Treatment of interface keratitis with oral corticosteroids

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ABSTRACT

Purpose: To describe the results of treating interface keratitis using a combination of intensive topical and oral corticosteroids.

Setting: Casey Eye Institute, Portland, Oregon, USA.

Methods: Thirteen eyes treated for grade 2 to 3 interface keratitis using an oral corticosteroid (prednisone 60 to 80 mg) as well as an hourly topical corticosteroid were retrospectively reviewed. The best corrected visual acuity (BCVA) was used as an objective guide of whether to treat with intense topical and oral corticosteroids, flap irrigation, or both. Predisposing factors such as intraoperative epithelial defects or a history of severe allergies or atopy were also looked for.

Results: All 13 eyes responded favorably to the combination of intensive topical and oral corticosteroids and had a BCVA of 20/20 after the keratitis resolved. In 6 eyes (46%), the patients had a history of severe seasonal allergies. One day postoperatively, 3 eyes (23%) had an epithelial defect and 2 eyes (15%), lint particles or debris embedded in the interface. With oral corticosteroid use, 3 patients (23%) noted mild stomach irritation and 2 (15%) noted nervousness. All 5 side effects resolved without sequelae. No patient developed a serious side effect.

Conclusion: A short, intense course of an oral corticosteroid was an effective treatment in patients with grade 2 or higher interface keratitis when combined with a topical corticosteroid administered hourly. The BCVA is a helpful objective measure of the severity of interface keratitis and can be used to guide the clinician in the therapeutic strategy.

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Interface keratitis or diffuse lamellar keratitis (DLK) can be a serious complication after laser in situ keratomileusis (LASIK).[1–5] Its onset is often insidious and the etiology, thought to be multifactorial, is unclear.[6–16] While there have been many theories about the cause of interface keratitis, there are a limited number of treatment strategies. Currently, the 2 main strategies involve relifting the flap and irrigating the flap interface to remove inflammatory cells and any antigenic stimulus that may be provoking the inflammation and using intensive topical corticosteroid drops to suppress the inflammation locally. We propose a third strategy that includes the use of a high-dose oral corticosteroid. We also identify several risk factors that may predispose patients to interface keratitis.[17]

Patients and Methods

The cases comprised 13 eyes of 13 patients who developed interface keratitis (DLK) after LASIK (Table 1). They occurred from April 1998 to October 2000. The cases were identified by a retrospective review of the

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medical history and surgical records. During this period, all eyes that developed grade 3 or higher interface keratitis (Linebarger classification)[18] were treated with a high-dose oral corticosteroid (prednisone).

Patients were questioned about past medical conditions to exclude a history of tuberculosis, fungal infections, amebiasis, peptic ulcer disease, or diabetes, which can be exacerbated by oral corticosteriod use. The high-dose oral corticosteroid dosage was 60 to 80 mg per

Table 1. Oral corticosteroid use with interface keratitis.

Patient	Age (Years)	Sex	Allergy History (Oral)	Day of Onset and Postoperative Treatment	Oral Prednisone Dose
1	41	F	Penicillin	Day 1	60 mg, 1-week taper
2	38	F	Severe atopic, asthma GPC	Day 1	60 mg, 1-week taper
3	43	F	PCW, aspirin, rosacea,		

keratitis, but the contralateral eye was less severe than grade 3 interface keratitis. In all eyes, the interface keratitis was recognizable on the first day postoperatively. All eyes responded to treatment with a combination of intensive full-strength topical and oral corticosteroids. In 3 severely affected eyes (23%), the flap was lifted and the flap interface irrigated.

All eyes recovered a BCVA of 20/20 or better after treatment (Table 1). In all patients, the oral and topical corticosteroids were discontinued by 2 weeks.

Predisposing Factors

Six patients (46%) had a history of severe seasonal allergies, atopy, and adult or childhood asthma. On the first day postoperatively, 3 eyes (23%) had an epithelial defect and 2 eyes (15%) had lint particles or debris embedded in the interface.

Complications

Three patients (23%) noted mild stomach irritation that was relieved by antacids. Two patients (15%) noted anxiety and nervousness: This resolved spontaneously in 1 patient and subsided in the second after the oral steroid was tapered from 60 mg/d to 40 mg/d after 2 days of treatment. No patient developed serious side effects as a result of the oral corticosteroid therapy. No patient was noted to have an elevation in intraocular pressure (IOP) or signs of glaucoma.

Table 1. (cont.)

Maximum Acute Reduction BCVA	Interface Keratitis	Final BCVA 20/20	Comments
20/60	Grade 3	20/20	Epi defect; LASIK retreatment over PRK; flap lifted and irrigated
20/40	Grade 3	20/20 OU 6 mo postop	Took Alomide FML intermittently over first 6 months for itching allergic conjunctivitis
20/200	Grade +3	20/20 2 mo postop	Rosacea, aspirin allergy
20/60 (6-line loss)	Grade +3 OD	20/20 5 mo postop	Severe atopic with ABM dystrophy; epithelial defect day postop; flap lifted and irrigated day 2
20/40	Grade 3	$20/20^{-1}$	Other eye had PRK with haze previously
20/25 BCVA day 1; 20/80 day 4	Grade 3	$20/20^{-1}$	Flap lifted and irrigated on day 4 postop
20/40 (3-line loss)	Grade 3	20/20 OS 6 mo postop	Possible hypersensitivity to tape; epithelial defect
20/70	Grade 3 OD; grade 1 OS	20/20 OU	Presumed allergy to Dexacidin; bilateral IK other eye grade 1
20/30 day 2 (2-line loss)	Grade 3	20/20	Superior interface lint; local IK superiorly
20/30 (3-line loss) from 20/15 postoperatively	Grade +2–3 OD; grade 2 OS	20/20 +1 3 mo postop	Quick repsonse to oral steroids; bilateral IK other eye grade 2
20/20 to 20/60 (5-line loss)	Grade +3	$20/20^{-2}$	Other eye had severe haze response to PRK
BCVA dropped 2 lines from 20/15 to 20/25	Grade 2–3	20/15	Moderate allergic history; no other predisposing factors
20/40	Grade +3	20/20	Lint in interface inf. temp; flap lifted and lint removed on day 2 postoperatively

