



Case report

Corneal edema and keratitis following selective laser trabeculoplasty

Erica Tan Liu^a, Loren S. Seery^{b, c}, Analisa Arosemena^d, Tania Lamba^e, Craig J. Chaya^{c, f, *}^a New England Eye Center, 800 Washington St., Box 450, Boston, MA 02111, USA^b Pacific Cataract & Laser Institute, 6695 W. Rio Grande Avenue, Kennewick, WA 99336, USA^c Seventh-day Adventist Guam Clinic, 388 Ypao Road, Tamuning, GU 96913, USA^d Aran Eye Associates, 1097 Le Jeune Rd, Miami, FL 33134, USA^e George Washington University, 2150 Pennsylvania Ave NW, Washington, DC 20037, USA^f John A. Moran Eye Center, University of Utah, 65 Mario Capecchi Dr., Salt Lake City, UT 84132, USA

ARTICLE INFO

Article history:

Received 30 May 2016

Received in revised form

14 September 2016

Accepted 14 November 2016

Available online 16 November 2016

Keywords:

Selective laser trabeculoplasty

SLT

HSV keratitis

Herpes simplex keratitis

ABSTRACT

Purpose: To describe three cases of keratitis following Selective Laser Trabeculoplasty (SLT).**Observations:** Three females with a history of glaucoma presented with corneal edema, keratitis (endothelial, epithelial) and decreased visual acuity shortly after SLT. There was variable resolution of symptoms after starting treatment with oral antiherpetics and topical steroids.**Conclusions and importance:** With the increase in usage of SLT as a treatment for glaucoma and subsequent reports of keratitis, it is imperative for ophthalmic surgeons to be aware of herpes simplex as a possible risk factor. Prompt treatment with antivirals and steroids can potentially prevent scarring and permanent damage to the cornea.Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Selective laser trabeculoplasty (SLT) was first approved by the Food and Drug Administration in 2001. Advantages of the procedure include less coagulative damage and structural changes when compared with argon laser trabeculoplasty,¹ low cost compared to bleb filtering procedures,² and a decreased need for medications.³ It is increasingly being performed in place of traditional treatments. Complications are similar to other laser trabeculoplasty modalities, including inflammation and transient post operative elevation of intraocular pressure.⁴

SLT is a relatively new procedure and complications are being documented as they arise. Rare cases of corneal edema following SLT have been reported. Symptoms specifically consistent with endotheliitis have been documented in two.⁵ Endotheliitis is characterized by corneal edema, keratic precipitates with or without anterior chamber reaction, and an increase in intraocular pressure. In severe or protracted cases, chronic edema may persist, or scarring and neovascularization may result. Several cases in the literature report post-operative, virus associated instances of

endotheliitis that resolve upon treatment.⁶ We report three additional cases of corneal edema (epithelial and endothelial involvement) following SLT. These were treated presumptively for herpetic-induced keratitis.

2. Findings

2.1. Case 1

A 64 year-old Japanese female with low tension glaucoma received SLT in the left eye, IOP max of 17 mmHg. Laser settings were: 110 shots; total power of 102mJ, 360° treated. Two days post-procedure, she returned with decreased vision. Her visual acuity (VA) had declined from 20/20 before SLT to 20/50. IOP was 20 mmHg, and exam showed corneal edema with a fine dusting of cells on the endothelium. She had a history of cold sores, but no prior history of intermittent “pink eye”. Our working diagnosis was endotheliitis, presumed to be secondary to reactivation of the herpes simplex virus (HSV). Treatment was begun with acyclovir 400 mg by mouth four times daily, and loteprednol drops every hour while awake. Two days later VA was 20/50 in the left eye, pinholing to 20/25. Left eye pachymetry showed a corneal thickness of 600 μm (pre-laser pachymetry was 522 μm in the left eye, performed four months earlier). VA improved to 20/25 in the left

* Corresponding author. John A. Moran Eye Center, University of Utah, 65 Mario Capecchi Dr., Salt Lake City, UT 84132, USA.

E-mail address: craig.chaya@hsc.utah.edu (C.J. Chaya).

eye one week post-op. The endothelial deposits and corneal edema had resolved. Pachymetry returned to baseline. Acyclovir was decreased to three times daily, and loteprednol was tapered. One month after SLT, she was back to her baseline and acyclovir was discontinued. At her six month follow-up, VA and IOP remained stable.

