# A case of severe diffuse lamellar keratitis after small-incision lenticule extraction operation

Dear Editor,

Diffuse lamellar keratitis (DLK) is a normal reaction of the corneal healing process following a stimulus. This reaction is intensified by the swift and unobstructed movement of inflammatory cells originating from the bone marrow through the cornea, especially within the lamellar interface. The most common cause is intraoperative or late injury to the epithelium. When the corneal epithelium is damaged, IL-1a, IL-1b, and TNF-a are immediately released from the epithelium into the underlying stroma. These cells not only have a chemotactic effect on bone marrow-derived cells themselves but also attract other bone marrow-derived cells such as monocytes, macrophages, and neutrophils from corneal blood vessels into the cornea. Cytokines and chemokines produced by these cells also attract other bone marrow-derived cells, thereby enhancing the inflammatory response.[1,2] Based on the severity and location of the inflammatory reaction, DLK can be categorized into four grades[3]: grade I, white granular cells in the periphery with sparing of the visual axis; grade II, white granular cells in the visual axis; grade III, clumping of granular cells with haze and reduced vision; and grade IV, stromal necrosis and melt, often leading to secondary hyperopia and irregular astigmatism. In this case, we describe in detail the complications of DLK after small-incision lenticule extraction (SMILE) and the related diagnosis and treatment process.

## Case Report

A 27-year-old woman came to our hospital for SMILE surgery due to myopia in her right eye. Her medical history was unremarkable, as was her preoperative eye examination. Before the operation, the diopters were − 2.25 DS/−0.50 DCx50 for the right eye and +0.50 DS/+0.25 DCx40 for the left eye; both eyes had a best corrected visual acuity (BCVA) of 20/16. On the first postoperative day, a sands of Sahara reaction appeared between the corneal layers of the right eye on a slit-lamp examination, and the BCVA was 20/40. The patient used antibiotic eye drops, eye ointments, and glucocorticoid eye drops postoperatively. The treatment process is shown in Table 1. Over the next 5 months, the patient's central corneal opacity narrowed and the central corneal maximum optical density value improved [Fig. 1]. The Pentacam (OCULUS

**Table 1: Changes in patient condition and treatment process**

| Time after surgery | UDVA/BCVA (Snellen) | IOP (mmHg) | Densitometry values | Cornea | Treatment |
|---|---|---|---|---|---|
| 1 day | 20/60-20/40 (−0.50 DS/−2.00 DC ×175) | 14 | / | DLK grade II | 1. 0.3% LED qid<br>2. 1%PAED Q1h<br>3. TDEO bid<br>4. 0.1% SHED qid |
| 2 day | 20/16 | 15 | / | DLK grade II | 1. 0.3%LED 6 times/day<br>2. 1%PAED 12 times/day<br>3. TDEO bid<br>4. 0.1%SHED qid |
| 7 day | 20/63–20/32 (−1.00 DS) | 14 | 84.7 | DLK grade III | 1. 0.3% LED 6 times/day<br>2. 1%PAED q1h<br>3. TDEO bid<br>4. 0.1% SHED qid<br>5. DT qd (5 days) |
| 2 weeks | 20/50–20/32 (−1.50 DC ×165) | 11 | 36.9 | Stromal opacity (3±3 $mm^2$) | 1. 0.3% LED qid<br>2. 1%PAED 8 times/day<br>3. 0.3% SHED qid<br>4. TDEO qn |
| 1 month | 20/32–20/32 (−1.25 DC ×165) | 12 | 25.9 | Stromal opacity (2±2 $mm^2$) | 1. 0.1% FED qid (2 week) Tid (2 week)<br>2. 0.1% SHED qid |
| 2 month | 20/50–20/25 (+3.00 DS) | 15 | 21.2 | Milder stromal opacity (2±2 $mm^2$) | 1. 0.1% FED tid (3 days) bid (3 days) qd (3 days)<br>2. 0.1% SHED qid |
| 3 month | 20/40–20/20 (+2.50 DS) | 11 | 20.4 | Corneal cloudiness | None |
| 4 month | 20/40–20/20 (+2.00 DS) | 12 | 20.3 | Corneal cloudiness | FT |
| 5 month | 20/25–20/20 (+1.75 DS) | 13 | 21.6 | Corneal cloudiness | FT |

