Epithelial Inoculation After Small-Incision Lenticule Extraction (SMILE): A Case Report

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Abstract

Epithelial ingrowth is a rare condition that is generally seen after laser *in situ* keratomileusis (LASIK) and has been reported in the literature in a small number of cases after small-incision lenticule extraction (SMILE) surgery. "Epithelial inoculation" should also be considered in patients presenting with decreased vision and an appearance similar to epithelial ingrowth in the early period after SMILE surgery. A 23-year-old woman presented to our clinic with a request for refractive surgery. Her manifest refractions were -7.50 -1.00 x 180° in the right eye and -7.25 -1.00 x 150° in the left eye, and best corrected distance visual acuity was 10/10 in both eyes. The SMILE procedure was performed with the Visumax femtosecond laser (Carl Zeiss Meditec AG). Slit-lamp examination at postoperative 1 week revealed a small grayish-white intrastromal opacity resembling epithelial ingrowth in the central optic axis of the right eye. Irrigation of the interface was performed with balanced salt solution using an irrigation cannula and the epithelial cluster was removed. The patient remained clinically stable 6 months after surgery and has experienced no recurrence. When epithelial inoculation is observed early after SMILE surgery, immediate irrigation of the interface appears to be an effective and safe treatment.

Keywords: Astigmatism, epithelial ingrowth, epithelial inoculation, LASIK, myopia, SMILE

Introduction

Small-incision lenticule extraction (SMILE) surgery has been used in the surgical treatment of refractive errors such as myopia and myopic astigmatism since 2008. Flapless removal of an intrastromal lenticule with SMILE has led to a paradigm shift in which the complications of traditional flap-based ablation methods can be avoided.[1,2] Epithelial ingrowth, a flap-related complication, is common after laser *in situ* keratomileusis (LASIK).[3] In contrast to LASIK, a small lateral incision ranging from 3 to 5 mm is made to remove the lenticule created in SMILE, so it is expected that interface epithelial ingrowth will be less likely.[4] However, in SMILE, epithelial cells can still be seeded into the interface by surgical instruments and epithelial cell proliferation can follow, leading to an ingrowth-like appearance. The result can be corneal irregularity and decreased vision, especially if the affected area is close to the visual axis.[5]

In this case report, we present a case of epithelial inoculation following SMILE surgery that was managed with interface irrigation.

Case Report

A 23-year-old female patient presented to our clinic with a request for refractive surgery. Her manifest refraction values were -7.50 -1.00 x 180° and -7.25 -1.00 x 150° in the right and left eyes, respectively. Best corrected distance visual acuity (BCVA) was 10/10 in both eyes. Central corneal thickness was 557 µm in the right and 548 µm in the left eye. Ocular and systemic histories were unremarkable. Ophthalmological examinations including corneal topography were normal in both eyes. Emmetropia was targeted and bilateral SMILE was planned for the patient.

The SMILE procedure was performed with the Visumax femtosecond laser (Carl Zeiss Meditec AG, Jena, Germany) under topical anesthesia (0.5% proparacaine hydrochloride; Alcaine;

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Alcon Laboratories, Inc, Fort Worth, TX, USA; one drop in each eye). The cap diameter was 7.8 mm, with an intended thickness of 120 µm, and the optical zone in both eyes was 6.5 mm. Superotemporal lateral incisions 3 mm long were made in both eyes for lenticule extraction. The repetition rate was 500 kHz, and the pulse energy was 140 NJ. Both ocular areas were prepared for surgery. After proper centralization and corneal contact, incisions were made with the laser system without any complications. A Duckworth & Kent double-ended dissector with a bullet-shaped tip was used to enter the interface. Although there was no evidence of loose epithelium or corneal dystrophy on preoperative examination, penetration under the epithelium was observed even though the tip of the dissector was directed towards the interfacial area. After several unsuccessful attempts, it was possible to enter the interface without an epithelial defect and perform a proper dissection of the lenticule. The procedure was uneventful for the left eye.

In both eyes, the interface was irrigated with balanced salt solution (BSS) and the side cut was dried with a sponge. After this stage, the interface was checked in both eyes with the slit lamp of the device and there was nothing noticeable. We do not routinely use postoperative bandage contact lenses in our SMILE cases. Although there was no epithelial defect in the side cut area, we used them prophylactically in both eyes for epithelial ingrowth due to loose epithelium in this case.

On the same day, half an hour after the procedure, the interfaces of both eyes were checked by slit-lamp biomicroscopy. The interfaces of both eyes were transparent and no suspicious findings were observed.