2.2. Case 2

A 75 year-old female with primary open angle glaucoma (POAG) had SLT performed in the left eye, IOP max 19 mmHg. Laser settings were: 103 shots; power of 0.9mJ/shot, 360° treated. Four days post-procedure, she returned with “burning and decreased vision”. VA had declined from 20/30 before SLT to 20/40. Exam showed a central area of corneal epithelial edema with folds, positive fluorescein stain and superficial punctate keratitis. She denied known history of herpetic disease. Prophylactic treatment was begun with valacyclovir 1000 mg by mouth two times daily for 14 days. She was seen four days later in follow-up “feeling better”. VA was 20/100 in the left eye. Pachymetry was performed for the left eye, and showed a corneal thickness of 525 μm, the same as pre-laser pachymetry. Left eye IOP was 13 mmHg. The corneal infiltrate improved. Zylet was started four times a day in the left eye for two days at which point the patient self-discontinued. At one month post-procedure, patient continued to improve. Vision in the left eye was 20/50 pinholing to 20/40 with IOP of 11 mmHg. There was minimal central corneal haze on exam. Follow up two years post-procedure was stable with complete resolution of corneal edema.

2.3. Case 3

A 58 year-old white female with pigment dispersion glaucoma had SLT in the right eye, IOP 27 mm Hg. Laser settings were: 101 shots; power of 0.9–1.0 mJ/shot; total energy = 99.4mJ; 360° treated. The patient presented one day post-laser with “very blurry vision” in the right eye. Her vision had declined from 20/20

before SLT to 20/100, pinholing to 20/40. IOP was 21 mm Hg, and exam showed a central area of corneal edema with folds and superficial punctate keratitis. She denied history of herpetic disease. Based on the endotheliitis like picture, she was started on acyclovir 400mg five times daily for 14 days and continued diclofenac drops. Three days post laser the patient reported improved vision but still had some visual distortion. Her vision had improved to 20/50 in the right eye and central corneal edema had completely resolved with mild anterior stromal corneal haze seen nasally. Pachymetry showed a CCT of 539 μm (prior to laser 477). The diclofenac was discontinued. Two weeks post laser the vision was back to 20/20 with mild anterior stromal haze and complete resolution of her corneal edema.

3. Discussion

Non-ulcerative keratitis has been reported as associated with a variety of viral infections. Most commonly, herpes simplex HSV^{7–10} and CMV.¹¹ These have occurred presumptively sporadically as well as associated with intraocular surgery.^{6,12} The first cases of corneal edema following SLT were reported in two patients in 2009.⁵ Case 1 was a 60 year-old female who presented with a decrease in visual acuity, focal epithelial haze and stromal edema one week following SLT. The patient had a known history of oral herpes. Symptoms resolved with topical prednisolone and oral valacyclovir. Corneal haze and keratitis did not resolve until antiviral therapy was commenced. Case 2 was a 54 year-old female who presented with haloes and mild central stromal edema one week post SLT. Symptoms resolved with topical prednisolone.

Seven additional cases of corneal edema following SLT were reported in 2010,¹³ 2011¹⁴ and 2014.¹⁵ All were only treated with topical steroids and had residual corneal thinning with hyperopic shift. All cases were female. One case had tear fluid tested for HSV which returned negative; the rest were not tested and did not mention a known history of HSV.

Case 1 described by us and Case 1 described by Moubayed both had a clinical history of herpes labialis⁵ and were presumptively

Table 1

Summaries of index cases and cases that have been reported in the literature.

Case	Age	Gender	Symptoms	Corneal exam	Onset	Treatment	Outcome
1 ^a	64	F	Blurred vision	Edema, endothelial fine deposits	2 d	PO acyclovir, loteprednol	No thinning, BCVA down 1 line at 1 mo
2 ^a	75	F	Burning, blurred vision	Central edema with folds, SPK	4 d	PO valacyclovir, loteprednol/tobramycin	No thinning, BCVA down 1 line at 1 mo
3 ^a	58	F	Haloes, blurred vision	Central edema with folds, SPK	1 d	PO acyclovir, diclofenac	BCVA stable at mild stromal haze at 2 wk
4 ⁵	60	F	Haloes	Central epithelial and stromal edema	1 wk	PO valacyclovir, prednisolone, sodium chloride	BCVA stable at 4mo
5 ⁵	54	F	Pain, blurred vision	Mild central stromal edema	1 wk	prednisolone	BCVA stable at 2mo
6 ¹³	55	F	Pain, blurred vision	Anterior stromal haze, rare AC cell	5 d	loteprednol	Thinning, BCVA decreased by one line, refractive shift
7 ¹⁴	55	F	Blurred vision	Central edema, AC fibrin	1 d	“intensive topical steroid”	Thinning, BCVA stable, central corneal haze, refractive shift at 2 mo
8 ¹⁴	59	F	Blurred vision	Anterior stromal haze	2 d	“intensive topical steroid”	Thinning, BCVA stable, central stromal scar, no refractive shift at 3 mo
9 ¹⁵	63	F	Photophobia, blurred vision	Central corneal edema, haze	2 d	prednisolone	Thinning, BCVA decreased two lines, mild central stromal haze at 8 mo
10 ¹⁵	56	F	Blurred vision	Central stromal edema and haze	1 d	prednisolone, nepafenac	Thinning, BCVA decreased one line, faint central stromal haze at 6 mo
11 ¹⁵	46	F	Blurred vision	Diffuse dense stromal opacification	2 d	prednisolone	Thinning, BCVA decreased one line, cornea clear at 11mo
12 ¹⁵	56	F	Blurred vision	Central stromal haze	2 wk	defluprednate, hypertonic saline	Thinning, BCVA decreased one line, cornea clear at 7mo

