Infectious Keratitis Progressing to Endophthalmitis A 15-Year Study of Microbiology, Associated Factors, and Clinical Outcomes

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Infectious Keratitis Progressing to Endophthalmitis

A 15-Year Study of Microbiology, Associated Factors, and Clinical Outcomes

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Purpose: To describe the incidence, microbiology, associated factors, and clinical outcomes of patients with infectious keratitis progressing to endophthalmitis.

Design: Nonrandomized, retrospective, consecutive case series.

Participants: All patients treated for culture-proven keratitis and endophthalmitis between January 1, 1995 and December 31, 2009, at the Bascom Palmer Eye Institute.

Methods: Ocular microbiology and medical records were reviewed on all patients with positive corneal and intraocular cultures over the period of the study. Univariate analysis was performed to obtain *P* values described in the study.

Main Outcome Measures: Microbial isolates, treatment strategies, and visual acuity (VA) outcomes.

Results: A total of 9934 corneal cultures were performed for suspected infectious keratitis. Only 49 eyes (0.5%) progressed to culture-proven endophthalmitis. Fungi (n = 26) were the most common responsible organism followed by gram-positive bacteria (n = 13) and gram-negative bacteria (n = 10). Topical steroid use (37/49 [76%]) was the most common associated factor identified in the current study, followed by previous surgery (30/49 [61%]), corneal perforation (17/49 [35%]), dry eye (15/49 [31%]), relative immune compromise (10/49 [20%]), organic matter trauma (9/49 [18%]), and contact lens wear (3/49 [6%]). There were 27 patients in whom a primary infectious keratitis developed into endophthalmitis, and 22 patients in whom an infectious keratitis adjacent to a previous surgical wound progressed into endophthalmitis. Patients in the primary keratitis group were more likely to be male (22/27 [81%] vs 8/22 [36%]; $P = 0.001$), have history of organic matter trauma (8/27 [30%] vs 1/22 [5%]); $P = 0.030$), and have fungal etiology (21/27 [78%] vs 5/22 [23%]; $P<0.001$). Patients in the surgical wound–associated group were more likely to use topical steroids (20/22 [91%] vs 17/27 [63%]; $P = 0.024$). A VA of $\geq$20/50 was achieved in 7 of 49 patients (14%), but was $<$5/200 in 34 of 49 (69%) at last follow-up. Enucleation or evisceration was performed in 15 of 49 patients (31%).

Conclusions: Progression of infectious keratitis to endophthalmitis is relatively uncommon. The current study suggests that patients at higher risk for progression to endophthalmitis include patients using topical corticosteroids, patients with fungal keratitis, patients with corneal perforation, and patients with infectious keratitis developing adjacent to a previous surgical wound. Patients with sequential keratitis and endophthalmitis have generally poor visual outcomes.

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Infectious keratitis uncommonly progresses to endophthalmitis. Although a number of small case series describing infectious keratitis associated with endophthalmitis exist, there are few consecutive case series on the subject.[1–20] In addition, because patients with infectious keratitis often present with marked visual loss, pain, hypopyon, and a poorly visualized posterior segment, distinguishing keratitis from endophthalmitis can sometimes be difficult. The current study describes a consecutive series of patients with infectious keratitis progressing to endophthalmitis and reports the associated microbiology, associated factors, and clinical outcomes in these challenging patients.

Patients and Methods

Institutional review board approval was obtained from the University of Miami Miller School of Medicine Sciences Subcommittee for the Protection of Human Subjects. The ocular microbiology department database was searched to identify all patients with positive corneal and intraocular cultures (anterior chamber, vitreous, or both) between January 1, 1995, and December 31, 2009. To be considered for the

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current study, the same organism was required to be positive from both corneal and intraocular cultures. Therefore, only culture-proven cases of sequential keratitis and endophthalmitis were included. Microbiology department records were reviewed to identify the responsible microbial isolates and antibiotic sensitivities.