LED: Levofloxacin eye drops PAED: Prednisolone acetate eye drops; TDEO: tobramycin dexamethasone eye ointment DT: dexamethasone tablets; SHED: Sodium hyaluronate eye drops; FED: Fluorometholone eye drops; q1h: 1 time per hour; qd: 1 time per day; bid: 2 times per day; tid: 3 times per day; qid: 4 times per day; qn: 1 time before going to bed; FT: Flipper training

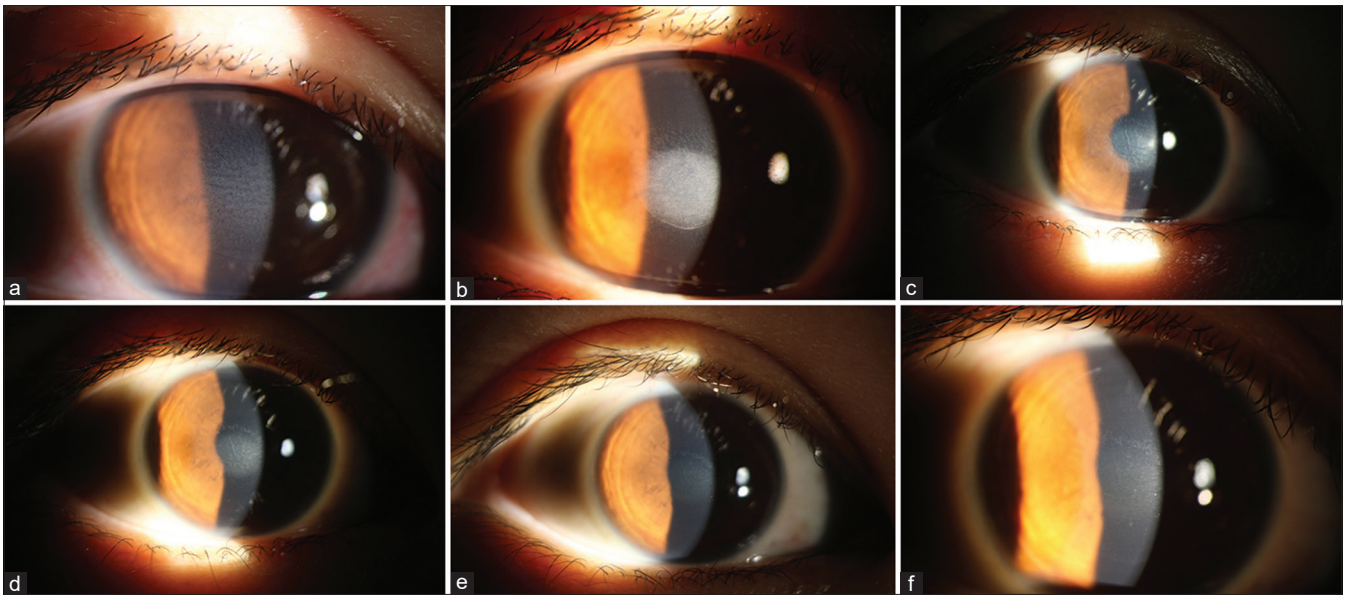


**Figure 1:** Changes in the patient's cornea under the slit lamp. a: On the 1st day after surgery, there was diffuse, sand-like opacity and mild edema between the layers within 6 mm in the central area of the cornea, which became more severe closer to the pupil area; b: One week after surgery, there was interlaminar inflammation within 4 mm of the pupil area of the cornea. The degree of reaction opacity was dense; c: Two weeks after surgery, the stromal opacity within 3 mm of the pupil area was less severe than before; d: One month after surgery, the stromal opacity within 2 mm of the pupil area was less severe than before; e: Two months after surgery, the stroma was slightly opaque within 2 mm of the pupil area; f: Three months after the operation, the center of the cornea basically returned to transparency, with only slight cloudiness remaining

