Endophthalmitis After Descemet Stripping Endothelial Keratoplasty: Microbiological Yield and Visual Outcomes

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• PURPOSE: To describe the clinical presentation, management, and visual outcomes of 6 eyes with endophthalmitis after Descemet stripping endothelial keratoplasty (DSEK).
• DESIGN: Retrospective case series.
• METHODS: SETTING: Tertiary, academic eye center. STUDY POPULATION: Individuals developing endophthalmitis after DSEK at the Duke Eye Center from January 1, 2009, to January 1, 2018, with at least 6 months of follow-up. OBSERVATION PROCEDURE: Retrospective chart review. OUTCOME MEASURES: Diagnostic procedures, microbiological yield, and visual outcomes.
• RESULTS: Six eyes of 6 patients were identified. Mean time from surgery to presentation was 51 days (range, 4-137 days). Dense vitreous opacities were present in all cases. Five of 6 cases (83%) had culture-proven infectious endophthalmitis (2 *Candida glabrata*, 2 coagulase-negative *Staphylococcus*, 1 *Streptococcus pneumoniae*). Aqueous tap yielded positive culture in 2 of 2 cases with adequate sample (100%); needle vitreous tap yielded positive culture in 0 of 3 cases. One eye underwent vitrectomy on presentation, and 3 eyes (50%) underwent subsequent vitrectomy for persistent endophthalmitis after a mean of 37 days. Mean pre-endophthalmitis visual acuity (VA) was 20/64; mean VA at 6 months was 20/2069 (average 15 ETDRS lines lost). VA at 6 months was light perception or no light perception in 3 of 6 cases (50%). One eye underwent enucleation at 6 months, and 1 eye became phthisical 1 year after endophthalmitis.
• CONCLUSIONS: DSEK-related endophthalmitis may lead to severe vision loss, even with prompt and appropriate treatment. Aqueous tap had a higher culture yield than needle vitreous tap in our series. (Am J Ophthalmol 2021;222:34–40. © 2021 Elsevier Inc. All rights reserved.)

ENDOPHTHALMITIS IS A RARE COMPLICATION OF intraocular surgery defined by a prominent inflammatory reaction in the vitreous body, often in response to an environmental pathogen. In many cases, endophthalmitis arises as a complication after intraocular surgery, such as cataract surgery, glaucoma filtering surgery, or corneal transplantation.[1,2] Although prompt diagnosis and treatment with intravitreal antimicrobials or pars plana vitrectomy (PPV) can decrease the likelihood of vision loss, certain cases still have poor outcomes, sometimes requiring evisceration or enucleation of the globe.[3]

Endothelial keratoplasty (EK), or selective surgical replacement of the corneal endothelium, is effective in patients with corneal decompensation in the setting of endothelial cell dysfunction. Descemet stripping endothelial keratoplasty (DSEK) is a common subtype of EK that allows for quicker rehabilitation and a better safety profile when compared with traditional penetrating keratoplasty (PK).[4,5] As with any intraocular procedure, there is a risk of intraocular infection after DSEK. In 2013, the Eye Bank Association of America reported that approximately 1.4 cases per 10,000 corneal transplants (including EK and PK) developed postoperative fungal keratitis or endophthalmitis.[6] Other studies have estimated an overall incidence of endophthalmitis after PK between 0.67% and 0.7%.[7,8] Borkar et al[8] recently reported an incidence of endophthalmitis after EK of 0.2%, which was significantly lower than the rate of endophthalmitis after PK (0.7% vs 0.2%, $P = .01$). In 2009, a systematic review of 34 studies found no cases of endophthalmitis after DSEK.[9] However, numerous case reports have been published regarding DSEK-related endophthalmitis in recent years.[10–15] In these reports, DSEK-related endophthalmitis was commonly due to a fungal etiology (predominantly *Candida* species)[12,14,15]; however, bacterial etiologies were also reported.[10,11,13]