Corneal cultures were obtained at presentation, or within days of presentation, in all cases. Specimens were obtained via corneal scraping with a Beaver blade and plated directly onto several different culture media, which typically included chocolate agar, 5% sheep blood agar, and Sabouraud agar. Gram stains and Giemsa stains were also performed. Blood and chocolate agars underwent incubation at 35°C for a period of up to 2 weeks. Sabouraud agars underwent incubation at 35°C for a period of 24–36 hours and then at 25°C for up to 2 more weeks. Additional culture media, including thioglycollate broth, Lowenstein-Jensen medium, and agar agar media were performed at the discretion of the ophthalmologist performing the culture.

Anterior chamber cultures were most often obtained at the time of penetrating keratoplasty. In a few instances, anterior chamber cultures were obtained from an anterior chamber paracentesis. In these instances, care was taken to pass the needle through clear cornea to avoid contamination of the specimen by infected corneal tissue and to avoid introduction of microbes into the anterior chamber. Vitreous cultures were obtained either at the time of vitreous tap and inject or during vitrectomy. Fluids from anterior chamber paracentesis or vitreous tap were plated directly on to culture media and were handled in an identical fashion to corneal specimens. For vitrectomy specimens, 30–50 cc of vitreous washings were filtered using a 0.45-μm filter. The resultant filter paper was divided into sections and was plated on to different culture media, which typically included chocolate agar, 5% sheep blood agar, and Sabouraud agar.

All cultures were read and classified by Ocular Microbiology Department staff. Antibiotic sensitivities were performed on all gram-positive and -negative bacteria. Antifungal sensitivities were not routinely assessed.

After analyzing microbiology records, the corresponding medical records of these patients were reviewed. Patient demographics, clinical characteristics, risk factors, treatment strategies, and clinical outcomes were assessed. Exclusion criteria included patients with endophthalmitis occurring within 6 weeks of a previous surgery, inadequate clinical records (<30 days of follow-up), bleb-associated infections, penetrating trauma, and cases of viral keratitis.

The remaining patients were divided into 2 categories: patients in whom a primary keratitis developed into endophthalmitis (defined as "primary keratitis") and patients in whom an infectious keratitis associated with a previous surgical wound developed into endophthalmitis (defined as "surgical wound–associated keratitis"). In the current study, endophthalmitis was defined by the presence of positive intraocular cultures. When anterior segment opacities prevented a view of the posterior segment, echography was consistently performed.

Pearson chi-squared test and Fisher exact test were used to compare basic characteristics of the 2 groups using SISA online statistical analysis (Uitenbroek DG, 1997; SISA; available at: http://www.quantitativeskills.com/sisa/index.htm; accessed September 4, 2011). The *t*-test was used for 2 independent samples. All *P* values are 2-sided and nominal.

Results

Demographics and Clinical Features

Over the 15-year period of the study, 9934 corneal cultures were performed for cases of suspected infectious keratitis, of which 3724 corneal cultures (37.5%) were positive. During this time period, 68 eyes were identified to have both positive corneal and intraocular cultures, of which 19 were excluded from the study. Reasons for exclusion included endophthalmitis occurring within 6 weeks of a previous surgery (9 patients), inadequate clinical records (5 patients), bleb-associated endophthalmitis (3 patients), and penetrating ocular trauma (2 patients). Thus, of 9934 cases of clinically suspected keratitis, 49 eyes (0.5%) that had progressed to culture-proven endophthalmitis were included.

The average age of patients in the current series was 61.4±17.6 years (median, 57 years; range, 10–96 years) and 30 of 49 were male [61.2%]. Patients in our series were divided into 2 classifications: patients in whom a primary keratitis developed into endophthalmitis (defined as "primary keratitis") and patients in whom an infectious keratitis adjacent to a previous surgical wound developed into endophthalmitis (defined as "surgical wound–associated keratitis"). Demographics and risk factors for these patients are presented in Table 1, and representative cases are shown in Figure 1. Patients in the primary keratitis group were younger (average, 54.8 years; range, 10–96 years) compared with patients in the surgical wound–associated keratitis group (average age, 69.4 years; range, 26–91 years). In addition, patients in the primary keratitis group were more likely to be male (22/27 [81%]), to have a history of trauma (12/27 [44%]), to have a foreign body injury (11/27 [41%]) or organic matter trauma (8/27 [30%]), and to have a fungal causative organism (21/27 [78%]). Patients in the surgical wound–associated keratitis group were more likely to be female (14/22 [64%]), to have used topical steroids (20/22, [91%]), and to have a bacterial causative organism (17/22 [77%]).

