral changes initiated once one eye is diagnosed with keratoconus (e.g. decreasing eye rubbing, sleeping on one's backs, using antihistamines, and receiving prophylactic corneal crosslinking of the unaffected eye), which may confound the presentation of unilateral keratoconus.

Fibrous dysplasia, a rare condition associated with GNAS mutations in which fibrous tissue replaces normal bone, has previously been reported to be associated with keratoconus.[6] This case report is consistent with previous observations as our patient with fibrous dysplasia developed ipsilateral keratoconus in the absence of other risk factors such as family history or eye rubbing. However, in previously reported cases, patients initially presented with findings consistent with keratoconus in the setting of unilateral proptosis, prompting further investigation with neuroimaging that found orbital masses. In these cases, following resection of the mass, patients had subsequent normalization of visual acuity and keratometric measures. Our patient, on the other hand, was diagnosed with and already underwent resection of his unilateral orbital fibrous dysplasia six years prior to presentation, but he did not show any signs of keratoconus at the time of diagnosis or for many years after as evidenced by his excellent uncorrected visual acuity, near-plano retinoscopic refraction, and unremarkable corneal exam. However, it is important to note that neither corneal tomography nor topography was performed at his previous eye examinations. Furthermore, while current detection of subclinical keratoconus relies of corneal topography, other studies have demonstrated that it may not detect all cases at risk.[8,9] In early keratoconus, focal steepening at the apex may be masked by compensatory corneal epithelial thinning, and thus epithelial thickness mapping with OCT may be a more sensitive way of identifying subclinical keratoconus.[10] We hypothesize that his history of fibrous dysplasia increased his risk of corneal ectasia secondary to mechanical pressure on the globe even after partial resection was completed. It is possible that even the mild progression of the mass on his most recent CT scan could have been associated with the progression of keratoconus as well.

Corneal collagen cross-linking improves the biomechanical stability of the cornea by using ultraviolet radiation to activate riboflavin and form covalent bonds between collagen fibrils in the corneal stroma. It is considered the first-line treatment in reducing keratoconus progression and has been shown to be a safe and effective procedure with minimal complications.[11,12] In this reported case, as the patient's vision loss was attributed to the development of unilateral keratoconus associated with his orbital tumor rather than compressive optic neuropathy secondary to the tumor growth, it enabled a risk versus benefits discussion for the less invasive corneal cross-linking procedure over repeat orbital surgery. Fortunately, the patient demonstrated improvement in visual acuity with scleral contact lenses and keratoconus disease stabilization one year after cross-linking, suggesting that corneal cross-linking may be effective for patients with unilateral keratoconus in the setting of stable orbital disease. However, more research is needed to understand the relationship between progressive unilateral orbital disease and ipsilateral keratoconus progression both before and after corneal collagen cross-linking.

4. Conclusion

In conclusion, unilateral keratoconus may present in the context of ipsilateral orbital pathology. This case describes using corneal collagen cross-linking to successfully prevent keratoconus progression in the setting of stable orbital pathology.

Patient consent

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

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Authorship

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

CRediT authorship contribution statement

Alice C. Jiang: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft. **Maanasa Indaram:** Conceptualization, Funding acquisition, Investigation, Methodology, Supervision, Writing – review & editing.

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.

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