The patient was treated topically with 0.5% moxifloxacin (Moxai; Abdi Ibrahim, Istanbul, Türkiye), loteprednol etabonate 0.5% (Lotemax; Bausch & Lomb, Florida, USA), and preservative-free artificial tears 4 times daily for 1 week postoperatively.

Uncorrected distance visual acuity (UDVA) was 6/10 in the right eye and 8/10 in the left eye on the first postoperative day. After removal of the bandage contact lenses, slit lamp examination of both eyes showed no epithelial defect in the lateral incision areas and the interfaces were clear.

At postoperative 1 week, UDVA was 2/10 in the right and 10/10 in the left eye. No results could be obtained from autorefractometer measurements in the right eye. Biomicroscopic examination revealed a small grayish-white intrastromal opacity similar to epithelial growth in the central corneal interface in the optic axis of the right eye which was not associated with the lateral incision. The opacity was also detectable with Cirrus HD (Carl Zeiss Meditec AG) optical coherence tomography (OCT) B-scan, and corneal topographic examination revealed a central irregularity immediately above the area of opacity (Figure 1). In order to determine the cause, the surgical recording was reviewed several times with the surgical team on the Visumax device and there was no manipulation that could lead to an epithelial defect. However, during the interfacial penetration phase, the patient's epithelium appeared to loosen when the dissector tip unexpectedly penetrated under the epithelium. Although precautions were taken by irrigating the interface and placing bandage contact lenses, it was concluded that a few invisible epithelial cells were introduced to the interface and multiplied there after repeated penetrations under the epithelium before entering the interface.

Since the lesion was on the optical axis and UDVA was affected, interface irrigation was performed with a diagnosis of "epithelial inoculation" due to repeated manipulation of loose epithelium. After dissection of the interface with the spoon tip of a double-ended dissector, the interface was irrigated with BSS by an irrigation cannula. During irrigation, it was observed that the epithelial cluster became mobile easily and detached from the interface (Figure 2). After making sure that there was no epithelial residue at the interface, the anterior surface of the cornea was rubbed towards the side cut with the back of the irrigation cannula to drain the fluid from the interface. The side

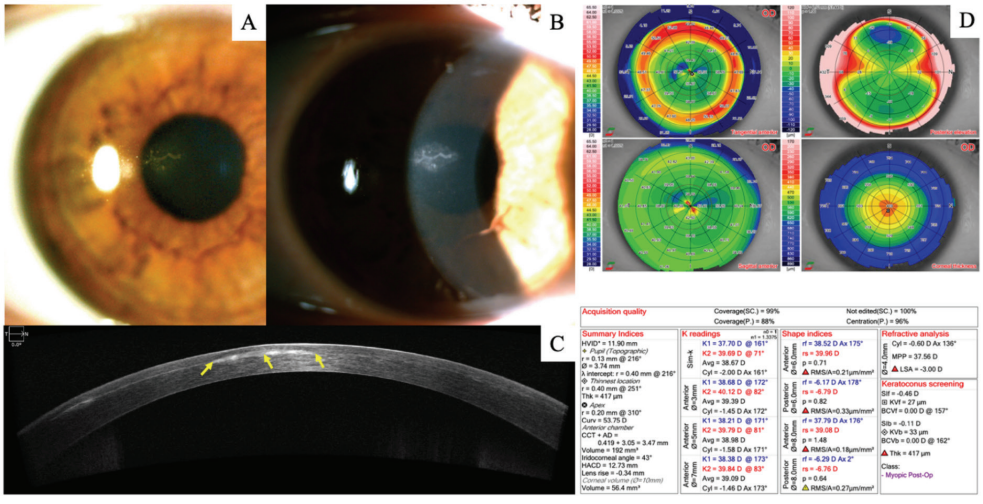

Figure 1. The right eye at postoperative 1 week. A, B) Irregularly circumscribed grayish-white opacities similar to epithelial ingrowth at the interface in the optical axis were observed on slit-lamp examination. C) Anterior segment optical coherence tomography showed increased hyperreflectivity at the interface limited to the central cornea (yellow arrows). D) Corneal steepening above the inoculation area and an irregular astigmatism-like appearance were observed on corneal topography

cut was dried with a cotton-tipped sponge. After irrigation, the patient was treated with topical 0.5% moxifloxacin (Moxai; Abdi Ibrahim, Istanbul, Türkiye), dexamethasone (Dexasine SE; LIBA, Kaysersberg, France), and preservative-free artificial tears 8 times a day for 1 day. The steroid and antibiotic drops were gradually tapered over 1 month. Treatment with artificial tears 4 times a day was planned for the following 6 months.