At the time of presentation, most patients were using topical steroids (37/49 [76%]), representing the most common associated factor identified in the current study. Only 3 of 49 patients (6%) were contact lens wearers, and all had a fungal etiology. A history of intraocular surgery was noted in 30 of 49 patients (61%). The average number of previous intraocular surgeries for all patients was 1.27

Table 1. Comparison of Characteristics of Patients with Keratitis and Subsequent Endophthalmitis

	Primary Keratitis	Surgical Wound–Associated Keratitis	*P* Value*
Average age (yrs)	54.8±15.1	69.4±17.5	0.003†
Male sex	22/27 (81.5%)	8/22 (36.4%)	0.001
Female sex	5/27 (18.5%)	14/22 (63.6%)	—
Contact lens wear	3/27 (11.1%)	0/22 (0.0%)	0.242‡
History of trauma	12/27 (44.4%)	3/22 (13.6%)	0.029‡
Foreign body injury	11/27 (40.7%)	2/22 (9.1%)	0.021‡
Organic matter trauma	8/27 (29.6%)	1/22 (4.5%)	0.030‡
Corneal perforation	11/27 (40.7%)	6/22 (27.3%)	0.325
Dry eye syndrome or blepharitis	6/27 (22.2%)	9/22 (40.9%)	0.158
Diabetes mellitus	3/27 (11.1%)	3/22 (13.6%)	1.000‡
Immune suppression	3/27 (11.1%)	1/22 (4.5%)	0.617‡
Oral steroid use	1/27 (3.7%)	0/22 (0.0%)	1.000‡
Topical steroid use	17/27 (63.0%)	20/22 (90.9%)	0.024
Previous surgery	8/27 (29.6%)	22/22 (100%)	<0.001
Average number previous surgeries	0.37	2.36	—
Fungal etiology	21/27 (77.8%)	5/22 (22.7%)	<0.001
Bacterial etiology	6/27 (22.2%)	17/22 (77.3%)	—

*Chi-square test.
†Student *t*-test.
‡Fisher exact test.

