Management of infectious keratitis following laser in situ keratomileusis

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Laser in situ keratomileusis (LASIK) is the most commonly performed refractive surgical procedure for the correction of ametropia. The advantages of LASIK include rapid visual rehabilitation, decreased stromal scarring, less irregular astigmatism, minimal regression, less postoperative pain, and the ability to treat a greater range of refractive disorders. Unlike surface-ablation procedures, LASIK preserves the integrity of Bowman's membrane and the overlying epithelium, thus decreasing the risk for microbial keratitis. However, microbial keratitis following LASIK has become an increasingly recognized, sight-threatening complication of refractive surgery.

The incidence of infectious keratitis following LASIK is difficult to estimate and can vary widely depending on the source of the information. One large retrospective study investigating the complications associated with LASIK found an incidence of 2 infections in 1062 eyes; a similar study found an incidence of 1 infection in 1019 eyes. A more recent case series of LASIK-associated infections encountered at a single institution reports an estimated incidence between 1:1000 and 1:5000. Based on a comprehensive review and analysis of the literature on infections following LASIK, Chang et al. state that the incidence of infection after LASIK can vary widely (0% to 1.5%). In a survey by the American Society of Cataract and Refractive Surgery (ASCRS), the incidence reported by LASIK surgeons who had experienced an infectious keratitis was 1 in 2919 cases performed during the year 2001. In this study of 116 cases, 76 presented the first week after surgery, 7 during the second week, 17 between the second week and the fourth week, and 16 after 1 month. The most common organisms cultured were atypical mycobacteria (33 of 116 cases, 28%) and staphylococci (23 of 116 cases, 20%) species. In 47 of the 116 cases, infectious keratitis was not diagnosed on initial presentation. Nine patients required flap excision, and 1 flap sloughed spontaneously. One case required enucleation, and 10 required penetrating keratoplasty for visual rehabilitation.

In most cases, it is difficult to determine the origin of the infection. A recent ASCRS survey of infectious keratitis following photorefractive keratectomy (PRK) and LASIK for the year 2004 (Donnenfeld, ASCRS 2005) revealed a significant decrease in atypical mycobacteria, with only 2 cases reported. Prophylaxis with a fourth-generation fluoroquinolone was not done in either case. Sixty-one percent of cases reported in this survey were due to Staphylococcus bacteria. Forty-eight infections were reported by 46 surgeons who had performed an estimated 102,300 procedures; an incidence of 1 infection for every 2131 procedures performed during the year 2004.

A review of the published reports of LASIK-associated microbial keratitis in the peer-reviewed literature reveals over 100 cases with a striking preponderance of atypical mycobacterial (47%) and staphylococcal (19%) species. Another interesting yet concerning observation regarding these atypical mycobacterial LASIK infections involves their ability to occur in clusters or epidemics. Separate clusters of atypical mycobacterial infections following LASIK have been published in the peer-reviewed literature. Chandra et al. report a series of 7 eyes in 4 patients, all of whom had hyperopic LASIK at the same surgery center by the same surgeon on the same day. The causative organism, Mycobacterium chelonae, presumably originated from a contact lens that was used intraoperatively to mask a portion of the laser's ablation. Another cluster is reported by Fulcher and coauthors in 7 eyes of 7 patients; Mycobacterium szulgai was traced back to the ice that was used to chill BSS on the surgical field. Freitas et al. report a cluster of infections in 11 eyes of 10 patients; M. chelonae was found in the portable steaming unit used to clean the microkeratome. Another large cluster that has not been published but has been investigated by the Centers for Disease Control and Prevention (CDCP) occurred in a surgery center in Georgia and involved 24 patients presumed to be infected with Mycobacterium gordonae. Karp et al. report a series of sporadic cases of atypical mycobacteria. Based on their
findings, the CDCP concluded that LASIK-associated keratitis from atypical mycobacteria may be more common than previously thought and also suggested that LASIK could be a risk factor for the development of atypical mycobacterial keratitis.

Infectious keratitis is a potentially devastating complication of LASIK. In addition to the ASCRS survey findings regarding the morbidity of these infections, the series of clustered atypical mycobacterial infections (25 eyes of 21 patients) shows that 4 patients experienced bilateral infections, almost 50% of the affected eyes required flap amputation, and all patients required aggressive topical and oral antimicrobial therapy for a 2- to 3-month period.

The organisms encountered in infectious keratitis following LASIK can be unusual, difficult to predict, and will often not respond to empiric therapy with older-generation topical fluoroquinolone antibiotic agents. For this reason, we highly recommend lifting the flap and taking corneal scrapings for appropriate stains and cultures if any suspicious infiltrate appears following LASIK. The results of these stains and cultures can be helpful in guiding antimicrobial therapy. A high degree of suspicion coupled with a rapid diagnosis and appropriate therapy can result in eradication of the infection and visual recovery. We recommend that any focal infiltrate following LASIK should be considered infectious, and we discourage the practice of empirical antibiotic treatment without culturing.

Diffuse lamellar keratitis (DLK) is a sterile inflammation of the lamellar interface following LASIK and is associated with epithelial abrasions and trauma. It traditionally occurs within the first few days after LASIK unless there is postoperative ocular trauma. Therapy is high-dose topical corticosteroids; in severe cases, oral corticosteroids and interface irrigation may be necessary.

