# Infectious Endophthalmitis After Boston Type 1 Keratoprosthesis Implantation

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**Purpose:** To determine the incidence, clinical features, and outcomes of infectious endophthalmitis after Boston Type 1 Keratoprosthesis (KPro) implantation.

**Methods:** Retrospective, consecutive case series. Chart review of 105 patients (126 eyes) who had KPro implantation at Cincinnati Eye Institute between November 2004 and November 2010 and who were followed up for at least 1 month (range, 1 month to 66 months; mean 25 months) revealed 3 cases who developed infectious endophthalmitis.

**Results:** One patient had a history of congenital glaucoma, and 2 patients had Stevens–Johnson syndrome. Two had KPro implantation for penetrating keratoplasty failure and 1 had necrosis of a previous KPro cornea. The incidence of endophthalmitis was 2.4%. All patients wore a contact lens and were on vancomycin and a fourth-generation fluoroquinolone (moxifloxacin). Vitreous fluid cultures yielded *Ochrobactrum anthropi*, *Candida parapsilosis*, and *Candida albicans*. All patients received intravitreal amphotericin, vancomycin, and/or ceftazidime. Topical and oral antiinfective agents were tailored based on sensitivities. One patient required KPro removal and therapeutic penetrating keratoplasty. Vision did not recover for 2 patients who presented with vision decreased to light perception. One patient, who presented with decreased vision of 20/400, recovered to 20/60.

**Conclusions:** Infectious endophthalmitis is a devastating complication that can occur after Boston KPro implantation even with prophylactic vancomycin, a fourth-generation fluoroquinolone, and a therapeutic contact lens. Fungal and gram-negative organisms are a growing cause for concern. Further study is needed on optimal prophylaxis regimens, including the use of antifungals, especially for high-risk eyes, such as those with autoimmune cicatrizing disease.

**Key Words:** Boston keratoprosthesis, endophthalmitis, fungal infection, bacterial infection

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The Boston Type 1 keratoprosthesis (KPro) has been used in the management of eyes with multiple failed penetrating keratoplasties (PKs), chemical injuries, bullous keratopathy, Stevens–Johnson syndrome (SJS), ocular cicatricial pemphigoid, herpes simplex virus keratitis, aniridic fibrosis syndrome, and other ocular diseases.[1] Infectious endophthalmitis is a devastating complication associated with poor visual outcomes.[2,3] There are just a few reports in the literature that examine the characteristics of patients who develop this complication after KPro implantation.[4–7] The addition of vancomycin and a quinolone to the bacterial prophylaxis regimen after KPro implantation has reduced the occurrence of bacterial endophthalmitis.[7,8] However, the risk of fungal colonization and infection in KPro has since appeared.[5] We present the characteristics, management, and outcomes of 3 patients who developed endophthalmitis after KPro implantation at the Cincinnati Eye Institute.

## METHODS

A retrospective chart review of 105 patients (126 eyes) who had undergone KPro implantation at the Cincinnati Eye Institute between November 2004 and November 2010 and were followed up for at least 1 month postoperatively (range, 1 month to 5.92 years; mean, 3.42 years) was conducted. Three cases were identified to have developed endophthalmitis after KPro implantation. Information on the incidence, presenting features, causative organisms, management, and patient demographical and visual acuity outcomes was recorded.

## RESULTS

The incidence of endophthalmitis was 2.4% (3 of 126 eyes) and occurred at 4, 11, and 35 months after surgery. There were 3 cases of endophthalmitis over 2582 accumulated patient-months of follow-up, or 0.014 infections per patient-year. Patient characteristics are summarized in Table 1. Mean patient age was 52 years. All 3 patients were women. Two patients had KPro implantation because of PK failure and 1 patient had necrosis of a previous KPro cornea. One patient had a history of congenital glaucoma. Two patients had a diagnosis of SJS, 1 of whom had previous living-related conjunctival limbal allograft combined with keratolimbal allograft ("Cincinnati Procedure") limbal stem cell transplant surgery.[9]