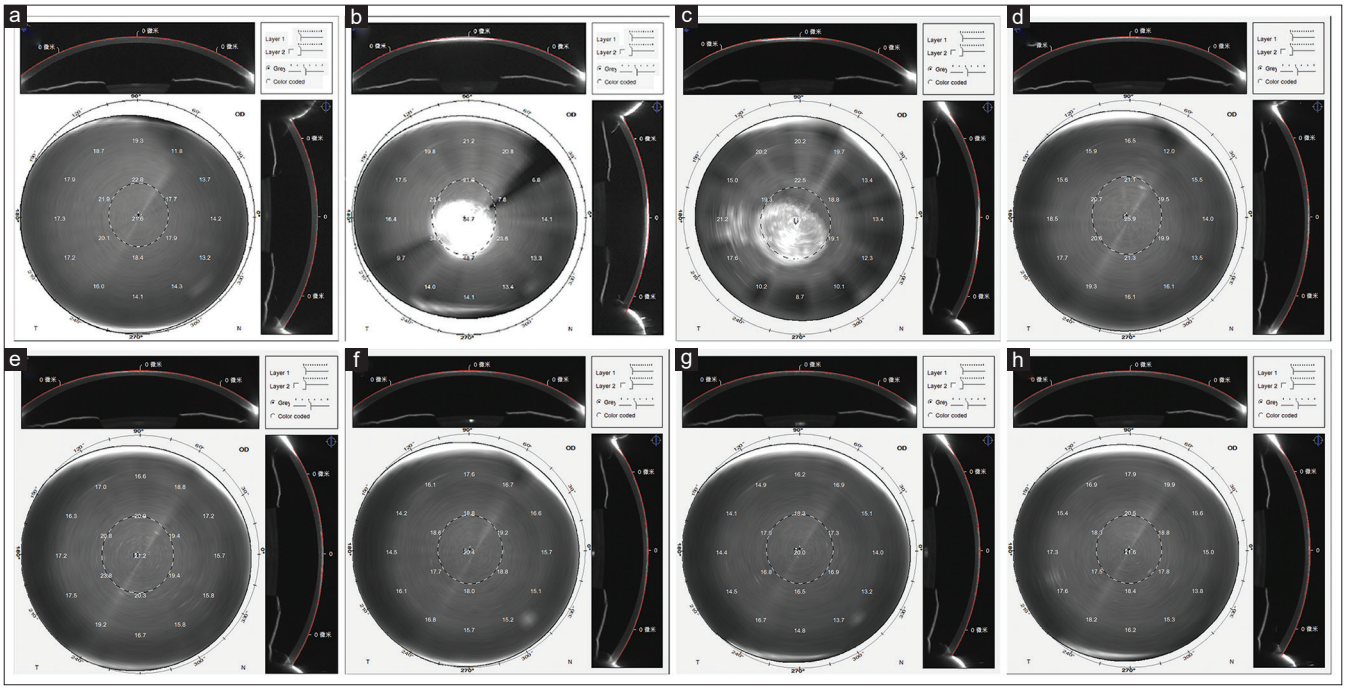


**Figure 2:** Corneal optical density change chart. This picture shows the changes in optical density before surgery (a) and at 1 week (b), 2 weeks (c), 1 month (d), 2 months (e), 3 months (f), 4 months (g), and 5 months after surgery. The optical density continued to decrease after surgery, and the corneal stroma gradually returned to transparency, especially within the 2-mm range of the center of the pupil

PENTACAM, GERMANY) optical density function was used to evaluate the degree of corneal interlayer opacity, and the optical density of the patient gradually decreased [Fig. 2]. This patient's corneal curvature first decreased and then increased after surgery [Fig. 3], and she developed hyperopic drift. Optical coherence tomography (VG2001, CHINA) was used to measure central corneal epithelial thickness, and it was found that epithelial thickening following surgery reduces the hyperopic shift during the healing period [Fig. 4]. Four months post-surgery, the uncorrected visual acuity (UDVA) of the right eye was 20/40 and BCVA was 20/20. After the visual function examination, it was found that the positive relative

