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CASE REPORT

Late Onset Corneal Haze Post Photorefractive Keratectomy

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Abstract

Introduction: Photorefractive keratectomy (PRK) is a surface ablation procedure to correct refractive errors. Regardless of the safety and efficacy, corneal haze may occur after PRK, and it remains one of the most feared complications because it can impair good visual outcomes. **Case Presentation:** A 20-year-old woman complained of blurred vision in her right eye (RE) after undergoing PRK elsewhere six months before admission with a history of refraction of S-12.75 C-1.75 x 10° preoperatively and S-0.75 postoperatively. Six-month postoperative uncorrected visual acuity (UCVA) was 0.01, best corrected visual acuity (BCVA) was 0.5 with S-7.00 C-0.75 x 50°. A slit lamp examination revealed grade three corneal haze. Anterior optical coherence tomography (OCT) showed the hyperreflective area with 132 µm deep into the stroma. The patient underwent phototherapeutic keratectomy (PTK) and mitomycin-C (MMC) treatment to a depth of 50 µm Ø6.5mm transition zone 0.5 mm. Two months later, UCVA was 0.2, BCVA was 0.63 with S-2.50 C-0.50 x 90°, and slit lamp examination revealed no haze remaining. **Conclusions:** This case illustrates the potential risk for corneal haze development, mainly when PRK is performed at greater treatment depths. However, with phototherapeutic keratectomy and mitomycin-C treatment, an excellent visual outcome and vision restoration can be obtained.

Keywords: corneal haze; photorefractive keratectomy complications; phototherapeutic keratectomy; mitomycin-C

Introduction

Photorefractive keratectomy (PRK) is a surface ablation procedure to correct refractive errors.[1] Although laser-assisted in situ keratomileusis (LASIK) has been widely and commonly used for refractive surgery, PRK is still preferable in some cases.[2]

The improvement in laser technologies has lessened the frequency of corneal haze following PRK, however, even with the implementation of all precautions and recommended measures, clinicians may still encounter post-PRK haze in approximately 2-3.6% of patients, and it remains one of the most feared complications because it can impair good visual outcome after PRK.[3],[4],[5]

Case Presentation

A 20-year-old woman presented to our hospital complaining of blurred vision. She gradually decreased visual acuity for the past four months on her right eye (RE) after undergoing PRK elsewhere six months before admission, with a history of refraction of S-12.75 C-1.75 x 10° preoperatively and S-0.75 postoperatively. The patient had no medical history that may impair her cornea. Six-month postoperative uncorrected visual acuity (UCVA) was 0.01, and best corrected visual acuity (BCVA) was 0.5 with S-7.00 C-0.75 x 50°. Slit lamp examination revealed grade three corneal haze (Figure 1A) according to the grading scale by Fantes et al.[6] (Table 1). The anterior optical coherence tomography (OCT) showed a hyperreflective area with 132µm deep into the stroma (Figure 2), while corneal topography (Figure 3) and corneal epithelial map (Figure 4) were within normal limits.

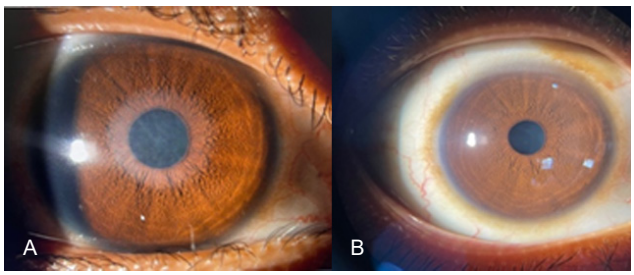

Figure 1. (A) Corneal haze of right eye and (B) Excellent outcome of the RE two months postoperatively.

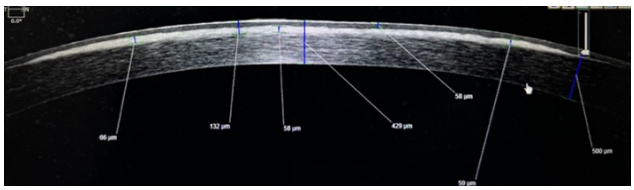

Figure 2. Anterior OCT of the RE before PTK and MMC treatment.

Adequate topical steroids and eye lubricant were initiated, with the haze being unresponsive. Following three month treatment, due to signs of no clinical improvement, the patient then underwent phototherapeutic keratectomy (PTK) assisted by alcohol solution for epithelial loosening and intraoperative mitomycin-C (MMC) 0.02% treatment was conducted to a depth of 50µm, Ø6.5mm, transition zone 0.5 mm and for 40 seconds followed by application of balanced salt solution and a bandage contact lens after the procedure. Two months after the procedure, the patient's UCVA was 0.2, and BCVA was 0.63 with S-2.50 C-0.50 x 90°. Slit lamp examination revealed no haze remaining (Figure 1B).