One day after interface irrigation, UDVA was 5/10 and CDVA was 10/10 (-1.00 -0.75 x 180°) in the right eye. On slit-lamp examination, the interface was hazy and smooth. A more regular map was observed on topography, while OCT imaging of the interface revealed no trace of hyperreflectivity due to epithelial deposition (Figure 3).

One month after refractive surgery, UDVA was 10/10 in both eyes. On slit-lamp examination, the interface was clear and smooth and a more regular corneal map was observed on topography of the right eye compared to the first postoperative day. On OCT imaging of the right eye, there was still no trace of hyperreflectivity due to epithelial deposition at the interface (Figure 4).

Discussion

Epithelium at the interface is frequently encountered as a postoperative complication in the form of epithelial ingrowth after femto-LASIK surgery.[6] Since SMILE does not require a corneal flap like LASIK, epithelial ingrowth is a rare postoperative complication.[7] The possible causes of epithelial cell migration to the interface during SMILE are varied: a) frequent instillation of topical anesthetic drops, resulting in a loose epithelium-like state, b) migration of corneal epithelium from the lateral incision to the interface, c) disruption of the epithelium close to the incision site and seeding of disrupted epithelial cells via severe and repetitive surgical manipulations,[5] and d) migration of epithelial cells to the interface through a fistula formed between the interface and epithelium by a vertical epithelial gas breakthrough.[8,9] Each of these may be the cause or multiple causes may coexist.

Loose epithelium that is not detected in the preoperative biomicroscopic evaluation may be encountered intraoperatively. During entry into the interface through the side cut, the dissector may be directed under the epithelium due to loose epithelium and surgical manipulations may increase during the operation. Therefore, with epithelial cells detached from the loose epithelium, interfacial inoculation can take place through a side incision. In the present case, while intending to enter the interface, the dissector went under the epithelium due to the presence of loose epithelium. Then, although the

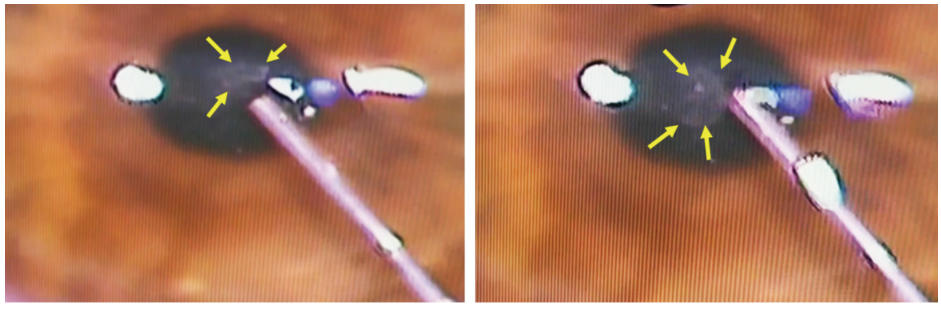

Figure 2. The interface was irrigated with balanced salt solution using an irrigation cannula. The gray epithelial accumulation became mobile and detached from the cornea as the interface was irrigated. Yellow arrows indicate the epithelial inoculation margins

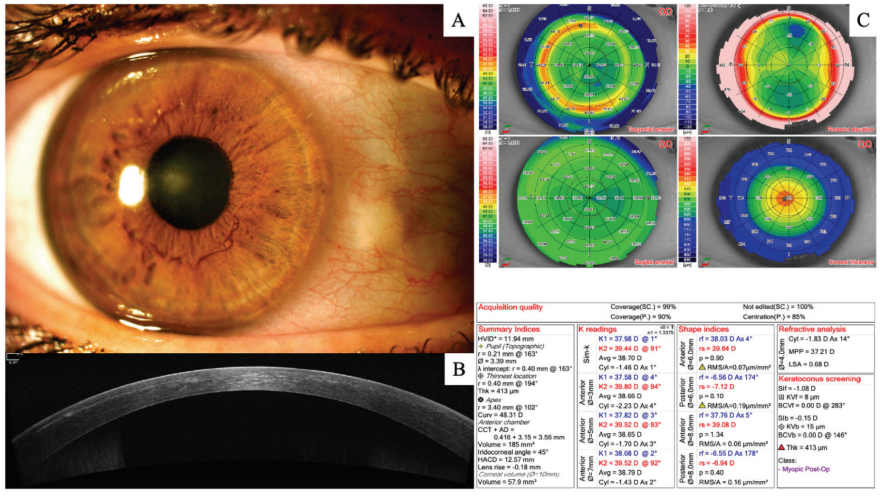

Figure 3. The right eye 1 day after interface irrigation. A) The epithelial ingrowth-like appearance disappeared, with only a slight haze remaining. B) Anterior segment optical coherence tomography imaging showed no hyperreflectivity. C) Corneal irregularity was significantly decreased on topography