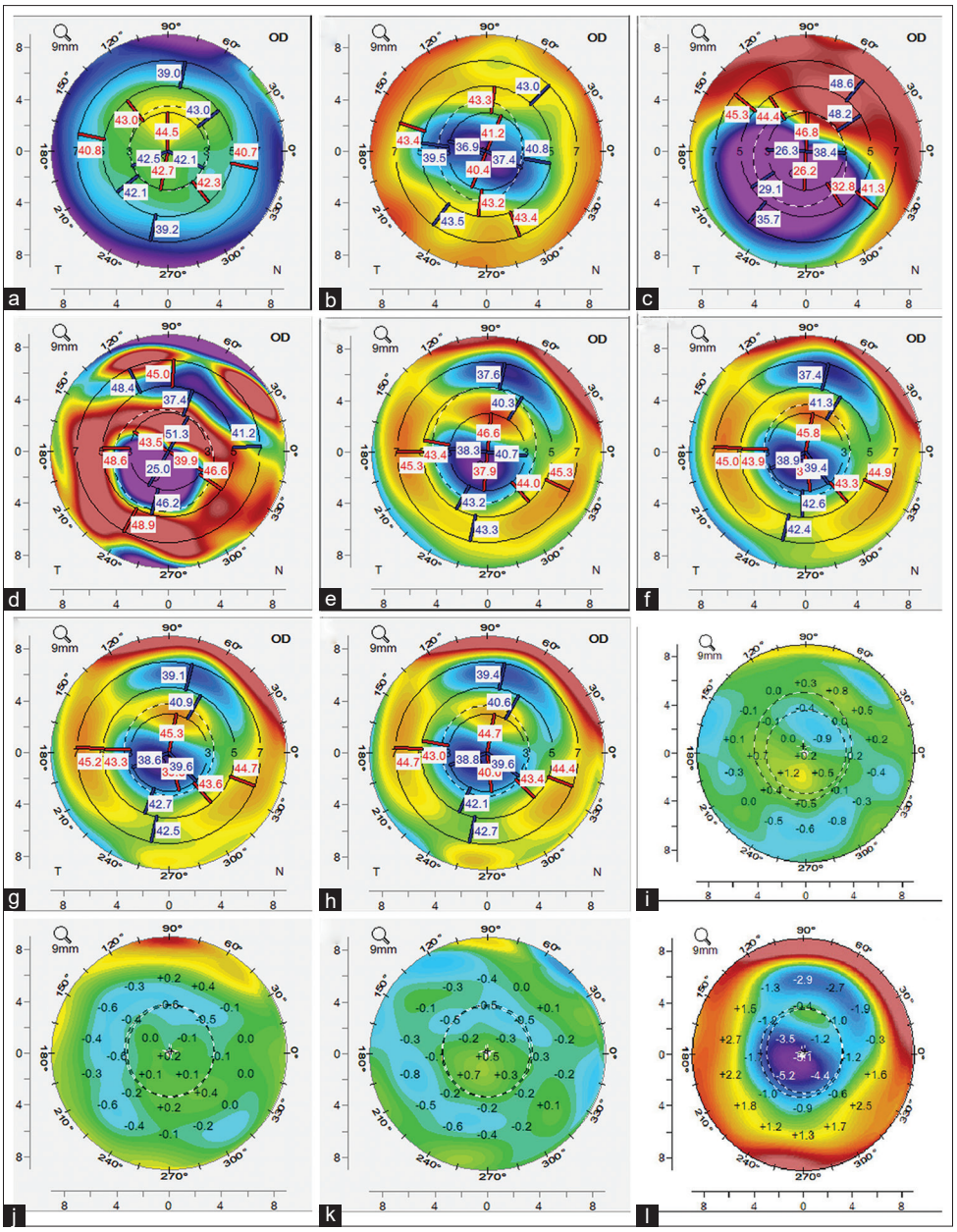

**Figure 3:** Changes in corneal curvature before and after surgery. (a) Preoperative corneal curvature map; (b) Corneal curvature map 1 week aftersurgery; (c) Corneal curvature map half a month after surgery: the curvature was lower than that at 1 week after surgery; (d) Corneal curvaturemap 1 month after surgery; (e and f) Corneal curvature 2 and 3 months after surgery, respectively; (g and h) Corneal curvature 4 and 5 monthsafter surgery, respectively; (i) difference in corneal curvature between 2 months and 1 month after surgery, showing that the central cornealcurvature increased; (j) difference in corneal curvature between 3 months and 2 months after surgery, showing that the central corneal curvatureincreased; (k) difference in corneal curvature between 5 months and 4 months after surgery, showing that the central corneal curvature increased; (l) difference in corneal curvature between 5 months and before surgery, showing that the central corneal curvature decreased

accommodation (PRA) of the right eye was −0.50 D, prompting the patient to practice with a ± 2.00 D flipper. After one month of practice, the UDVA improved to 20/25, and BCVA remained at 20/20, essentially returning to normal.