Because of the rarity of DSEK-related endophthalmitis, there is a dearth of evidence regarding practice patterns and visual outcomes in this condition. In the Endophthalmitis Vitrectomy Study (EVS), which assessed patients with endophthalmitis after cataract surgery, eyes undergoing PPV on presentation had better visual outcomes only if presenting visual acuity (VA) was light perception (LP).[16] Although it is possible that physicians encountering DSEK-related endophthalmitis refer to this practice pattern, there is little published evidence to guide the treatment of DSEK-related endophthalmitis, specifically. In addition, the microbiological pathogens and visual outcomes in DSEK-related endophthalmitis may differ from

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endophthalmitis after cataract surgery. Thus, it is important to better understand clinical practice patterns and outcomes specific to DSEK-related endophthalmitis.[17]

This study describes the ocular history, presenting findings, initial management, microbiological yield, and visual outcomes of individuals with DSEK-related endophthalmitis at a single tertiary academic medical center over a 9-year period (2009-2018).

METHODS

PRIOR ETHICAL APPROVAL FOR THIS RETROSPECTIVE STUDY (Pro00091062) was obtained from the Duke University Health System institutional review board, and the requirement for informed consent was waived. This study complied with the Health Insurance Portability and Accountability Act of 1996 and followed the tenets of the Declaration of Helsinki.

• **PATIENT IDENTIFICATION AND DATA COLLECTION:** All patients seeking care at the Duke University Eye Center between January 1, 2009, and January 1, 2018, were analyzed using the Duke Enterprise Data Unified Content Explorer (DEDUCE, Duke University Health System, Durham, North Carolina, USA). Individuals with a diagnosis of endophthalmitis were identified. Medical records were manually reviewed to determine patient inclusion in the study. Included patients were between 18 and 89 years of age and had at least 6 months of follow-up after initial diagnosis of endophthalmitis. From this group, we identified patients with endophthalmitis related to recent DSEK surgery as determined by an experienced retina specialist at the time of diagnosis. Eyes with a recent history of trauma, recent intravitreal injection, or other more likely source of endophthalmitis were excluded. By retrospective chart review, we assessed VA before endophthalmitis, VA on presentation with endophthalmitis, and VA 6 months after initial diagnosis. In addition, we recorded initial management, subsequent management, and eventual complications associated with DSEK-related endophthalmitis.

• **STATISTICAL ANALYSIS:** XLSTAT (Addinsoft, Paris, France) was used to perform statistical analysis for this study. Descriptive statistics were performed to assess demographic data and to compare variables across patients. Continuous variables were compared using 2-tailed *t* tests, and categorical variables were compared using Fisher's exact tests. Visual acuity was converted from Snellen equivalent to the logarithm of the minimum angle of resolution for the purpose of statistical analysis.

RESULTS

FIVE HUNDRED AND THIRTEEN PATIENTS WITH ENDOPHthalmitis were identified on our initial query; of these, 383 patients were excluded because of inadequate clinical data or limited follow-up. Of our final cohort of 133 eyes of 130 patients, 6 eyes (4.5%) of 6 patients had endophthalmitis related to a recent DSEK procedure based on initial assessment documented by an experienced retina specialist. For the 6 eyes with DSEK-related endophthalmitis, 50% were right eyes, 67% were female, mean age was 76 years (range, 59-85 years), and mean time from surgery to presentation was 51 days. All cases received intravitreal antimicrobials after initial diagnostic testing with aqueous tap, needle vitreous tap, and/or PPV with mechanical vitreous biopsy. Pertinent ocular history, surgical information, and corneal status on presentation for 6 eyes with DSEK-related endophthalmitis are detailed in Table 1. Clinical images from 4 of the 6 eyes are shown in Figure 1.