Discussion

Our management of interface keratitis or DLK includes a third strategy besides the use of frequent (hourly) topical corticosteroid drops and lifting the flap and irrigating the interface in severe cases.[1,5–7,14,17,18] We found the use of an intense, short-term oral corticosteroid helpful in controlling interface keratitis when it affects vision. Within 24 to 48 hours, the interface keratitis usually began to resolve and the vision slowly improved. The oral corticosteroid dosage was based on a methylprednisolone plasma half life of 78 to 188 minutes and a biologic half life of 18 to 36 hours.[19]

We began using an oral corticosteroid after discussions about the mechanism of interface keratitis with several dermatologists and an ocular immunologist. Two of the dermatologists noted the similarity in the time course of interface keratitis and poison oak contact dermatitis. They used a combined approach of topical and oral corticosteroids (60 to 80 mg/d) to control the swelling and inflammatory damage caused by the contact dermatitis associated with poison oak as well as atopic dermatitis.[20,21]

We found the use of an oral corticosteroid to treat interface keratitis advantageous for several reasons. First, an oral corticosteroid taken once or twice daily is more likely to be properly carried out (compared with an hourly topical corticosteroid that requires more diligent compliance throughout the day). Second, an oral corticosteroid provides around-the-clock antiinflammatory

treatment when the patient is sleeping. An hourly topical corticosteroid is typically not given while the patient is sleeping or if attempted, proper compliance may be difficult. Third, an oral corticosteroid can be used in a complementary fashion with the topical corticosteroid. This allows both local and systemic suppression of the immune response to minimize interface inflammation. If this aggressive corticosteroid combination is used before the inflammation progresses to grade 4 interface keratitis, intrastromal scarring may be avoided. Fourth, in eyes with large epithelial defects, the use of intense topical corticosteroid drops and their preservatives may inhibit reepithelialization and, in some instances, cause the epithelium to slough entirely.[22] The use of an oral corticosteroid helps reduce the inflammatory response without causing significant local epithelial toxicity or reducing reepithelialization. In eyes with severe epithelial defects, we used an intense oral corticosteroid dose, 60 to 80 mg, and reduced the topical corticosteroid from hourly to 4 to 6 times per day maximally to encourage reepithelialization while controlling inflammation.

There are many proposed causes of interface keratitis.[5–8,10,12,14,23] We think the most compelling theory is that an antigenic endotoxin on the gram-negative cell wall surface is capable of inciting an intense neutrophilic response.[2,24] This lipopolysaccharide (LPS) is stable for short cycles of steam sterilization used with most LASIK instruments. Holland et al.[2] suggest that the sterilizer water reservoirs may breed bacteria if not drained after use. The bacteria are killed during sterilization, but their biofilm excites an inflammatory reaction. This includes debris from the cell wall such as the LPS (endotoxin from gram-negative bacteria), and the peptidoglycan (gram-positive bacteria) may deposit on the surgical instruments during the sterilization process. The surgical instruments introduce this foreign debris into the interface during surgery.

The use of an intensive hourly topical steroid or oral corticosteroid should be approached with caution because it may aggravate an infection if a bacterial inoculum is the cause of the keratitis. Reports of infectious keratitis after LASIK are uncommon but do exist.[11,12]

Ocular hypertension can be particularly difficult to detect in post-LASIK eyes because a small cleft or pseudochamber may form in the stromal interface at the level of the flap, causing an artificially low or normal IOP. (The actual IOP may be 40 mm Hg or greater when measured on the peripheral cornea away from the cleft.)

There are 2 recent reports of glaucoma or ocular hypertension, which is difficult to detect and may be associated with atypical DLK after the use of an intensive topical corticosteroid. In the case reported by Najman-Vainer and coauthors,[3] a fluid-filled cavity developed in the interface. This led to an erroneous

strategy is used to treat acute asthmatic exacerbation with an oral high-dose corticosteroid.

Three eyes (23%) that had epithelial defects developed grade 3 interface keratitis. Interface keratitis associated with an epithelial defect was noted after corneal scraping without lifting the flap by Steinert and coauthors.[15]

and irrigation. A clinical case series cannot directly answer whether oral steroid use is superior to topical use because of the small and sporadic number of cases and the variation in presentation patterns that we see in our practice. A large multicenter study may be a consideration in the future. Alternatively, the issue of the etiology and optimal management of interface keratitis may be approached using an animal model as recently reported by Peters et al.[24] Despite these limitations, we have found the strategy described to be useful.

In summary, we believe it is important for the surgeon to realize that interface keratitis is a sight-threatening condition.[6,7,12] In this study, we noted that multiple allergies, atopism, an epithelial defect, or significant debris in the interface may be associated with a significant interface keratitis reaction. In our experience, the prompt use of intensive topical and oral corticosteroids is warranted when the BCVA is worse than 20/40. If more severe visual loss occurs, relifting and irrigating the flap may be indicated. The potential risks of the use of intensive topical and oral corticosteroids are not to be minimized. They should be balanced with the need to minimize inflammation and enhance visual recovery after LASIK.

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