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Corneal Thinning and Opacity following Selective Laser Trabeculoplasty: A Case Report

Julia Song[1*] David Yu[2], Alice Song[3], Trisa Palmares[1], Harold S. Song[3] and Michael Song[3]

[1]Huntington Medical Plaza, 800 S. Fairmount Ave., #207, Pasadena, CA 91105, California, USA.
[2]Pasadena Eye Medical Group, 10 Congress Street, # 340, Pasadena, CA 91105, California, USA.
[3]Long Beach Memorial, 2840 Long Beach Blvd., #330, Long Beach, CA 90806, California, USA.

Authors' contributions

This work was carried out in collaboration between all authors. Authors JS and DY examined the patient before and after treatment. Authors MS, HSS, AS, and TP performed the literature search. Author AS took photos of the patient. All authors read and approved the final manuscript.

Case Study

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ABSTRACT

Aims: Selective laser trabeculoplasty (SLT) (Lumenis, Santa Clara, CA) was developed in 1999 as a means to lower IOP in patients with glaucoma. It is a relatively safe procedure. We report a rare side effect of corneal opacity and stromal haze with corneal thinning and hyperopic shift following SLT.
Presentation of Case: Case report.
Results: A 50 year-old Asian male who underwent SLT OD developed mild corneal edema and slightly elevated intraocular pressure (IOP) one day after procedure. He was prescribed anti-inflammatory drops. One week afterwards, he developed a small corneal abrasion centrally. He was given topical antibiotics and asked to continue anti-inflammatory drops. On postoperative day 8, his corneal abrasion healed, but he developed stromal corneal haze. Topical steroids were begun. By postoperative week #2, his visual acuity and stromal haze had improved. His corneal thickness decreased from 600 µms to 468 µms. After one year, he had almost complete resolution of his

**Corresponding author: Email: jsongmd@drsongvision.com;*

corneal pathology but had residual corneal thinning and flattening.
Discussion: Corneal stromal haze following SLT is a rare side effect. This can result in corneal scarring with corneal thinning and a hyperopic shift due to corneal flattening. Physicians and patients should be aware of this potentially vision threatening side effect.
Conclusion: More studies are needed to identify risk factors for the development of corneal pathology following selective laser trabeculoplasty.

Keywords: Selective laser trabeculoplasty; corneal thinning; side effect; glaucoma.

1. INTRODUCTION

Selective laser trabeculoplasty (SLT) (Lumenis, Santa Clara, CA) was developed in 1999 as a means to lower IOP in patients with glaucoma [1]. It was purported to be a gentler laser than argon laser trabeculoplasty (ALT) with no histologic scarring or coagulative damage to the trabecular meshwork [2], because it selectively targets the pigmented trabecular meshwork cells, thus reducing collateral damage to surrounding tissues and incidence of iritis and elevated IOP compared to ALT [3]. The thermal relaxation time of SLT is less than that of melanin, which allows for the selective targeting of only the pigmented cells. SLT did not induce inflammation with 90º treatment [4]. Although studies [5-7] have demonstrated various efficacies depending the amount of trabecular meshwork treated, the efficacy of SLT generally has ranged from 40-70%. Several studies [8,9] have demonstrated that SLT and ALT have similar efficacies. Due to minimal side effects, quick recovery, and relative ease of the procedure, SLT remains a good method to lower IOP, either as adjunct therapy or as primary therapy in both adults and children with glaucoma [10,11,12].

The mechanism of SLT is not entirely known. The mechanism involves the recruitment of macrophages from the spleen to the trabecular meshwork [13,14]. The side effects of SLT are minimal. These include pain, inflammation, and elevated IOP [14,15]. There have been several case reports of rare but serious side effects, including elevated IOP, [16] corneal edema [17,18], diffuse lamellar keratitis [19,20], hyphema [20,21] and choroidal effusion [22]. Our report describes corneal opacity and haze following SLT in a previously healthy patient, resulting in corneal thinning and a hyperopic shift.

2. PRESENTATION OF CASE

Our patient was a 50 year-old Asian male who presented to the office one year ago with elevated IOPs. He was otherwise healthy and was taking no systemic medications. He had been diagnosed with mild open-angle glaucoma with maximum IOPs in the high 20's. He had undergone ALT in both eyes in 5 years prior by another ophthalmologist with a minimal response. He was taking Xalatan (latanoprost, Pfizer) which controlled his IOPs for several years. Due to mild progression of his visual fields and elevating IOPs, he had been placed on a second topical glaucoma medication (Azopt, Alcon, Fort Worth, TX) but did not respond well. He also was a high myope and had mild retinal pigmentary changes OD as well as mild amblyopia OD.