All eyes underwent DSEK for endothelial decompensation—the presumed cause of endothelial failure was Fuchs' endothelial dystrophy in 3 of 6 cases (50%), pseudophakic bullous keratopathy in 2 of 6 cases (33%), and prior glaucoma drainage device placement (tube tip not touching corneal endothelium) in 1 of 6 cases (17%). One eye with pseudophakic bullous keratopathy also had an existing glaucoma drainage device; however, the tip of the tube in the anterior chamber was not touching the corneal endothelium. Surgical history for the 6 eyes is detailed in Table 1; only 1 eye was surgery-naïve, and 4 eyes had a prior history of either glaucoma filtering surgery (2 eyes with prior trabeculectomy, 2 eyes with prior glaucoma drainage device) or corneal surgery (1 eye underwent prior PK; 2 had undergone prior DSEK). Two eyes underwent primary DSEK, 2 eyes underwent repeat DSEK due to a prior failed graft, 1 eye underwent DSEK on a failed PK, and 1 eye underwent combination DSEK and cataract extraction with intraocular lens implantation. No other combination procedures (eg, DSEK + glaucoma surgery + PPV) were identified with DSEK-related endophthalmitis.

On presentation, the DSEK interface was centrally attached in all cases. One graft had a small inferotemporal detachment, and 1 graft had Descemet folds. Five of 6 cases had notable corneal findings on initial examination, which are detailed in Table 1. Corneal culture performed in 2 cases grew *Streptococcus pneumoniae* and *Propionibacterium acnes*. Dense vitreous opacities were present in all 6 cases.

All 6 patients presented with blurred vision and ocular pain, 1 of 6 eyes (17%) had elevated intraocular pressure (>21 mm Hg), 1 of 6 (17%) had low intraocular pressure (<9 mm Hg), 2 of 6 (33%) had a hypopyon, and 3 of 6 (50%) had anterior chamber fibrin.

Initial management, microbiological yield of diagnostic procedures, and visual outcomes are detailed in Table 2. All 6 eyes received intravitreal vancomycin (1 mg) on

TABLE 1. Demographic Data, Ocular History, Surgical Information, Corneal Status, and Presenting Exam Findings in 6 Eyes With DSEK-Related Endophthalmitis

Case	Age (y)	Sex	Time From DSEK to Diagnosis (d	Presumed Cause of Endothelial Failure	Surgical History	Procedure	Interface Status on Presentation	Corneal Status on Presentation	Corneal Culture Results	Vitreous Involvement?
1	59	F	76	Fuchs' dystrophy	None	DSEK/CE	Attached	Diffuse edema, diffuse KP	N/A	2+ vitritis
2	69	F	31	Fuchs' dystrophy	PPV	Primary DSEK	Attached centrally, inferotemporal small detachment	Temporal 4 × 1mm corneal ulcer	*Streptococcus pneumoniae*	Dense vitreous membranes on B-scan
3	75	F	4	Fuchs' dystrophy	Trabeculectomy x2	Primary DSEK	Attached	Normal	N/A	2+ vitritis
4	82	M	137	Ahmed tube	PK, tube	DSEK on Prior PK	Attached	Diffuse corneal stromal infiltrate with no epithelial defect	*Propionibacterium acnes*	No view; vitritis on B-scan
5	84	M	38	PBK/Baerveldt tube	DSEK, tube	Repeat DSEK	Attached	Inferior edema, diffuse KP	N/A	1+ vitritis
6	85	F	19	PBK	DSEK x2, trabeculectomy, EDTA chelation for band keratopathy	Repeat DSEK (#3)	Attached with Descemet folds	Diffuse edema, band keratopathy temporally	N/A	No view; vitritis on B-scan

CE = cataract extraction; DSEK = Descemet stripping endothelial keratoplasty; EDTA = ethylenediaminetetraacetic acid; KP = keratic precipitates; PBK = pseudophakic bullous keratopathy; PK = penetrating keratoplasty; PPV = pars plana vitrectomy.