## Discussion

SMILE has a low incidence of DLK, with an incidence rate of 0.45% in the population.[4] DLK after SMILE typically presents as grade I or II, with mild disease and short duration, which may be related to the high precision of the femtosecond laser and minimal damage to the surrounding tissues.[5] The DLK classification for this patient was grade II and III, which is relatively rare. The cause of DLK is not fully understood, but it may result from endotoxins released by Gram-negative bacteria in sterilized containers, irrigation fluids used during surgery, the temperature and humidity in the operating

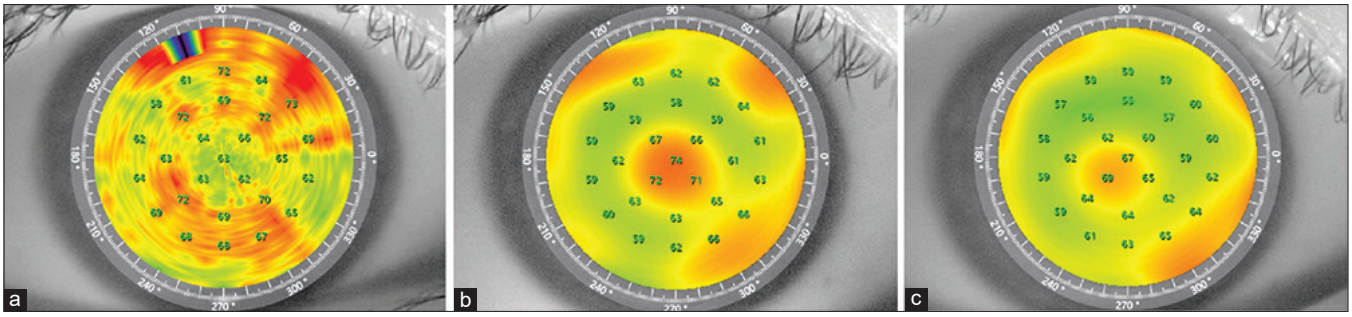

**Figure 4:** Changes in epithelial thickness after surgery. a: Corneal epithelial thickness 1 week after surgery; b: Corneal epithelial thickness 2 months after surgery; c: Corneal epithelial thickness 5 months after surgery, showing that the central corneal epithelial thickness first increased and then decreased

room, talc in surgical gloves, and oily secretions from the meibomian glands. A corneal flap that is too thin or too large in diameter, among other factors, may also contribute.[5-7] This patient had normal meibomian gland function before surgery, and powder-free gloves were used; the surgery was smooth with no significant bleeding. Other patients who underwent SMILE surgery in the same batch did not develop DLK; thus, the equipment, talc, hemoglobin, and other causes can be ruled out. It is important to distinguish DLK from interface fluid syndrome (IFS), which often presents as diffuse opacity and edema between corneal layers, mainly due to prolonged steroid use.[8] This patient's postoperative intraocular pressure was normal, and no interlayer corneal edema was observed under the slit lamp; thus, IFS could be excluded.

Early diagnosis and the application of glucocorticoids after DLK are critical. After the patient's condition worsened 1 week after surgery, she was prescribed oral dexamethasone tablets for 5 days and responded well to steroid treatment. Post surgery, corneal curvature changes first decreased and then increased. The curvature changes during the healing response were the result of inflammation resolution and scarring. Postoperative hyperopia was the result of excessive flattening of the pupil area, exceeding the expected curvature value after SMILE of −2.5 D. The mechanism is possibly due to the release of collagenase and metalloproteinase by inflammatory cells and corneal fibroblasts/keratinocytes within the layers. These enzymes can alter the matrix around the lamellar interface and even promote the melting of the DLK matrix, thereby reshaping the cornea.[9] Contrary to the changes in corneal curvature, the thickness of the central corneal epithelium first increased and then decreased after surgery. It can be seen that the proliferation of the corneal epithelium has a certain compensatory effect on the reduction of curvature.