Preoperatively, the patient's visual acuity with correction was OD: 20/60 pinhole 20/40-2 and OS: 20/25. His preoperative refraction was OD: -19.25 +1.25 x 104 and OS: -15.75 +1.75 x 074. His preoperative IOPs were 20.5 mmHg OU. He had open angles to grade IV with rare pigment. Dilated examination revealed 0.9 optic nerve cupping OU with myopic degeneration

OD but no subretinal fluid or hemorrhage. His preoperative central corneal thicknesses (CCTs) 600 and 610 µms, respectively, by ultrasound pachymetry. After discussing the available treatment options with him and given the fact that he had undergone previous ALT, as well as the moderate status of his glaucoma, he elected to undergo SLT OD in lieu of additional medications or incisional surgery. The settings included a burst energy of 0.8-1.0 mJ 360º for a total of 120 spots. Postoperatively, his IOP was 19 mmHg.

The next day, the patient reported foggy vision, photosensitivity, injection, and a foreign body sensation OD. He stated that the evening prior, he had no symptoms. On examination, his visual acuity OD with correction was 20/200. His IOPs were OD: 23 and OS: 17 mmHg. Slit lamp examination revealed trace conjunctival injection, mild diffuse corneal edema but no epithelial defect, and 1+ cell/flare. He was given Acuvail OD bid (ketorolac, Allergan, Irvine, CA) and Zymaxid (gatifloxacin, Allergan, Irvine, CA) OD qid.

Two days after SLT, his visual acuity improved to 20/80. He had trace conjunctival injection, very mild corneal edema which had improved compared to the day before, and rare flare. His IOPs were OD: 26 and OS: 18 mmHg. Muro drops were added, and he was asked to resume Xalatan OD.

Seven days following SLT, his visual acuity worsened to OD: Count fingers (pinhole 20/200). His IOPs were OD: 25 and OS: 20 mmHg. Corneal sensitivities were intact and equal. His corneal edema was localized centrally, and he had developed a small epithelial defect. Acuvail and Muro were discontinued. He was given topical Zymaxid and bacitracin eye ointment as well as a pressure patch OD overnight.

The following day, his reported that his pain had disappeared. His visual acuity was OD: 20/400. The corneal epithelial defects had disappeared, but there was corneal haze centrally. He was asked to continue topical Zymaxid and bacitracin ophthalmic ointment, as well as topical Pred Forte (prednisolone acetate, Allergan, Irvine, CA) qid. He was also asked to patch his eye at night to prevent inadvertent rubbing.

Three weeks following SLT, his uncorrected visual acuity was 20/400 (pinhole 20/50). Refraction yielded a hyperopic shift to -1.00 + 7.00 x 010. Slit lamp examination revealed a fairly well-defined central stromal haze involving the anterior 2/3 of the cornea. There was no corneal edema or Descemet's folds. Optical coherence tomography (OCT) of the anterior segment revealed stromal haze and corneal thinning to 484 µms (Table 1).

Postoperative week #4, his visual acuity was OD: 20/200 (pinhole 20/60) with continued improvement of his corneal haze (Fig. 1). Pred Forte was decreased to every 2-3 hours. Optical coherent tomography (OCT) of his anterior segment revealed corneal thinning.

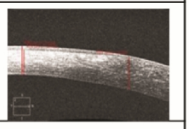
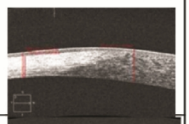
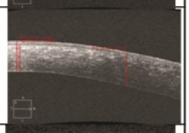
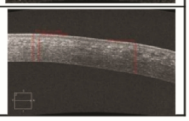
Postoperative week #51/2, his visual acuity improved to OD: 20/80 (pinhole 20/70). His IOPs were OD: 10 and OS: 19 mmHg. His corneal haze continued to improve. Central corneal thicknesses revealed thinning of his cornea to 468 µm OD (OS remained at 602 µms).

On postoperative month 2, his refraction was -8.50 + 3.00 x 017. OCT demonstrated less stromal haze but still a thin cornea of 496 µms.

By postoperative month 3, his visual acuity OD was 20/70 (pinhole 20/40). His manifest refraction was -8.00 + 1.25 x 105 (20/100). His corneal thickness elevated slightly to 524 µms. His IOPs were OD: 28 mmHg and OS: 14 mmHg. By tonopen, they were OD: 18 and

OS: 11. His corneal haze improved (Fig. 2). Pred Forte was continued at bid as well as Xalatan OU qhs. Istalol OD qam (timolol, Bausch & Lomb, Madison, NJ) was added.

