CASE REPORT

Bilateral central toxic keratopathy after laser in situ keratomileusis

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SUMMARY

One week after LASIK, our patient presented with bilateral haloes and reduced vision. Examination revealed the typical central toxic keratopathy triad: corneal thinning, hyperopic shift and a reduction in best corrected visual acuity to 6/12, which, after commencing high-dose topical steroids, improved 6 months later to 6/6.

BACKGROUND

LASIK surgery is now the most performed surgery in the world. With such high volume, complications are bound to occur. Central toxic keratopathy (CTK) is a fairly recently described complication that, regarding its pathophysiology and treatment, is not yet fully understood. These rare cases are important for other clinicians to look up, and as the basis for larger studies.

CASE PRESENTATION

A 47-year-old man presented at our centre, seeking LASIK for both eyes (OU). His medical history was unremarkable. Refraction in the right eye (OD) was myopic ($-3.25/-0.50 \times 20^\circ$) and, in the left eye (OS), it was a simple myopia (-3.50). Keratometric readings were $44.5/44.0 \times 30$ in the right eye and $44.25/44 \times 145$ in the left eye. His uncorrected visual acuity was 6/60, which reached 6/6 with full correction. His intraocular pressure was 16 mm Hg with applanation tonometry in both eyes, and anterior chamber and fundus examination were normal. Preoperative investigations showed pachymetry of $510 \mu\text{m}$ in both eyes, and the topography was unremarkable. Keratometry showed 43 and 44 D for both eyes. A decision to perform bilateral simultaneous LASIK with under correction of the non-dominant right eye—as a sort of monovision to assist the patient in near work—was taken after a discussion with the patient.

Bilateral simultaneous wavefront optimised LASIK was performed using an ALLEGRETTO Wave Eye-Q Excimer laser platform manufactured by Alcon surgical. After routine draping and under strict aseptic technique, a suction ring was placed, and a Moria M2 Evolution 3 automated device manufactured by Moria Surgical Group was used to create a $130 \mu\text{m}$ corneal stromal flap. The stromal bed was then subjected to excimer laser with an optical zone of 6.50 mm and a treatment zone of 9 mm. Central ablation of $39 \mu\text{m}$ of stromal tissue was carried out after treatment of myopia of -2 D, and astigmatism of -0.50 at an axis of 20° was entered into the device to under

correct the right eye for monovision. A similar technique was then performed for the left eye, with an optical zone of 6.50 mm and a treatment zone of 7.1 mm, and a full correction of -3.50 D of myopia to centrally ablate $53 \mu\text{m}$ of stromal tissue.

A postoperative treatment regimen was started with an hourly dose of topical tobramycin 0.3%/dexamethasone 0.1% combination, along with lubricant eye drops. The patient's binocular uncorrected visual acuity was 6/6 on postoperative day 1, and his autorefractometer was stable at -1.25 OD and emmetropia OS. His dose was then lowered to a four times per day of the combination drops and maintaining the hourly dose of the lubricant eye drops OU. Exactly 1 week after surgery (day 7), he reported reduction of vision and light haloes. His best spectacle-corrected visual acuity (BSCVA) was reduced to 6/12 OU with a refraction of -0.25 , $-1.50 \times 90^\circ$ OD and $+2.50$, $-2.00 \times 35^\circ$ OS, denoting a hyperopic shift. Examination showed a grade 2 diffuse lamellar keratitis (DLK) with a central corneal opacification OU extending approximately 20% deep into the stromal bed, and stromal thinning and folds, as shown in figure 1. No epithelial defect was present.

DIFFERENTIAL DIAGNOSIS

DLK, an acute inflammatory-mediated condition, is associated with an anterior chamber reaction, conjunctival hyperaemia or ciliary flush.¹ A rarer complication of LASIK is CTK, a condition suggested to be a non-inflammatory process, which is characterised by the typical CTK triad of non-inflammatory central corneal opacification, striae and stromal bed tissue loss. This results in a hyperopic shift, causing a reduction in quality of vision.^{2–4} Differentiation of DLK from CTK is shown in table 1.

Figure 1 Central toxic keratopathy before treatment.

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Table 1 Differential diagnosis of CTK

	DLK	CTK
Time of onset	First day	3–9 days
Response to steroids	Steroid responsive	No response to steroids
Inflammation	Widespread opacification confined to interface	Central opacification, extending posteriorly
Examination	No striae or refractive changes. Associated with anterior chamber reaction, conjunctival hyperaemia and ciliary flush	Striae and refractive changes present. Not usually associated with anterior chamber reaction, conjunctival hyperaemia and ciliary flush
Prognosis	Usually resolves in a week	Resolves in 2–18 months
Confocal microscopy	No loss of keratocytes, inflammatory cells present	Loss of keratocytes, no inflammatory cells present
Inciting procedure	LASIK	LASIK, PRK

CTK, central toxic keratopathy; DLK, diffuse lamellar keratitis; PRK, photorefractive keratectomy.