All patients since the time of K-pro implantation wore a bandage contact lens (Kontur Kontact Lens Co, Inc, Hercules, CA) that was changed every 3 months. Antibiotic prophylaxis consisted of 250 mg of cephalexin 4 times daily

**TABLE 1.** Patient Characteristics at the Time of Diagnosis of Endophthalmitis

| Case No. | Age at KPro (yr) | Diagnosis | Indication for KPro | Previous Surgery | Comorbid Ocular Disease | Medical Problems | Ocular Medications at Diagnosis | Systemic Immunosuppression |
|---|---|---|---|---|---|---|---|---|
| 1 | 21 F | Congenital glaucoma | Failed PK | PK | Glaucoma RD repair | Asthma, hypertension, gastric reflux | Vancomycin twice a day, moxifloxacin twice a day, prednisolone twice a day, brimonidine twice a day, timolol twice a day | — |
| 2 | 58 F | SJS | Failed PK | AMT, LR-CLAL/ KLAL, PK, tarsorrhaphy | Glaucoma, symblephara | Gastric reflux, hypertension | Vancomycin twice a day, moxifloxacin twice a day, prednisolone once a day | Mycophenolate mofetil, tacrolimus, prednisone |
| 3 | 76 F | SJS | KPro melt | Phaco/PCIOL, tarsorrhaphy, KPro | Glaucoma, symblephara, noncompliance | Psoriasis, hypertension | Vancomycin twice a day, moxifloxacin twice a day, difluprednate twice a day, latanoprost before bed | — |

AMT, amniotic membrane transplant; F, female; KLAL, keratolimbal allograft stem cell transplant; LR-CLAL, living-related conjunctival limbal allograft stem cell transplant; PCIOL, posterior chamber intraocular lens; Phaco, phacoemulsification cataract extraction.

for 1 week after surgery, with 14 mg/mL of vancomycin and a fourth-generation fluoroquinolone (moxifloxacin) 4 times daily immediately after surgery for 1 month and then tapered to twice daily. All patients were also on a topical steroid for management of chronic inflammation 4 times daily immediately after surgery for 1 month and then tapered to twice daily. One patient with SJS was taking systemic immunosuppression medications at the time of endophthalmitis development.

Features of the endophthalmitis are summarized in Table 2. All patients presented with decreased vision. Only 1 patient complained of pain [probably because of the hypotony associated with her chronic retinal detachment (RD)]. The other patient who presented with an RD complained of new onset floaters and on examination had a dense retroprosthetic membrane that was not noted 2 months before.

All patients were referred to the retina service. Causative pathogens were found in vitreous fluid cultures for all patients: *Ochrobactrum anthropi*, *Candida parapsilosis*, and *Candida albicans*. One patient (case 1) had a contact lens that was culture-positive for *Staphylococcus aureus* but sensitive to vancomycin. Initial broad-spectrum antibiotics and antifungals were used based on clinical findings (Table 2). Oral antibiotics and antifungals were added only after culture-positive results were known. Patient 1 [who presented with anterior chamber (AC) infiltrates] and patient 2 (who presented with vitritis) immediately received 5 μg of amphotericin, 1 mg of vancomycin, and/or 2.25 mg of ceftazidime intravitreally. No intravitreal steroids were given because of a high suspicion for fungus as the causative pathogen for endophthalmitis after KPro. Patient 3 (who presented with hypotony and an RD, with no AC infiltrates or visible vitritis) received intravitreal anti-infectives only after positive culture results were returned. Additional management was tailored according to culture and sensitivity results, and levofloxacin (case 1), amphotericin,