Table 1. Corneal stromal thinning and hyperopic shift after SLT

Date	Corneal thickness affected area(µm)	Epithelial thickness affected area (µm)	Corneal thickness unaffected area (µm)	Refraction	
Pre-op	600			-19.25 +1.25 x 104	
3 wks	448	62	584		
2 mos	496	64	584	-17.25 + 1.25 x 105	
3 mos	524	64	584	-8.00 + 1.75 x 085	
4 mos	508	64	592	-7.00 sphere	
1 year	516	60	575	-11.75 +2.25 x 180	

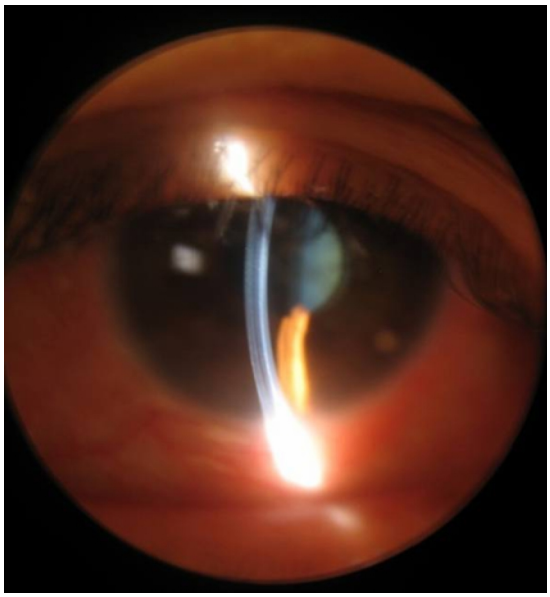


Fig. 1. Central corneal haze OD, 4 weeks after SLT.

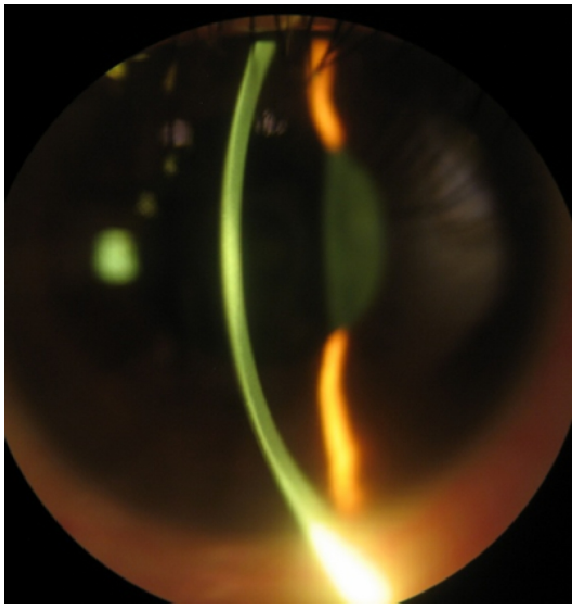


Fig. 2. Diffuse central corneal haze OD, 3 months after SLT.

By postoperative month 6, his best-corrected visual acuity was OD: 20/30 with a final hyperopic shift of 11 diopters (-8.50 + 3.00 x 175). He could not tolerate the anisometropia. His corneal haze was almost completely gone. His corneal thickness stabilized at 506 μms OD.

At one year following SLT OD, his manifest refraction stabilized to 6 diopters more hyperopic than his preoperative refraction. His corneal thickness was 516 μms, which was 84 μms thinner than his original corneal thickness prior to SLT. Although his corneal haze was significantly improved, it did not resolve completely.

3. DISCUSSION

Although SLT is a relatively safe procedure, there is an increasing number of reported side effects, including elevated IOP [16], corneal edema [17,18], diffuse lamellar keratitis [19,20], hyphema [20,21] and choroidal effusion [22]. To date, including our patient, there are 7 reported cases of SLT-induced keratitis with a refractive shift [18-20]. (Jun J, Ansari H, Regina M, Moster M. Corneal complications associated with selective laser trabeculoplasty**.** Poster presented at the Am Glauc Soc Meeting 2012, New York, NY.). Our patient has one-year follow-up with OCT photos.

In order to understand its side effects, one must have an understanding of how SLT works. The theory of SLT involves stimulation of cytokine production from the trabecular meshwork. These cytokines include interleukin-alpha (IL-1α), interleukin-1 beta (IL-1β), and tumor necrosis factor-alpha (TNF-α) [23,24]. The result is recruitment of macrophages from the spleen that phagocytose debris in the trabecular meshwork extracellular matrix. In addition, there is an increase in lipid peroxidase and a decrease in free radical scavenging superoxide dismutase and glutathione S-transferase in aqueous fluid, suggesting free oxygen radical formation that may account for the postoperative inflammation [23]. A study by Wood, et al.

[25], demonstrated that SLT causes trabecular meshwork cell death. Other laser treatments (such as diode laser cyclophotocoagulation) have been found to increase central corneal thickness [26], which may represent corneal endothelial decompensation. A comparison of SLT and ALT found that inflammation was greater in SLT patients (possibly due to the greater spot side), which could affect a larger surface area of tissue (the ciliary body and the iris root), thus possibly accounting for the spread of inflammation to the cornea in our patient.