During the 3-month postoperative follow-up, the patient's corneal optical density continued to decrease, with the most significant change in the pupil diameter range of 0–2 mm. Although corneal transparency gradually improved, the UDVA did not significantly improve, which may be related to the postoperative hyperopia. The patient had anisometropia in both eyes before surgery and myopia in the right eye. Long-term myopia may lead to insufficient accommodation, resulting in decreased distance vision after surgery. To confirm this, the patient's visual function was examined 4 months after surgery, and the right eye's relative accommodation was −0.50 D, indicating insufficient accommodation. After 1 month of flipper training, the patient's UDVA improved to 20/25 and PRA to −1.25 D, despite a persistent +1.75 DS in her right eye. The significant hyperopia remaining after DLK from the SMILE takes 3–6 months to stabilize, and surgery is not advisable before then. Thus, refraction should be monitored to be stable before considering vision enhancement surgery.

## Conclusion

Corticosteroid treatments for DLK after SMILE surgery are generally successful. Severe DLK repair can engender hyperopia. If the patient's accommodation is not sufficient, hyperopic drift could degrade UDVA. Vision function training may enhance this and waiting until refraction stabilizes before considering vision augmentation surgery is advised.

### Ethical approval

This study complied with the tenets of the Declaration of Helsinki. Written informed consent was obtained from the patient's mother for publication of this case report and any accompanying images.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Financial support and sponsorship:** Medical, Scientific Research Foundation of Guangdong Province, China (A2020512).

**Conflicts of interest:** There are no conflicts of interest.

*Mengxia Yuan, Ruifeng Ji, Riping Zhang*

Joint Shantou International Eye Center of Shantou University and the Chinese University of Hong Kong, Shantou, Guangdong Province, China

Correspondence to: Dr. Riping Zhang, Joint Shantou International Eye Center of Shantou University and the Chinese University of Hong Kong, 69 North Dongxia Road, Shantou - 515041, Guangdong Province, China. E-mail: zhangrp0412 @163.com

## References


1. Hong JW, Liu JJ, Lee JS, Mohan RR, Mohan RR, Woods DJ, *et al*. Proinflammatory chemokine induction in keratocytes and inflammatory cell infiltration into the cornea. Ophthalmol Vis Sci 2001;42:2795-803.
2. Wilson SE, Schultz GS, Chegini N, Weng J, He YG. Epidermal growth factor, transforming growth factor alpha, transforming growth factor beta, acidic fibroblast growth factor, basic fibroblast growth factor, and interleukin-1 proteins in the cornea. Exp Eye Res 1994;59:63-71.
3. Wilson SE, de Oliveira RC. Pathophysiology and treatment of diffuse lamellar keratitis. J Refract Surg 2020;36:124-30.
4. Reinstein DZ, Stuart AJ, Vida RS, Archer TJ, Carp GI. Incidence and outcomes of sterile multifocal inflammatory keratitis and diffuse lamellar keratitis after SMILE. J Refract Surg 2018;34:751-9.
5. Zhao J, He L, Yao P, Shen Y, Zhou Z, Miao H, *et al*. Diffuse lamellar keratitis after small-incision lenticule extraction. J Cataract Refract Surg 2015;41:400-7.
6. Holland SP, Mathias RG, Morck DW, Chiu J, Slade SG. Diffuse lamellar keratitis related to endotoxins released from sterilizer reservoir biofilms. Ophthalmology 2000;107:1227-33.
7. Zhao J, Sun Z, Fan Y, Cao T. Effect of operating room temperature and humidity on diffuse lamellar keratitis after LASIK. Gansu Med 2015;12:919-20.
8. Cai L, Jiang Y, Xiao Y, Zhang S, Li D, Li Y. A case of interlaminar effusion syndrome caused by repeat LASEK surgery after LASIK. Chinese Journal of Optometry and Visual Science 2014;16:122-4.
9. Ollivier FJ, Gilger BC, Barrie KP, Kallberg ME, Plummer CE, O'Reilly S, *et al*. Proteinases of the cornea and preocular tear film. Vet Ophthalmol 2007;10:199-206.




**Access this article online**

**Quick Response Code:**

**Website:** https://journals.lww.com/ijo

**DOI:** 10.4103/IJO.IJO_2974_23

**Cite this article as:** Yuan M, Ji R, Zhang R. A case of severe diffuse lamellar keratitis after small-incision lenticule extraction operation. Indian J Ophthalmol 2024;72:1219-23.