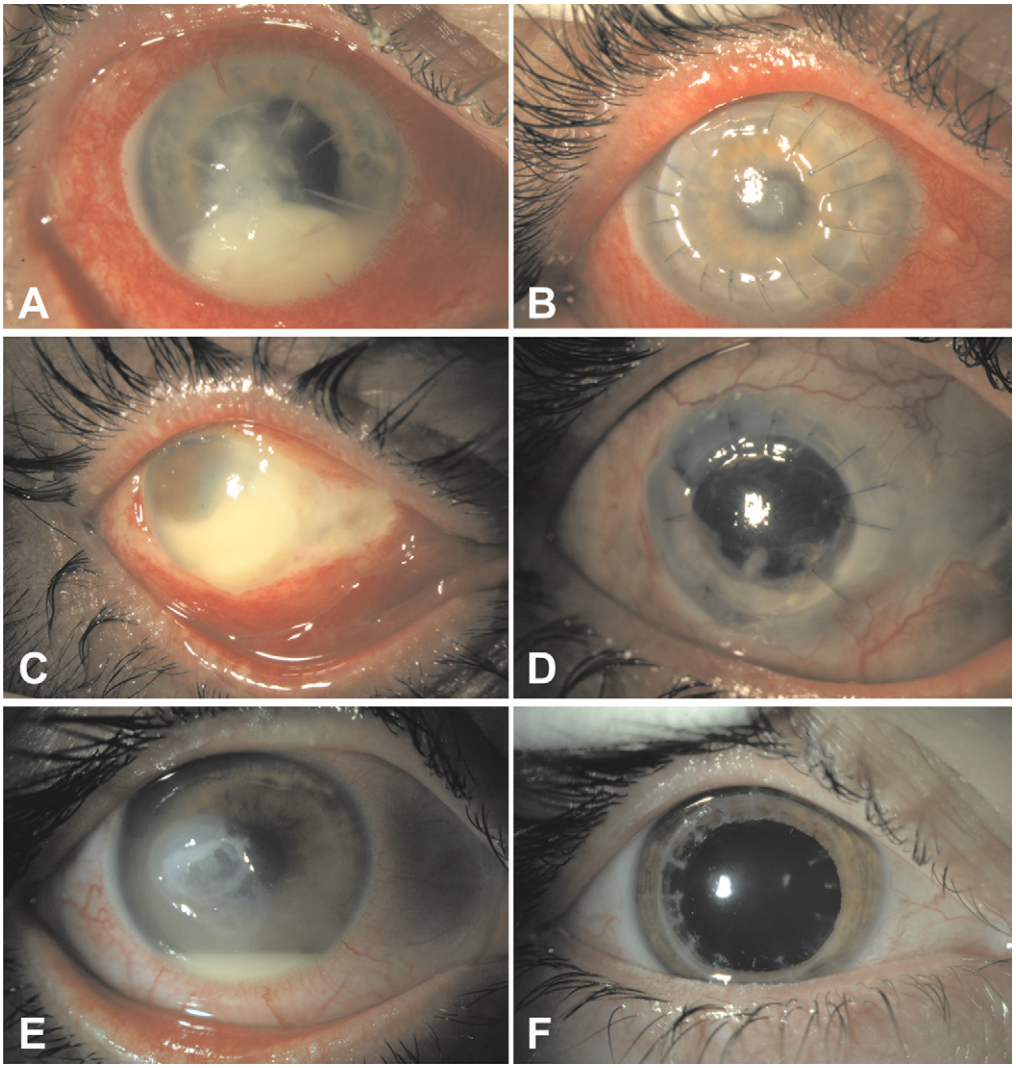

Figure 1. A, A 56-year-old man with a history of radial keratotomy developed *Fusarium* keratitis and consequent endophthalmitis after a weekend of camping. Presenting visual acuity was 6/200. **B**, Appearance of the patient from **A** 1 month after undergoing treatment with topical natamycin, intracameral voriconazole, and penetrating keratoplasty. The patient eventually regained 20/20 visual acuity with use of a hard contact lens. **C**, A 47-year-old man developed *Pseudomonas aeruginosa* keratitis and subsequent endophthalmitis after a nonperforating corneal abrasion from a tree branch. **D,** Appearance (of the patient from panel **C)** 2 years after management with topical tobramycin, intravitreal ceftazidime, penetrating keratoplasty, and subsequent extracapsular cataract extraction with secondary intraocular lens. He regained hand motions vision. **E**, A 26-year-old man developed *Mycobacterium chelonae* endophthalmitis after a 4-month history of chronic keratitis after LASIK surgery. Presenting vision was hand motions. **F**, Appearance of the patient (from panel **E)** 8 months after management with topical amikacin, topical clarithromycin, subconjunctival amikacin, and penetrating keratoplasty with anterior chamber washout. The patient recovered 20/30 visual acuity.

(range, 0–7). In patients with a surgical history, the average length of time from most recent surgery to the date of presentation was 1087 days (median, 255.5 days; range, 48–8349 days). All patients with keratitis and endophthalmitis occurring within 6 weeks of a previous surgery were excluded from the current study.

Clinical features at presentation included conjunctival injection (49/49 [100%]), hypopyon (45/49 [92%]), documented vitritis on clinical examination and/or echography (25/49 [51%]), and moderate to severe pain (38/49 [78%]). Corneal perforation was common, occurring in 17 of 49 eyes (35%). Of patients in the primary keratitis group, 11 of 27 eyes (41%) had a corneal perforation, compared with 6 of 22 eyes (27%) in the surgical wound–associated keratitis group, which was not a significant difference ($P = 0.325$).

The clinical diagnosis of endophthalmitis was suspected by physicians based on characteristic features in 44 of 49 patients (90%). In 5 of 49 patients (10%), physicians were uncertain of the diagnosis at the time of intraocular cultures because of equivocal clinical findings or patients presenting early in the disease course. Because of the retrospective nature of this study, a full description of which clinical features led to the diagnosis of endophthalmitis were not always available in the medical record.