This reaction appears to be idiopathic. A possibility is that it could have been performed incorrectly. However, the surgeon performing SLT has over 10 years of clinical experience, performing this laser since 2002. One of the advantages of SLT is the larger spot size and increased ease of the procedure when compared to ALT.

In our patient, the early post operative slit lamp appearance was that of diffuse corneal edema with mild aqueous cell and flare. Over the first seven days, the corneal haze became more defined centrally. The first OCT analysis at 3 weeks following SLT showed marked corneal thinning with stromal haze sparing the posterior corneal storma. Flattening of the anterior corneal curvature was grossly evident on OCT and coincided with a large hyperopic shift in refraction. Sequential OCT analysis over the next several months showed a gradual increase in corneal thickness along with a qualitative reduction in corneal stromal haze. The thickness of the corneal epithelial layer remained unchanged during this period, and the corneal thickness changes appear to be only in the stroma.

His IOPs postoperatively were initially elevated then lowered. Due to the significant thinning of his CCT, his postoperative IOP readings may actually have been higher than what was recorded. He did eventually need 2 glaucoma medications to control his IOP.

The findings in our patient suggest changes in the corneal stroma with no endothelial involvement. The mechanism appears to be that of stromal collagen damage leading to an inflammatory reaction and removal of damaged collagen. This phase would correspond to corneal haze and stromal thinning. The inflammatory phase is followed by the laying down of additional collagen by keratocytes, leading to corneal thickening. How SLT treatment may cause corneal stromal collage damage is unknown. Possibilities would include direct light damage, indirect thermal damage, or chemical damage during treatment or early post operative period.

Other reported side effects of SLT can help elucidate the mechanism of action. Aykan, et al. [27] reported increased ciliary body and iris thicknesses within the first month of treatment. This is in line with the increased inflammation seen with SLT compared to ALT. Following ALT, the greatest inflammatory response was 48 hours post-treatment, implying that the trabecular meshwork can synthesize prostaglandins that act as mediators of inflammation. Interestingly, the thickest area of the ciliary body was in the superior quadrant, away from the area treated (inferior angle), implying that the SLT's biologic response affected areas not directly irradiated by SLT. This may explain why our patient's cornea was affected by SLT although the laser does not directly target the corneal endothelium. Another theory is that the inflammatory cascade induced by SLT could have reactivated an occult herpes simplex infection, particularly in those patients on concomitant topical prostaglandins. Although our patient was taking latanoprost, he denied any history of herpes keratitis or infection.

Upregulation of metalloproteinases (MMP), particularly MMP-9, has been associated with pseudophakic corneal edema [28]. SLT has been known to increase the amount of metalloproteinases in the aqueous humor. MMP-2 is the major metalloproteinase secreted

after laser therapy and is inhibited by tissue inhibitor of metalloprotineases (TIMP)-2. In pseudoexfoliative glaucoma, the enzyme balance between MMP-2 and TIMP-2, already impaired by the pseudoexfoliative syndrome, is seriously altered even compared with primary open-angle glaucoma. The ratio of metalloproteinases (MMP-2) to TIMP-2 after SLT is increased in pseudoexfoliative glaucoma. Over-expression of matrix metalloproteinases by resident corneal cells has been shown to impede re-epithelialization after some types of corneal injury [29]. This may partially account for our patient's corneal pathology.

It is helpful to identify risk factors that predispose to various side effects. Elevated postoperative intraocular pressures can occur in eyes with heavy pigmentation, previous ALT, or multiple medications. Previous corneal haze has been reported in patients with possible predisposing conditions, such as prior LASIK [3] or a history of herpes labialis. Proposed mechanisms of corneal stromal inflammation may involve migration of monocytes-macrophages into the corneal stroma. A study by Hong, et al. [30] demonstrated that Cytokines IL-1 and TNF-α activated monocytes chemotactic and activating factor (MCAF) and granulocyte colony-stimulating factor (G-CSF). Patients taking bimatoprost have significantly higher levels of IL-1β and TNF-α in their tears [31]. Our patient was taking a topical prostaglandin at the time of his SLT treatment, which may have contributed to more inflammation.

More studies are needed to identify those patients at high risk of developing side effects from SLT. Patients with identifiable risk factors can be counseled about the potential for side effects.

4. CONCLUSION

Although SLT is relatively safe and efficacious, the side effect of corneal stromal haze is serious.This can result in corneal scarring with corneal thinning and a hyperopic shift due to corneal flattening. Physicians and patients should be aware of this potentially vision threatening side effect. More studies are needed to identify risk factors for the development of corneal pathology.

CONSENT

All authors declare that ‘written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

Not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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