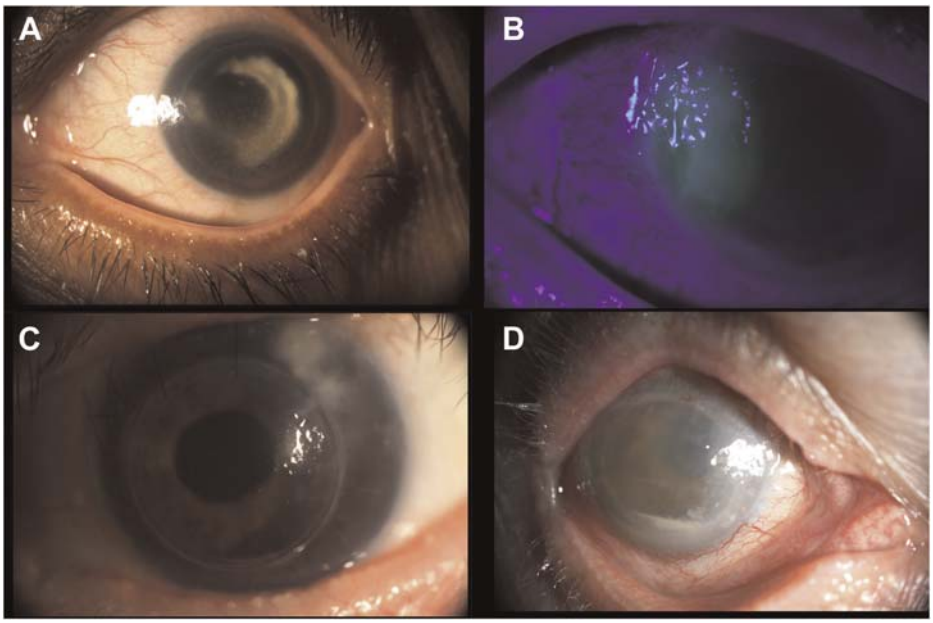

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FIGURE 1. Clinical images of 4 eyes with endophthalmitis after Descemet stripping endothelial keratoplasty. In panel A (corresponding to case 1 in the tables), a left eye is shown with diffuse corneal edema and white precipitates on the intraocular lens. Initial needle vitreous tap was culture-negative in this case; subsequent vitrectomy cultures grew *Candida glabrata*. In panel B (corresponding to case 2 in the tables), a right eye is shown with fluorescein staining of infectious keratitis that developed after DSEK and led to endophthalmitis. *Streptococcus pneumoniae* grew on aqueous tap cultures. In panel C (corresponding to case 4 in the tables), a left eye is shown with a superotemporal corneal infiltrate on the host side with small extension into the graft—this patient was found to have corneal cultures positive for *Propionibacterium acnes*, and aqueous tap positive for coagulase-negative *Staphylococcus*. This patient also had a prior penetrating keratoplasty in 2003. In panel D (corresponding to case 6 in the tables), a right eye is shown with diffuse corneal edema, a hypopyon, and conjunctival injection. Aqueous and vitreous cultures in this case were insufficient for analysis.

presentation, 5 of 6 eyes (83%) received intravitreal ceftazidime (2.25 mg), and 2 of 6 eyes (33%) received intravitreal amphotericin B (5 μg). Five of 6 eyes (83%) received topical steroids, and 2 of 6 eyes (33%) received systemic steroid therapy. No eyes received intravitreal or sub-Tenon steroids. After initial antimicrobial administration, 2 eyes underwent subsequent intravitreal injections for persistent inflammation. In both cases, fungal culture from subsequent PPV with mechanical vitreous biopsy (performed 15 days and 84 days after initial presentation, respectively) grew *Candida glabrata*—1 patient underwent 2 subsequent injections of amphotericin B (5 μg) after having received intravitreal vancomycin and ceftazidime on initial presentation, and 1 patient underwent 4 subsequent injections of amphotericin B (5 μg) after having received intravitreal vancomycin, ceftazidime, and amphotericin B on initial presentation.

On presentation, 3 eyes (50%) underwent aqueous tap, 4 eyes underwent needle vitreous tap (67%), and 1 eye (17%) underwent PPV with mechanical vitreous biopsy. Two eyes (33%) underwent both aqueous and needle vitreous taps. Three eyes (50%) required subsequent PPV at a mean of 37 days after initial presentation for definitive culture and/or treatment of persistent intraocular inflammation and lack of clinical improvement.