Microbial Isolates and Antibiotic Sensitivities

Of the 49 eyes included in the current study, all had documented keratitis before the development of endophthalmitis. A single organism was identified in 39 eyes and multiple organisms were

identified in 10 eyes. Fungi (n = 26) were the most common responsible organism followed by gram-positive bacteria (n = 13) and gram-negative bacteria (n = 10). A summary of all responsible microbial isolates is shown in Table 2 (available online at http://aaojournal.org). Corneal cultures were performed in 49 patients, anterior chamber cultures in 34, and vitreous cultures in 22. All 49 patients had positive corneal cultures; 31 patients had positive anterior chamber cultures and 22 patients had positive vitreous cultures. Four patients had positive corneal, anterior chamber, and vitreous cultures. Fungi responsible for endophthalmitis were isolated from the anterior chamber alone in 20 cases, from the vitreous alone in 5 cases, and from both in 1 case. Bacteria responsible for endophthalmitis were isolated from the anterior chamber alone in 7 cases, from the vitreous alone in 13, and from both in 3.

In the primary keratitis group, fungi accounted for the majority of cases (21/27 [78%]) progressing to endophthalmitis. There were 6 of 27 cases in the primary keratitis group where bacterial keratitis progressed to endophthalmitis, each of which had special circumstances that predisposed the patients to serious infection, including a recent history of organic matter trauma (n = 2), Mooren's ulcer (n = 1), neurotrophic keratopathy (n = 1), and a history of herpes zoster ophthalmicus in the setting of HIV infection (n = 1). A final patient with sequential *Pseudomonas* keratitis and endophthalmitis had a history of urine exposure to the eye as an attempted treatment for conjunctivitis.

In the surgical wound–associated group, bacteria accounted for the majority of cases (17/22 [77%]). Scenarios associated with infection included suture abscess (n = 6), wound dehiscence (n = 3), or wound leak (n = 3) occurring months to years after the original surgery. These cases were distinct from cases of postoperative endophthalmitis, which were excluded from the current study.

Antibiotic sensitivities were assessed for gram-positive and gram-negative bacteria. Among gram-positive isolates, 100% (13/13) were sensitive to vancomycin, 55% (6/11) were sensitive to fluoroquinolones, and 30% (3/10) were sensitive to trimethoprim/sulfa. The single case of *Mycobacterium chelonae* was sensitive to amikacin but was resistant to trimethoprim/sulfa and ciprofloxacin. Gram-negative isolates were found to be sensitive to a wide range of antibiotics, with 100% of gram-negative isolates (10/10) sensitive to amikacin, ceftazidime, tobramycin, gentamicin, and ciprofloxacin. All gram-negative bacteria were resistant to cefazolin and ampicillin.

Treatment Strategies

Nearly all patients—47 of 49 (96%)— were treated with topical antibiotics or antifungals before and/or after the diagnosis of keratitis and endophthalmitis (Table 3). The 2 patients who were not treated with topical antimicrobial agents underwent primary enucleation. Of the fungal cases, 26 of 26 patients (100%) received topical antifungal drops, most commonly natamycin (18/26 [69%]), amphotericin B (5/26 [19%]), or multiple antifungal agents (2/26 [8%]). Topical amphotericin B was used in all 5 cases caused by *Candida*. Of the bacterial cases, 20 of 22 (91%) received topical antibiotics that were tailored based on antibiotic sensitivities.

Intraocular antimicrobials were administered in 39 of 49 patients (80%). Among patients with fungal infections, intraocular antifungals were used in 23 of 26 cases (88%): most commonly, amphotericin B (16/23 [70%]), voriconazole (2/23 [9%]), or multiple antifungal agents (5/23 [22%]). In 3 patients with fungal keratitis and endophthalmitis, penetrating keratoplasty (PKP) and anterior chamber irrigation alone were performed. In these patients, the diagnosis of endophthalmitis at the time of PKP was uncertain, and intraocular antifungals were not administered. Among patients with bacterial infections, intraocular antibiotics were used in 16 of 23 cases (70%), with ceftazidime and vancomycin being the antibiotics of choice. Of the 7 patients with bacterial keratitis and endophthalmitis who were not treated with intraocular antimicrobial agents, 5 underwent primary enucleation and 2 underwent PKP with anterior chamber irrigation and culture. In these 2 patients, the anterior chamber culture was obtained at the time of surgery, and the diagnosis of endophthalmitis was not made until culture results returned.