**TABLE 2.** Characteristics of Endophthalmitis

| Case No. | VA Before KPro | VA Before Endophthalmitis | Presenting Symptoms and Signs | Initial Management | Culture Results | Management After Culture Results | Last Recorded VA |
|---|---|---|---|---|---|---|---|
| 1 | HM 6 ft | HM | ↓ VA (LP) × 1 wk, cornea and AC infiltrates/ hypopyon, 35 mo after KPro | Oral fluconazole; AC, CL, and vitreous cultures; intracameral amphotericin and vancomycin; intravitreal ceftazidime; topical fortified tobramycin | *Staphylococcus aureus* from CL, *Ochrobactrum anthropi* (GNB) from AC and vitreous | KPro removal and therapeutic PK; oral and topical levofloxacin | LP, 18 mo after |
| 2 | CF 1 ft | 20/40 | ↓ VA (20/400), ↑ floaters × 3 wk, dense RPM, vitritis 11 mo after KPro | PPV; RPM peel; endolaser; vitreous cultures; intravitreal vancomycin, ceftazidime, and amphotericin | *Candida parapsilosis* from vitreous | Topical amphotericin; oral fluconazole | 20/60, 11 mo after |
| 3 | HM | 20/200 | ↓ VA (LP) × 2 mo, pain, hypotony, RD, 4 mo after KPro | PPV, RD repair, endolaser, silicone oil fill, vitreous cultures | *Candida albicans* from vitreous | Oral fluconazole; intravitreal amphotericin | LP, 2 mo after |

AC, anterior chamber; CF, count fingers; CL, contact lens; GNB, gram-negative bacilli; HM, hand motions; LP, light perception; PPV, pars plana vitrectomy; RPM, retroprosthetic membrane; VA, visual acuity.

and/or fluconazole (cases 2 and 3) were used. The patient who did not undergo pars plana vitrectomy required removal of the KPro and a therapeutic PK.

Visual outcomes were poor for the 2 patients who presented with vision decreased to light perception (LP). Those 2 patients did not recover any further vision beyond LP. One patient, who presented with decreased vision of 20/400 recovered a visual acuity of 20/60.

## DISCUSSION

The incidence of endophthalmitis in our study, 2.4% (3 of 126 KPro eyes) more than 2582 months of accumulated follow-up for all 126 KPro eyes or 1.4% per patient-year, is lower than the incidence reported in other series: 11.4%[6] and 12%[4]—where vancomycin was not routinely used but more than 1 large series where gram-positive cocci were reported to have caused more than 80% of the cases (0.35% per patient-year).[7] Two of the 3 cases in our series occurred because of fungal organisms for an overall rate of 0.009 infections per patient-year of follow-up, which is identical to that reported by Barnes et al.[5]

Two patients (cases 2 and 3) in this series had a diagnosis of SJS. In a study published before the widespread use of vancomycin, eyes with autoimmune conjunctivitis were found to have a higher incidence of gram-positive bacterial endophthalmitis.[4] It is difficult to determine statistically significant predictors for fungal endophthalmitis in small case series, such as this study. Further investigation is certainly warranted to determine the risk factors for endophthalmitis with current anti-infective prophylaxis regimens. Another article reports just 1 case of sterile vitritis and no cases of endophthalmitis after KPro implantation in 16 eyes with SJS.[10] One patient in our series (case 3) had known issues with noncompliance that has been associated with more infections.[6] Case 1 likely had noncompliance issues as well because cultures from both the contact lens and the vitreous were positive for organisms sensitive to drugs that the patient was supposed to take.

The pathogens cultured from the vitreous in this series included a gram-negative bacillus, *O. anthropi*, and 2 *Candida* species (*C. parapsilosis* and *C. albicans*). Nouri et al[4] reported no gram-negative isolates, but Fintelmann et al[6] had 1 case of *Pseudomonas*. In the study of Barnes et al[5] on fungal colonization, *C. parapsilosis* predominated when both infections and surveillance colonization were considered. Both *O. anthropi* and *C. parapsilosis* have been reported to be related to indwelling catheters for venous access or other permanent plastic medical devices.[11,12] *Ochrobactrum anthropi* is also known to have caused endophthalmitis after intraocular surgery.[13–17]

One patient (case 2) was on systemic immunosuppression medications of mycophenolate mofetil, tacrolimus, and prednisone, at the time of her fungal endophthalmitis. In the report of Nouri et al[4], 1 patient developed *S. epidermidis* endophthalmitis while on systemic azathioprine and cyclosporine.