In terms of microbiological yield, 5 of 6 eyes (83%) were culture-positive, and the remaining 1 eye had insufficient aqueous and vitreous samples for microbiological analysis (after both aqueous and needle vitreous taps). Two of 2 (100%) aqueous taps with sufficient sample grew pathogens, whereas no needle vitreous taps grew pathogens. Three of 4 (75%) PPV specimens grew pathogens; in 1 case that did not grow a pathogen, aqueous tap performed 15 days prior had grown *S. pneumoniae*. Pathogens responsible for DSEK-related endophthalmitis included *C. glabrata* (x2), coagulase-negative *Staphylococcus* (x2), and *S. pneumoniae* (x1).

Mean VA before developing endophthalmitis was 20/64. Mean VA on presentation was 20/5,450, and mean VA at 6 months was 20/2,069. On average, patients lost 15 ETDRS lines of vision from pre-endophthalmitis VA to 6 months after the diagnosis of endophthalmitis. On presentation, 2 of 6 eyes (33%) were LP; at 6 months, 2of 6 eyes (33%) were LP, and 1 of 6 eyes (17%) was no light perception (NLP). After endophthalmitis, 1 eye was enucleated at 6 months due to NLP vision and painful eye, and 1 eye became phthisical after 1 year. No eyes developed a retinal detachment after endophthalmitis.

The presence of anterior chamber fibrin on presentation was associated with worse presenting VA (20/12,700 vs 20/

TABLE 2. Initial Management, Microbiological Yield, and Visual Outcomes in 6 Cases of DSEK-Related Endophthalmitis

Case	Initial Management	Subsequent Intravitreal Injection	Diagnostic Method?	Days From Presentation to PPV	Organism Isolated (Method)	VA Before Endophthalmitis[a]	Presenting VA	VA at 6 Months
1	V/C	Yes x2 (AB)	Needle vitreous tap	15	*Candida glabrata* (PPV)	20/60	20/800	20/60
2	V	No	Aqueous tap	12	*Streptococcus pneumoniae* (Aqueous tap)	20/40	20/16,000	20/32,000[b]
3	V/C/AB	No	PPV	0	*Coagulase-negative Staphylococcus* (PPV)	20/50	20/4,000	20/60
4	V/C	No	Aqueous tap and needle vitreous tap	N/A	*Coagulase-negative Staphylococcus* (Aqueous tap)	20/30	20/16,000	20/16,000
5	V/C/AB	Yes x4 (AB)	Needle vitreous tap	84 (with tube removal)	*Candida glabrata* (PPV)	20/200	20/4,000	20/2,667
6	V/C	No	Aqueous tap and needle vitreous tap	N/A	None	20/200	20/8,000	20/16,000[c]

AB = amphotericin B; C = ceftazidime; DSEK = Descemet stripping endothelial keratoplasty; PPV = pars plana vitrectomy; V = vancomycin; VA = visual acuity.

[a]Visual acuity before endophthalmitis was assessed at the patient's most recent clinic visit before presenting with presumed endophthalmitis.

[b]Eviscerated due to no light perception (NLP, 20/32,000) vision.

[c]Phthisis 1 year after endophthalmitis.

2,339, $P = .044$) and worse VA at 6 months (20/20,159 vs 20/213, $P = .024$). PPV during the course of treatment (n = 4, 1 initial and 3 subsequent) trended toward better VA at 6 months compared with those that did not undergo PPV (20/745 vs 20/16,000); however, this finding was not statistically significant ($P = .255$).

DISCUSSION

IN THIS RETROSPECTIVE STUDY, WE REPORT THE CLINICAL presentation, initial management, microbiological yield, and visual outcomes in eyes with DSEK-related endophthalmitis. We found that these eyes developed prominent visual morbidity, with 3 of 6 eyes (50%) being LP or NLP at 6 months. In addition, 1 eye underwent evisceration 6 months after endophthalmitis, and 1 eye became phthisical 1 year after endophthalmitis. Three of 6 eyes (50%) required PPV after initial presentation for persistent inflammation related to endophthalmitis; this may suggest that early vitrectomy may have been beneficial in these patients. However, further prospective research will be necessary to determine the optimal role of vitrectomy in this condition.