Table 3. Treatment Strategies in Patients with Keratitis and Subsequent Endophthalmitis

	Primary Keratitis	Surgical Wound–Associated Keratitis	*P* Value*
Topical antimicrobials	27/27 (100%)	20/22 (90.9%)	0.056
Intraocular antimicrobials	23/27 (85.2%)	16/22 (72.7%)	0.282
Intraocular steroids	1/27 (3.7%)	10/22 (45.5%)	<0.001†
Pars plana vitrectomy	7/27 (25.9%)	10/22 (45.5%)	0.153
Penetrating keratoplasty	22/27 (81.5%)	11/22 (50.0%)	0.019
Enucleation or Evisceration	7/27 (25.9%)	8/22 (36.4%)	0.430

*Chi-square test.
†Fisher exact test.

Intraocular steroids were used in 11 of 49 patients (22%), and were used more commonly in patients with surgical wound–associated keratitis and endophthalmitis (Table 3). Intraocular steroids were avoided in cases of suspected or confirmed fungal endophthalmitis, accounting for the relatively low rates of use.

Pars plana vitrectomy (PPV) was performed after the diagnosis of endophthalmitis in 17 of 49 patients (35%). The median length of time from presentation to vitrectomy was 2 days (average, 25 days; range, 0–195 days). Clinical data pertaining to the subset of patients undergoing PPV is highlighted in Table 4 (available at http://aaojournal.org). Globe salvage, defined as avoidance of enucleation or evisceration, was achieved in 13 of 17 patients (76%) undergoing PPV.

Penetrating keratoplasty was performed in 33 of 49 patients (67%). The median length of time from presentation to PKP was 12 days (average, 56.5 days; range, 0–641 days). In the primary keratitis group, 22 of 27 patients (81%) underwent PKP: 19 for therapeutic purposes and 3 for optical purposes. Of these, 12 of 22 (55%) had eventual graft failure and 9 of 22 (41%) underwent subsequent PKP. In the surgical wound–associated keratitis group, 11 of 22 patients (50%) underwent PKP: 9 for therapeutic purposes and 2 for optical purposes. Of these, 3 of 11 (27%) had eventual graft failure and 3 of 11 (27%) underwent subsequent PKP.

Patients with fungal keratitis and endophthalmitis underwent PKP more often (24/26 [92%]) than patients with bacterial keratitis and endophthalmitis (9/23 [39%]), which was a significant difference ($P<0.001$). Among patients with fungal keratitis and endophthalmitis undergoing PKP, 12 of 24 (50%) had eventual graft failure and 10 of 24 patients (42%) underwent subsequent PKP.

Clinical Outcomes

Best-corrected visual acuity (VA) outcomes at last examination ranged from 20/20 to no light perception (Table 5). Among all

Table 5. Visual Acuity at Last Follow-up Visit

	≥20/50	≥20/400	<5/200	No Light Perception
All patients	14% (7/49)	24% (12/49)	69% (34/49)	35% (17/49)
Primary keratitis	19% (5/27)	26% (7/27)	70% (19/27)	30% (8/27)
Wound-associated keratitis	9% (2/22)	23% (5/22)	68% (15/22)	41% (9/22)
Fungi	19% (5/26)	31% (8/26)	62% (16/26)	27% (7/26)
Fusarium sp	14% (2/14)	21% (3/14)	71% (10/14)	36% (5/14)
Candida sp	25% (1/5)	40% (2/5)	40% (2/5)	0% (0/5)
Other fungi	29% (2/7)	43% (3/7)	57% (4/7)	29% (2/7)
Gram-positive bacteria	8% (1/13)	23% (3/13)	69% (9/13)	31% (4/13)
Streptococcus species	0% (0/10)	0% (0/10)	90% (9/10)	40% (4/10)
Staphylococcus species	0% (0/2)	100% (2/2)	0% (0/2)	0% (0/2)
Gram-negative bacteria	10% (1/10)	10% (1/10)	90% (9/10)	60% (6/10)
Pseudomonas aeruginosa	13% (1/8)	13% (1/8)	88% (7/8)	50% (4/8)
Serratia marcescens	0% (0/2)	0% (0/2)	100% (2/2)	100% (2/2)

patients, only 7 of 49 (14%) achieved a VA of ≥20/50 at last follow-up. A VA of ≥20/400 was achieved in 12 of 49 patients (24%). No light perception vision was present in 17 of 49 patients (35%), including 15 of 49 patients (31%) who ultimately underwent enucleation or evisceration.