Discussion and conclusions

Corneal haze after surface ablation is the outcome of an intricate inflammatory process. It is widely observed that following PRK procedures, patients will experience a corneal epithelial reaction. Initially, this reaction involves an enlargement of epithelial cells to cover the surgical defect, succeeded by cell proliferation, migration, differentiation, and the formation of hemidesmosomes. Concurrently, the cytokines released due to the epithelial injury initiate a series of stromal events. This cascade includes keratocyte apoptosis, proliferation, migration, and fibroblast differentiation alongside extracellular matrix (ECM) remodeling.[7]

Damage to the basement membrane during surgery triggers a subepithelial fibrotic response, characterized by the production of disorganized stroma ECM by activated keratocytes, leading to increased corneal light scattering and visible corneal haze.[8]

Studies have mentioned several risk factors associated with developing postoperative haze: dry eye disease, epithelial basement membrane dystrophy (EBMD), vitamin D deficiency, ultraviolet exposure, hormonal changes, autoimmune, and atopy.[9],[10],[11],[12] In our case, the patient had no medical history that may impair her cornea. Instead, she had undergone PRK elsewhere, which corrected the RE up to -12D with residual refraction of S-0.75 postoperatively. This finding is in accordance with a previous study stating that the degree of intended myopic correction remains the most critical risk factor for developing haze because the higher myopic and/or cylindrical correction is planned, the greater treatment depth is required. As a consequence, it will increase the risk of the development of corneal haze.[13]

Once clinicians detect visually notable haze following PRK, they may aim to differentiate between early and late-onset haze. Early-onset haze manifests within the first three months post-surgery and might respond better to topical steroids[14], while late-onset haze typically emerges between three to five months and may persist to 12 months after PRK and often shows resistance to steroid treatments.[13],[14]

For late-onset haze, a short-term topical steroid regimen may be attempted with bi-weekly follow-ups. Surgical management is considerable if there is no response or progression within four weeks of treatment. Conversely, if the patient shows improvement with steroid therapy, the treatment can be gradually tapered until symptoms completely resolve.[15],[16]

Besides the topical steroid therapy, MMC has notably enhanced clinical outcomes since its introduction into refractive surgery in 1991.[17] MMC acts as an alkylating agent, disrupting DNA replication and

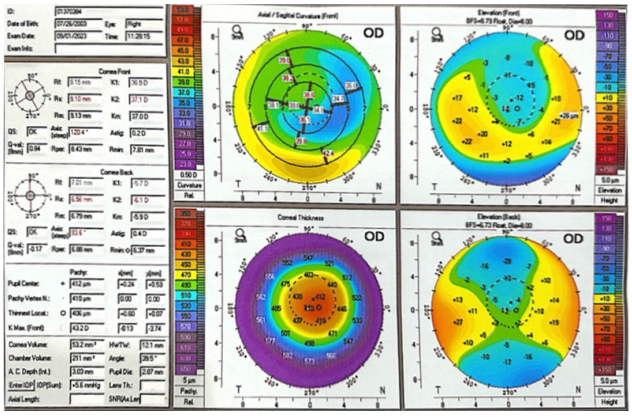

Figure 3. Normal corneal topography of RE.

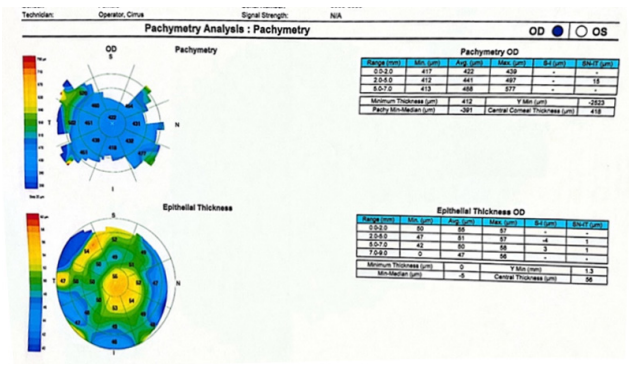

Figure 4. Normal corneal epithelial map of the RE.

Table 1. Corneal haze grading scale by Fantes et al.[6]

Stage	Slit-lamp Appearance
0	Clear cornea
0.5	Trace haze was seen with oblique illumination
1	Haze not interfering with iris detail visibility
2	Haze with mild obscuration of iris detail visibility
3	Haze with moderate obscuration of iris detail visibility
4	Complete opacity of the stroma

cellular proliferation by forming DNA crosslinks. It is a pro-drug that requires tissue reduction to unleash its DNA-alkylating capabilities. Although MMC enhances the initial surge of keratocyte apoptosis in the anterior corneal stroma, its principal role in preventing fibrosis in surface ablation procedures lie in inhibiting the mitosis of myofibroblast precursor cells during the first few weeks following the procedures.[18]

MMC helps treat eyes with higher degrees of myopia (≥ 6D), which are more prone to developing fibrosis and late-onset haze. Studies reveal the use of MMC at a concentration of 0.02% compared to lower doses (e.g., 0.01% or 0.002%) for the best reduction of fibrosis after surface ablation procedures. Longer exposure times exceeding 40 seconds with 0.02% MMC may confer benefits for moderate to high myopia (≥ 6D), while shorter exposure times appear equally effective for lower myopia.[18] A retrospective study also shows that the use of intraoperative MMC during PTK for patients with anterior corneal disorders is safe and that it does not inhibit epithelial healing and may aid in preventing recurrent anterior corneal disease in the MMC-treated area.[17],[19]

In our case, according to the anterior OCT result that revealed the haze affects more than one-fifth of the corneal thickness or extends beyond 15µm into the stroma and the failure to use adequate topical steroids for three months, deep PTK and intraoperative MMC 0.02% were the appropriate management for treating the haze.

The case we presented here illustrates the potential risk for corneal haze development, particularly when PRK is performed at greater treatment depths. However, with phototherapeutic keratectomy and mitomycin-C treatment, an excellent visual outcome and vision restoration can be obtained.

Acknowledgment

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