In 3 eyes with anterior chamber fibrin on initial examination, we observed worse VA at presentation and at 6 months. In a case report by Kaiura and associates,[10] anterior chamber fibrin was noted 1 day before a severe purulent episode of DSEK-related endophthalmitis treated with vitrectomy and intravitreal antibiotics—in that case, the causative agent was *S. pneumoniae*. We observed anterior chamber fibrin in 1 case with *S. pneumoniae*, 1 case with *coagulase-negative Staphylococcus*, and 1 case with negative cultures due to insufficient sample for analysis. This finding is consistent with prior studies describing bacterial endophthalmitis as more proinflammatory than the typically indolent course of fungal endophthalmitis.[18] As a result of more diffuse and severe inflammation, bacterial DSEK-related endophthalmitis may lead to worse visual outcomes. Larger studies describing causal organisms and visual outcomes in DSEK-related endophthalmitis may be beneficial to help guide clinical decision-making.

Notably, in our series, aqueous taps were more likely to yield positive cultures than vitreous taps. Traditionally, aqueous tap has been considered an insensitive and poorly predictive test for suspected infectious endophthalmitis.[19–21] However, it is possible that in the case of a contaminated DSEK graft leading to endophthalmitis, anterior chamber bacterial growth may be prominent. As the cornea is the source of infection in DSEK-related endophthalmitis, it is intuitive that aqueous taps may be more appropriate for yielding positive cultures than vitreous taps. There are no studies directly comparing the microbiological yield of aqueous and vitreous taps in cases of DSEK-related endophthalmitis; this can be a focus of future investigation,

as aqueous tap may be preferred in these cases. In our small sample size, we are unable to definitively conclude that aqueous tap is better than vitreous tap in these cases.

In 1 case with corneal ulcer after DSEK, which later developed into endophthalmitis, ulcer cultures and subsequent aqueous tap grew *S. pneumoniae*. We suspect that the ulcer, which developed shortly after surgery, eroded through the graft interface and seeded the anterior chamber, eventually leading to endophthalmitis. The patient developed dense vitreous membranes and was eventually NLP, and the globe was eviscerated 6 months after endophthalmitis.

This study is limited by its retrospective nature and small sample size. We are unable to conclude whether earlier vitrectomy would have resulted in visual benefit for the 3 eyes that underwent subsequent vitrectomy for persistent endophthalmitis. In addition, our sample size is too small for statistical comparisons of various treatment options and risk factors that could potentially affect visual outcomes. Although we observed that aqueous tap had higher culture yield than vitreous tap in these cases, it is not possible to draw definitive conclusions given our small sample size. Some reports have previously described the treatment of DSEK-related endophthalmitis with therapeutic PK.[12,13,15] None of our patients underwent therapeutic PK or explantation of the DSEK graft, so we were unable to describe whether these measures would be useful in improving visual outcomes. Although we reference the EVS as a potential source for practice patterns in DSEK-related endophthalmitis in the Introduction, it is important to note that eyes with NLP were excluded from the EVS and that corneal opacities in DSEK-related endophthalmitis may make early vitrectomy difficult in this patient population. Future research should seek to include larger patient numbers; however, this may be difficult at a single tertiary eye center, given the rarity of this condition.

In this paper, we describe, to our knowledge, the largest case series of DSEK-related endophthalmitis to date. Because of the rarity of this condition, multicenter prospective clinical trials will be necessary to guide medical and surgical management of these cases; however, these trials would be exceedingly difficult to conduct with sufficient sample sizes. Other directions for research may include larger, multicenter retrospective data sets or population-level studies using large registries or insurance claims data. From our data, we may conclude that DSEK-related endophthalmitis often causes severe visual loss. As such, early identification of this exceedingly rare condition and prompt referral to a retina specialist may be beneficial in suspected cases of endophthalmitis after DSEK.

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