The VA outcomes were similar among patients in the primary keratitis and surgical wound–associated keratitis groups. Although a greater percentage of patients in the primary keratitis group achieved a VA of ≥20/50 (5/27 [19%] vs 2/22 [9%]), this was not a significant difference ($P = 0.436$; Fisher exact test). For patients with gram-negative infections, VA outcomes were particularly poor; all patients with S*erratia marcescens* infections had no light perception at last follow-up visit, and 7 of 8 patients (88%) with *Pseudomonas aeruginosa* infections had hand motion VA or worse. For patients with streptococcal infections, 9 of 10 patients (90%) had hand motions or worse VA at last follow-up. More patients with fungal keratitis and endophthalmitis achieved a VA of ≥20/50 than those with bacterial keratitis and endophthalmitis (5/26 [19%]) vs 2/23 [9%]), but this was not a significant difference ($P = 0.430$, Fisher exact test). In patients who had a corneal perforation, only 2 of 17 patients (12%) achieved a VA of ≥20/50, whereas 13 of 17 patients (76%) had <5/200 VA at last visit, including 6 of 17 (35%) who ultimately underwent enucleation.

Secondary complications of patients included retinal detachment (5/52 [10%]), secondary glaucoma (20/52 [38%]), and irregular astigmatism (18/52 [35%]).

Among the 15 patients presenting with LP vision at presentation, 2 of 4 (50%) undergoing PPV achieved a VA of ≥20/400 at the last visit compared with 0 of 11 (0%) not undergoing PPV, which approached significance ($P = 0.057$). Patients undergoing PKP did relatively well, with 12 of 33 patients (36%) achieving a VA of ≥20/400 and 7 of 33 (21%) achieving a VA of ≥20/50. Two patients undergoing PKP achieved a VA of 20/20.

Discussion

Microbial keratitis is common, with an estimated incidence of 30 000 cases per year in the United States.[21–23] Progression of keratitis to endophthalmitis, however, is considered to be uncommon. This was confirmed in the current study, in which only 0.5% of eyes with clinically suspected keratitis progressed to culture-proven endophthalmitis (49 cases of endophthalmitis of 9934 corneal cultures performed). Some patients presenting with small or peripheral corneal ulcers did not undergo corneal cultures, meaning the true incidence of endophthalmitis developing from keratitis may be even lower. This was balanced somewhat by the fact that a few patients underwent multiple corneal cultures over the period of the study.

There were a number of associated factors that may have predisposed patients to infection in the current study. The use of topical corticosteroids was seen in 37 of 49 patients (76%) and was the most common associated factor identified. Patients tended to be older, with an average age of 61.4 years. Relative immune compromise from HIV, leukemia/lymphoma, or diabetes mellitus was seen in more than one fifth of patients (10/49 [20%]), which is higher than the prevalences in the general population of 8.3% for diabetes mellitus (25.8 million Americans) and 0.4% for HIV (1.2 million Americans).[24,25] Dry eye syndrome (15/49 [31%]), foreign body injury (13/49 [27%]), and organic matter exposure (9/49 [18%]) were also relatively common risk factors in our series. The use of contact lenses was not a common risk factor in our series because only 3 patients had contact lens–related ulcers progressing to endophthalmitis. Corneal perforation occurred in 17 of 49 cases (35%) and was particularly common in cases of primary keratitis progressing to endophthalmitis (11/27 [41%]).

Among the cases of primary keratitis progressing to endophthalmitis, fungi accounted for 21 of 27 cases (78%), suggesting that a fungal etiology may increases the risk of progression to endophthalmitis. This makes sense mechanistically, because fungi such as *Fusarium* have demonstrated the ability to penetrate an intact cornea.[14] In the current study, fungi causing keratitis and endophthalmitis were preferentially isolated from the anterior chamber, and in many cases infections seemed to be contained within the anterior chamber without spreading to the vitreous.