Infectious keratitis following LASIK often presents with inflammation in the corneal interface, which can mimic DLK. Because of this, many cases are typically treated with frequent topical corticosteroid therapy that can cloud the clinical picture with transient improvement in the inflammation. However, unlike DLK, the inflammation associated with LASIK-associated infections usually persists despite topical corticosteroids, and the underlying infections can potentially worsen with corticosteroid tapering. The appearance of an interface inflammation more than 1 week after LASIK should be presumed to be of an infectious etiology until proven otherwise. Diffuse lamellar keratitis characteristically has a diffuse appearance (Figure 1), as the name suggests, while infectious keratitis has a focal area of infiltration surrounded by diffuse inflammation (Figure 2) or even focal inflammation limited to the area of the infiltrate. Any focal infiltrate surrounded by inflammation should be presumed infectious until proven otherwise.
masks by the treating physician and assisting technician. A povidone–iodine solution (Betadine 10%) lid prep before cataract surgery has been shown to reduce the incidence of endophthalmitis postoperatively and is recommended by many clinicians when performing LASIK. Finally, several epidemics of atypical mycobacteria have been associated with the use of nonsterile water to clean instruments or the use of ice during LASIK. All fluids applied to the eye before, during, and after LASIK should be sterile.

TREATMENT OF INFECTIOUS KERATITIS FOLLOWING LASIK

We divide infectious keratitis following LASIK into early onset (occurring within the first 2 weeks of surgery) and late onset (occurring 2 weeks to 3 months after surgery). The organisms seen in early-onset infectious keratitis are common bacterial pathogens such as staphylococcal and streptococcal species. Gram-negative organisms are rare. The organisms seen in late-onset infectious keratitis are usually opportunistic such as fungi, nocardia, and atypical mycobacteria. The literature review of LASIK-associated infections by Chang and coauthors supports this classification of infection. Based on their study, gram-positive organisms were more likely to present within 7 days of surgery (P = .001) while mycobacterial infections were more likely to present 10 or more days after surgery (P < .001).

Since the organisms responsible for infectious keratitis following LASIK will often not respond to empiric therapy, we recommend lifting the flap, scraping and culturing suspicious cases, and selecting appropriate culture media including blood agar, chocolate agar, Sabouraud’s agar, and thioglycolate broth. For infectious keratitis after 2 weeks, we recommend a growth media for atypical mycobacteria such as Lowenstein-Jensen or Middlebrook 7H-9 agar in addition to the other culture media. If these special media are unavailable, we recommend using blood agar as atypical mycobacteria grow quite well on these plates. At the time of culture, we also recommend scraping the infiltrate and performing a Gram stain, Gomori-methenamine silver stain, and Ziehl-Neelsen stain to rule out unusual pathogens such as nocardia, atypical mycobacteria, and fungi. In cases in which cultures are negative and the infection continues to worsen, a corneal biopsy or polymerase chain reaction should be contemplated.

For the treatment of rapid-onset and delayed-onset infectious keratitis, the recommendation is to elevate the flap and culture. Irrigation of the flap interface with an appropriate antibiotic solution (fortified vancomycin 50 mg/mL for rapid-onset keratitis and fortified amikacin 35 mg/mL for delayed-onset keratitis) may be helpful. For rapid-onset keratitis, we recommend a fourth-generation topical fluoroquinolone such as gatifloxacin 0.3% or moxifloxacin 0.5% given in a loading dose every 5 minutes for 3 doses and then every 30 minutes, alternating with an antimicrobial that is rapidly bactericidal and has increased activity against gram-positive organisms, such as fortified cefazolin 50 mg/mL every 30 minutes. In patients who work in a hospital environment, there is an added risk for methicillin-resistant Staphylococcus aureus (MRSA). In these patients, we recommend the substitution of fortified vancomycin 50 mg/mL for cefazolin every 30 minutes to provide more effective therapy against MRSA (Figure 3). In addition, we advocate the use of oral doxycycline 100 mg twice a day to inhibit collagenase production and also discontinuation of corticosteroids.

For delayed-onset keratitis, which is commonly due to atypical mycobacteria, nocardia, and fungi, we recommend beginning therapy with amikacin 35 mg/mL every 30 minutes, alternating with a fourth-generation fluoroquinolone (gatifloxacin 0.3% or moxifloxacin 0.5%) every 30 minutes, starting oral doxycycline 100 mg twice a day, and discontinuing corticosteroids (Figure 3). This treatment will not affect fungal infections; therefore, treatment in all cases of infectious keratitis should be modified based on culture and scraping results and clinical response to therapy.

In conclusion, infectious keratitis is a potentially devastating complication following LASIK. Culture results reveal opportunistic infections and gram-positive bacteria as the most common organisms. Infectious keratitis may present as late as months after LASIK, and its frequent misdiagnosis at initial presentation may result in significant vision loss. We do not recommend empiric therapy as most organisms are opportunistic and do not respond to conventional therapy. A high degree of suspicion with flap elevation and culturing should be performed in all eyes suspected of having an infectious infiltrate(s) following LASIK.

We hope the information contained in this report will help LASIK surgeons assess their respective approaches to the management of post-LASIK infectious keratitis. The

**Figure 3.** Treatment of infectious keratitis following LASIK.
goal is to standardize treatment, minimize visual loss, and improve outcomes.

REFERENCES