Cases in order of mention.

Abbreviations: AC, anterior chamber; BCVA, best-corrected visual acuity; d, day/s; F, female; mo, month; PO, oral; wk, weeks.

^a Index cases that are described in this report.

treated for HSV keratitis. Cases of edema following SLT described thus far do not have definitive diagnoses, most resolving with empiric treatment. Whether these represent the same process is inconclusive, although lack of thinning in our cases suggests purely endothelial pathology versus stromal involvement. It is unclear whether early antiviral treatment would have affected the outcomes of the cases that did not have clinical history of HSV. The cases we describe were immediately started on antiherpetics, thus we are unable to conclude if symptoms may have resolved with only steroid treatment.

Based on the current literature, the cases described by us and the cases described by Moubayed are clinically consistent with corneal endotheliitis associated with viral infection (Table 1). Further tests were not warranted given the rapid and complete resolution of symptoms. Definitive diagnosis requires isolating the virus but is difficult without corneal endothelial tissue.⁶ Polymerase chain reaction can be performed to detect HSV in aqueous fluid¹⁶ as was done in one reported case of corneal edema following SLT, however sensitivity is low.¹⁷ The origin of the virus is unclear but may enter the anterior chamber through the trabecular meshwork⁸ with increased secretion of viral particles from disruption of the meshwork and subsequent increased inflammatory response.¹⁸ This viral shedding has been shown, in rabbits, to elicit an endotheliitis reaction clinically similar to that found in humans.¹⁹

Currently, a history of herpes simplex keratitis is not a contraindication when considering SLT. Despite lack of prior clinical history or dendrites, HSV should always be on the differential in idiopathic anterior chamber inflammation due to ubiquity of infection²⁰ and possible presentation with or without epithelial involvement. The HSV virus can affect any layer of the cornea, and can present in a multitude of ways. Cases have been reported following uncomplicated cataract surgery, lamellar corneal transplantation²¹ and laser in situ keratomileusis²². Some patients presented with epithelial disease, while others presented with corneal edema. Whether these cases resulted from the ocular inflammation associated with surgery, the postoperative steroids, or both, is unclear. Nonetheless, treatment with antiviral therapy is indicated, and often resolves the keratitis. In cases that present with corneal edema, antiviral therapy and steroids are both necessary for resolution. Because antiviral therapy is so well tolerated, and because diagnostic testing such as PCR is not readily available, a trial of anti-herpetic medications without culture positive results is often employed in practice. Alternatively, a missed or delayed HSV diagnosis can lead to permanent scarring and thinning.

Because ocular herpes simplex is common and easily misdiagnosed, it would be prudent for clinicians to query patients regarding prior history of recurrent, unilateral conjunctivitis, or “pink eye”; as well as history of prior cold sores. If the decision is made to proceed with SLT, patients should be informed of the risk of HSV reactivation, and consideration given to using prophylactic anti-viral medications. Given increasing usage of SLT as a promising treatment for glaucoma, more studies are warranted to determine the risk factors for and further elucidate the etiology of keratitis. Ophthalmic surgeons should be aware of the potential risk for keratitis and commence treatment promptly, preventing extensive and permanent scarring or endothelial cell loss.

Patient consent

Written patient consent was not obtained. As such, identifying information has not been included.

Funding

Supported in part by an Unrestricted Grant from Research to Prevent Blindness, Inc., New York, NY, to the Department of Ophthalmology & Visual Sciences, University of Utah.

Conflict of interest

None.

Financial disclosures are as follows

Erica Tan Liu, MD: Employed by Tufts Medical Center.
Loren S. Seery, MD: Employed by the Pacific Cataract & Laser Institute.
Analisa Arosemena, MD: Employed by Aran Eye Associates, owns stock of Allergan.
Tania Lamba, MD: Employed by George Washington University.
Craig J. Chaya, MD: Employed by University of Utah, owns stock of Abbott Labs, Inc., owns stock of AbbVie, Inc.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Acknowledgements

None.