Topical corticosteroids have been previously demonstrated to potentiate the growth and invasiveness of bacteria and fungi by suppressing immune defense mechanisms, particularly when used without concomitant antimicrobial agents.[14,23,26–31] In addition, the use of topical corticosteroids has been shown to increase the risk ulcerative keratitis in patients with preexisting corneal disesases.[23,31] The use of corticosteroids before the development of keratitis can lead to worse treatment outcomes and an increased likelihood of antibiotic failure.[23] Very recently, the Steroids for Corneal Ulcers Trial, a randomized, placebo-controlled, double-masked trial of 500 patients, compared clinical outcomes with and without the use of topical corticosteroids as adjunctive therapy in the treatment of bacterial corneal ulcers. In this study, no safety concerns were reported with the use of topical corticosteroids, including no cases of endophthalmitis and no increased risk of corneal perforation. Primary outcomes, however, were assessed only through 3 months in this trial, and safety outcomes after long-term use of corticosteroids in patients with a history of microbial keratitis remain unknown.[32]

Topical cyclosporine, in contrast, has been shown to inhibit the growth of fungi in vitro.[27] More recently, topical tacrolimus, also a calcineurin inhibitor, has also been shown to inhibit fungal growth in a murine model of *Aspergillus* keratitis when used in combination with topical amphotericin B, voriconazole, or polyhexamethylene biguanide.[33] Calcineurin inhibitors should be considered as an alternative agent to corticosteroids, especially in cases of fungal keratitis.

Topical and intravitreal antimicrobials were the mainstays of treatment in the current series. In cases that present with a bacterial etiology, antibiotic sensitivity results from the current study reinforce the standard use of intravitreal vancomycin and ceftazidime. However, antimicrobial agents did not prove sufficient in many cases because PPV, PKP, or both were required in 35% and 67% of cases, respectively. In the Endophthalmitis Vitrectomy Study, patients with light perception vision who underwent vitrectomy had superior visual outcomes compared with intravitreal antibiotics alone.[34] In our study, 15 patients presented with light perception vision, of whom 50% undergoing PPV achieved a vision of ≥20/400 at final outcome compared with 0% not undergoing PPV, a finding that approached significance ($P = 0.057$). The retrospective nature of this study and small sample size, however, prevented definitive conclusions regarding benefits of PPV in this population. In patients undergoing PKP in the current study, initial graft failure was common (15 of 33 cases [45%]); however, many of these patents ultimately did well, with 36% (12/33) achieving a VA of ≥20/400 and 21% (7/33) with ≥20/50 vision.

There are a few smaller case series in the literature that have evaluated sequential keratitis and endophthalmitis. A previous study by Scott et al[1] looked at patients presenting with positive corneal and intraocular cultures between 1990 and 1995. There were 1699 corneal cultures performed over the period of their study, of which 14 eyes (0.8%) progressed to culture-proven endophthalmitis. Similar to our study, topical corticosteroid use (93%) and a history of ocular surgery (57%) were common. In addition, VA outcomes in this series were poor with only 43% of patients achieving vision of ≥20/200. In contrast with our study, gram-negative bacteria were the most commonly isolated organisms, although the study size was smaller.

A second study by Dursun et al[14] looked at 159 cases of *Fusarium* keratitis, of which 10 (6.3%) progressed to endophthalmitis, which supports the theory that fungal keratitis is more likely than bacterial keratitis to progress to endophthalmitis.[14] Risk factors in this series included trauma (60%), topical steroid use (20%), contact lens use (10%), and LASIK surgery followed by minor trauma (10%). All patients in this series[14] were immunocompetent, and developed endophthalmitis via contiguous intraocular spread. Other case reports in the literature suggest relative immune compromise, topical steroid use, surgical history, and preexisting corneal disease as possible risk factors for progression of keratitis to endophthlamitis.[4–20]

Progression of infectious keratitis to endophthalmitis is relatively uncommon. The current study suggests that those at higher risk for progression to endophthalmitis include patients using topical corticosteroids, patients with fungal keratitis, patients with corneal perforation, and patients with infectious keratitis developing adjacent to a previous surgical wound. Patients with sequential keratitis and endophthalmitis have generally poor visual outcomes.

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