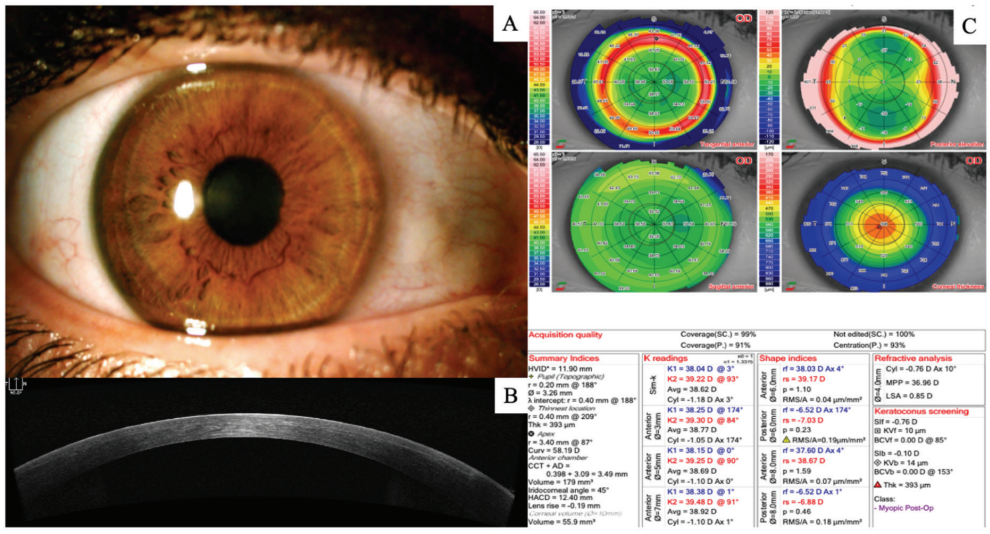

Figure 4. The right eye at postoperative 1 month. A) Slit-lamp examination showed the cornea is completely clear. B) Anterior segment optical coherence tomography imaging and C) corneal topography were completely normal

surgery proceeded correctly, the epithelial cells detached from this loose epithelium around the side cut were planted at the interface during lenticule dissection. The fact that the epithelial accumulation was distant from the incision site and not associated with the side cut supports the diagnosis of epithelial inoculation rather than ingrowth.

It is a common approach to observe epithelial ingrowth seen after LASIK without treatment. If the visual axis is affected, the surface becomes irregular, visual acuity is reduced, or stromal melting is observed, a more aggressive approach is required. Many treatment options have been described for epithelial ingrowth. The flap can be lifted and mechanically debrided, and adjuvant treatments such as mitomycin C or alcohol can be used. In addition, phototherapeutic keratectomy can be performed on the residual stromal bed after flap removal. Following these methods, the flap can be closed with sutures or tissue glue to prevent recurrence.[10] Although epithelial ingrowth is less common in SMILE, certain complications that affect the optical axis or reduce vision require treatment. Compared to LASIK, the epithelial infiltration area is relatively smaller in SMILE and therefore less aggressive methods may be sufficient.[5] Intervention is necessary when the optical axis is affected because it leads to an irregular ocular surface and reduced visual acuity. The treatment decision depends on the size of the epithelial ingrowth area, its connection with the side cut, and its distance from the side cut. In our case, the epithelial debris was easily detached and removed from the interface by irrigation and was not connected to the side cut, facts strongly suggestive of epithelial inoculation rather than ingrowth. Prompt action was taken as the condition was interfering with the optical axis and creating topographic irregularity. After irrigating the interface, a dramatic increase in visual acuity was observed which confirmed that our diagnosis and intervention were appropriate.

In conclusion, in the presence of loose epithelium that was not detected in the preoperative examination, as in our case, or when access is repeatedly attempted during the procedure, the interface should always be checked immediately after surgery with the slit lamp of the device or biomicroscope, and the patient should be followed closely after surgery. When epithelial inoculation occurs after SMILE, treatment is planned depending on factors such as the location of epithelial cells and the amount of epithelial proliferation, necrosis, or progression at the inoculation site. If epithelial inoculation is in the optic axis, interfacial irrigation and scraping may improve visual acuity and reduce topographically irregular astigmatism. As epithelial inoculation is observed early after SMILE surgery, immediate irrigation of the interface appears to be an effective and safe treatment.[5]

Ethics

Informed Consent: Obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.K., F.Ö.Y., Concept: N.K.B., Design: M.Ö.Ç., Data Collection or Processing: S.A., Analysis or Interpretation: A.K., Literature Search: S.A., Writing: S.A.

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