References

- Kramer TR, Noecker RJ. Comparison of the morphologic changes after selective laser trabeculoplasty and argon laser trabeculoplasty in human eye bank eyes. *Ophthalmology*. 2001;108:773–779.
- Cantor LB, Katz LJ, Cheng JW, Chen E, Tong KB, Peabody JW. Economic evaluation of medication, laser trabeculoplasty and filtering surgeries in treating patients with glaucoma in the US. *Curr Med Res Opin*. 2008;24:2905–2918.
- McIlraith I, Strasfeld M, Colev G, Hutnik CM. Selective laser trabeculoplasty as initial and adjunctive treatment for open-angle glaucoma. *J Glaucoma*. 2006;15:124–130.
- Glaucoma Laser Trial Research Group. The glaucoma laser trial: I. Acute effects of argon laser trabeculoplasty on intraocular pressure. *Arch Ophthalmol*. 1989;107:1135–1142.
- Moubayed SP, Hamid M, Choremis J, Li G. An unusual finding of corneal edema complicating selective laser trabeculoplasty. *Can J Ophthalmol*. 2009;44:337–338.
- Suzuki T, Hara Y, Uno T, Ohashi Y. DNA of cytomegalovirus detected by PCR in aqueous of patient with corneal endotheliitis after penetrating keratoplasty. *Cornea*. 2007;26:370–372.
- Amano S, Oshika T, Kaji Y, Numaga J, Matsubara M, Araie M. Herpes simplex virus in the trabeculum of an eye with corneal endotheliitis. *Am J Ophthalmol*. 1999;127:721–722.
- Olsen TW, Hardten DR, Meiusi RS, Holland EJ. Linear endotheliitis. *Am J Ophthalmol*. 1994;117:468–474.
- Sundmacher R, Neumann-Haefelin D. Herpes simplex virus isolations from the aqueous of patients suffering from focal iritis, endotheliitis and prolonged disciform keratitis with glaucoma. *Klin Monatsbl Augenheilkd*. 1979;175:488–501.
- Robin JB, Steigner JB, Kaufman HE. Progressive herpetic corneal endotheliitis. *Am J Ophthalmol*. 1985;100:336–337.
- Koizumi N, Suzuki T, Uno T, et al. Cytomegalovirus as an etiologic factor in corneal endotheliitis. *Ophthalmology*. 2008;115:292–297.
- Vajpayee RB, Sharma N, Verma K, Saxena T, Tandon R. Presumed herpetic endotheliitis following phacoemulsification surgery. *Clin Exp Ophthalmol*. 2006;34:617–621.
- Marqui RE. Keratitis and hyperopic refractive shift induced by SLT. *Glaucoma Today*. September 2010:18–22.
- Knickerbein JE, Singh A, Flowers BE, et al. Acute corneal edema with subsequent thinning and hyperopic shift following selective laser trabeculoplasty. *J Cataract Refract Surg*. 2014;40:1731–1735.
- Yamamoto S, Pavan-Langston D, Kinoshita S, Nishida K, Shimomura Y, Tano Y. Detecting herpesvirus DNA in uveitis using the polymerase chain reaction. *Br J Ophthalmol*. 1996;80:465–468.

16. Kudo E, Shiota H, Kinouchi Y, Mimura Y, Itakura M. Detection of herpes simplex virus DNA in tear fluid of stromal herpetic keratitis patients by nested polymerase chain reaction. *Jpn J Ophthalmol*. 1996;40:390–396.
17. Pavan-Langston D. Herpes simplex virus ocular infections: current concept of acute, latent and reactivated disease. *Trans Am Ophthalmol Soc*. 1990;88:727–796.
18. Zheng X, Yamaguchi M, Goto T, Okamoto S, Ohashi Y. Experimental corneal endotheliitis in rabbit. *Invest Ophthalmol Vis Sci*. 2000;41:377–385.
19. Hill JM, Ball MJ, Neumann DM, et al. The high prevalence of herpes simplex virus type 1 DNA in human trigeminal ganglia is not a function of age or gender. *J Virol*. 2008;82:8230–8234.
20. Jhanji V, Ferdinands M, Sheorey H, et al. Unusual clinical presentations of new-onset herpetic eye disease after ocular surgery. *Acta Ophthalmol*. 2012 Sep;90(6):514–518.
21. Jain V, Pineda R. Reactivated herpetic keratitis following laser in situ keratomileusis. *J Cataract Refract Surg*. 2009 May;35(5):946–948.