TREATMENT

The patient was started on a 2 hourly dose of prednisolone acetate 1% suspension OU, along with his previous topical lubricant treatment. The refraction remained the same OD, but changed to +2.0, $-1.0 \times 65^\circ$ OS at day 12.

OUTCOME AND FOLLOW-UP

The DLK started responding to the topical steroids, and the patient noticed an improvement in vision, reaching a BSCVA of 6/9 OU on day 14. Luckily, the patient's uncorrected vision was sufficient to perform his daily activities without correction, as the patient's non-dominant right eye, which was previously adjusted to be myopic for near vision, now had simple myopic astigmatism after the hyperopic shift, thus aiding him in near work and slightly for distance. The topical steroids were gradually tapered to a four times per day dose starting on day 14, and then stopped altogether 1 month postoperatively. The central opacity and thinning only slightly improved, but the DLK disappeared. The patient was later fitted with reading glasses to compensate for his presbyopia, in addition to his hyperopia OS, 1 month postoperatively. Six months postoperatively, the hyperopic shift was maintained, but his refraction was still changing, being -0.50 , $-0.75 \times 100^\circ$ OD, and $+1.00$, -0.25×50 OS, at the time. His reading glasses were adjusted accordingly. The central corneal opacity had not yet fully resolved, as shown in [figure 2](#).

DISCUSSION

The cause of CTK remains uncertain, although recent confocal microscopy studies by Hau and Allan and Hsu *et al* on CTK

confirm the existence of keratocyte apoptosis in the affected central stromal matrix, which is thought to be responsible for the clinical findings seen in CTK.^{5 6} Furthermore, it is possible that individuals who develop CTK have a background of or genetic predisposition to hypersensitivity towards substances in the tear film, which may trigger keratocyte apoptosis.⁷ Sonmez and Maloney³ suggested that the underlying cause of CTK was due to a toxic reaction to a substance that undergoes photoactivation by the laser.

Early reports advise giving steroid treatment in managing CTK, considering the cause as inflammatory.^{1 8 9} This was challenged by the notion of it being more of a toxic reaction, and that prolonged steroid treatment would only increase the morbidity of the patient by exposing the eye to risks, such as cataract and glaucoma, caused by the prolonged steroid treatment.^{10 11}

Anterior segment optical coherence tomography images have suggested that the rate of tissue apoptosis slowed as early as 1 week post-LASIK, with a rapid increase in corneal thickness at 5 weeks, due to the proliferation of keratocytes.^{4 12} This correlates with the cessation of postoperative topical steroids. Therefore, it was suggested not to use steroids in treatment of CTK due to their potential to inhibit the proliferation of keratocytes and fibroblasts, and to reconstruct the damaged cellular matrix.^{2 13}

Furthermore, recent in vivo confocal microscopy findings of CTK showed no evidence of inflammatory cells in CTK, but rather a loss of keratocytes, as opposed to DLK, which is steroid responsive.^{5 6} Collectively, these findings further support the limited role of steroids in managing CTK.

With these findings and our literature review of all available publications on CTK, the most effective management for CTK thus far is close-monitoring.^{2 4 8 12 14 15} Numerous studies and case series have proven that corneal opacification in CTK clears within 18 months without intervention or treatment.^{4 12} However, we recommend regular follow-up.

Surgeons should make a diagnosis of CTK as early as possible, stop steroids as soon as there is no flap interface inflammation due to DLK and then closely follow-up the patient. However, stage 4 DLK must be treated with steroids. DLK is relatively easily differentiated from CTK because patients will describe ocular pain and the presence of a 'foreign-body'.¹ The responsible surgeon should be able to distinguish between the many differential diagnoses of CTK, such as infectious keratitis, DLK, interface keratitis, epithelial ingrowth, trauma and superficial punctate keratitis, and should be competent to treat accordingly.^{1 2}

In our case, we chose to continue topical steroids for 6 months, gradually tapering off, which was probably not ideal

Figure 2 Central toxic keratopathy after treatment.

because this possibly delayed the proliferation of keratocytes and thus the improvement in best corrected visual acuity.

Other possible pharmacological approaches to managing CTK include doxycycline, which has been shown to decrease the expression of interleukin 1 and tumour necrosis factor- α , which are proven to induce keratocyte apoptosis, although no studies have been performed to test its effect on CTK.¹⁶ Topical vitamin E application after photorefractive keratectomy has also been shown to decrease keratocyte apoptosis.^{16 17} However, there have been few studies or trials of successful pharmacological inhibition of keratocyte apoptosis, although this could have important implications in the prevention and treatment of CTK in the future.

In summary, we believe that intensive steroid therapy did benefit the patient, although randomised, controlled trials are needed to determine the most appropriate management for CTK.

Learning points

- Rare complications are bound to occur with the widespread use of LASIK surgery.
- The clinician should harbour suspicion of central toxic keratopathy when faced with advanced diffuse lamellar keratitis.
- Treatment with steroids is controversial.

Competing interests None declared.

Patient consent Obtained.

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