Infectious endophthalmitis is a devastating complication usually associated with poor visual outcomes.[2,3] Presenting complaints are usually decreased vision, pain, red eye, and hypopyon.[3] In our series, all patients complained of decreased vision, 1 had AC hypopyon, and 1 complained of increased floaters with an acute dense retroprosthetic membrane noted on examination. Only 1 patient presented with pain, which was likely because of hypotony from a chronic RD. These presenting findings are similar to those reported by Fintelmann et al,[6] whose patients complained of painless visual decline. Presenting features of infectious endophthalmitis after KPro implantation in patients on vancomycin and fluoroquinolone prophylaxis from other reports are summarized in Table 3.

**TABLE 3.** Summary of Presenting Features in Reported Cases of Infectious Endophthalmitis After Boston Type 1 Keratoprosthesis Implantation Where Vancomycin and a Fluoroquinolone Were Used in the Standard Postoperative Prophylaxis Regimen

| Study | Case | Diagnosis | ↓ Vision | Pain | Hypopyon | Vitritis | Other | Culture Result | Vancomycin Use at Diagnosis |
|---|---|---|---|---|---|---|---|---|---|
| This study | 1 | Congenital glaucoma | + | − | + | No view | Corneal infiltrate | *Staphylococcus aureus*, *Ochrobactrum anthropi** | + |
| | 2 | SJS | + | − | − | + | Floaters, RPM | *Candida parapsilosis* | + |
| | 3 | SJS | + | + | − | − | RD, hypotony | *Candida albicans* | − |
| Fintelmann et al[6] | 4 | Herpetic keratouveitis | + | − | n/a | + | Red eye | *Pseudomonas aeruginosa**, *S. aureus* | + |
| | 5 | PBK, aniridia | + | − | n/a | + | Red eye | MRSA | − |
| | 6 | Anterior staphyloma | + | − | n/a | + | Red eye | MRSA | − |
| | 7 | PBK | + | − | n/a | + | Red eye | None isolated | − |
| Barnes et al[5] | 8 | OCP | + | + | n/a | n/a | Corneal infiltrate | *Candida glabrata* | + |
| | 9 | Congenital glaucoma | + | + | + | + | White deposits on BCL, red eye | *C. parapsilosis*, diphtheroids, *Alcaligenes** | + |
| | 10 | OCP | + | − | + | − | Choroidal effusions, leak | Possible *C. albicans* | − |
| | 11 | Herpetic keratitis | + | − | − | n/a | Corneal infiltrate, AC reaction | *Fusarium* | + |

*Gram-negative organism.

BCL, bandage contact lens; MRSA, methicillin-resistant *Staphylococcus aureus*; n/a, not available; OCP, ocular cicatricial pemphigoid; PBK, pseudophakic bullous keratopathy; RD, retinal detachment; RPM, retroprosthetic membrane.

Poor vision at presentation of endophthalmitis has been reported to be associated with poor visual outcome.[18] In our series, 2 patients (cases 1 and 3) who presented with decreased vision to LP more than 1 week and 2 months, respectively, did not recover any vision at the final follow-up. The patient (case 2) who presented with decreased vision from 20/40 to 20/400 and increased floaters for 3 weeks was managed most aggressively with initial vitrectomy, retroprosthetic membrane peel, and intravitreal injections of vancomycin, ceftazidime, and amphotericin. This patient recovered vision of 20/60 at 11 months of follow-up. Prompt recognition and aggressive treatment, including vitrectomy, can contribute to retention of the KPro and a more favorable visual outcome. Case 3 demonstrated that fungal endophthalmitis may be insidious and coexist with another complication, such as an RD. Thus, precautionary vitreous cultures at the time of vitrectomy and RD repair may be beneficial. Patients should be counseled regarding the importance of compliance with infection prophylaxis and to seek prompt medical attention should they experience progressive decreased vision, increased floaters, or pain.

The low rate of bacterial endophthalmitis in this study supports the use of a fourth-generation fluoroquinolone and the previously recommended use of topical vancomycin prophylaxis after KPro implantation.[7,8] However, fungal infections and gram-negative organisms are a growing cause for concern. Further study is needed on optimal prophylaxis regimens, including the use of antifungals, especially for high-risk eyes, such as those with autoimmune cicatrizing disease.

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