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Endophthalmitis caused by *Klebsiella* species

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Abstract

Purpose—To report the clinical presentation, antibiotic sensitivities, treatment strategies, and visual outcomes associated with endophthalmitis caused by *Klebsiella* species.

Methods—A non-comparative consecutive case series. Microbiology database records were retrospectively reviewed for all patients with endophthalmitis caused by *Klebsiella* species from 1990 to 2012 at a large university referral center. The corresponding clinical records were then reviewed to evaluate the endophthalmitis clinical features and treatment outcomes.

Results—Seven patients were identified. Clinical settings included endogenous (n=3), post-traumatic (n=2), trabeculectomy bleb-associated (n=1), and post-penetrating keratoplasty (n=1). Five patients presented with hypopyon. Presenting visual acuity ranged from 20/60 to light perception in non-endogenous cases and 1/200 to light perception in endogenous cases. *Klebsiella* was sensitive to aminoglycosides, 3rd generation cephalosporins, and 2nd and 3rd generation fluoroquinolones in all cases. Initial treatment strategies were vitreous tap and injection (n=4), pars plana vitrectomy with intravitreal antibiotics (n=2), and anterior chamber tap and injection (n=1). All three endogenous cases later underwent enucleation or evisceration. In non-endogenous cases, final visual acuity was 20/70 or better in all four patients.

Conclusions—Endophthalmitis caused by *Klebsiella* species is associated with poor visual outcomes. Endogenous cases had high rates of enucleation or evisceration.

Keywords

Endophthalmitis; Endogenous; *Klebsiella*; Bacterial Eye Infections

Introduction

Klebsiella species are gram-negative, encapsulated, anaerobic bacteria that may form part of the normal nasopharyngeal and gastrointestinal flora.¹ In recent years *Klebsiella* species have emerged as a leading cause of pyogenic liver abscesses in Asia.^{2,3} *Klebsiella pneumoniae* liver abscesses are associated with a 3 to 11 percent incidence of endogenous

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endophthalmitis.^{4,5} This rate of ocular involvement is much higher than ocular involvement with other systemic infections.⁶ More significantly, endophthalmitis caused by *Klebsiella* species is associated with increased mortality in patients with liver abscesses.⁷

Endophthalmitis caused by *Klebsiella* species has been recognized as an increasingly prevalent cause of endogenous endophthalmitis in Asia, accounting for 54 to 61 percent of cases in selected series.^{5,8-11} Reported risk factors for endogenous endophthalmitis caused by *Klebsiella* species include liver abscesses, diabetes mellitus, and systemic immunocompromise.^{5,8,12,13} In contrast, endophthalmitis caused by *Klebsiella*, whether endogenous and non-endogenous, is uncommon in the USA, described only in a small number of isolated case reports and series.¹⁴⁻¹⁹ Still, it is an emerging entity in the USA associated with poor visual outcomes.^{12,13,19}

Based on a PubMed literature search, the current study is the largest reported series in the USA to date of culture-positive cases of endophthalmitis caused by *Klebsiella*.

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 intraocular cultures (anterior chamber, vitreous, or both) for *Klebsiella* species between January 1, 1990, and December 31, 2012. Microbiology department records were reviewed to identify the responsible microbial isolates and antibiotic sensitivities.

Anterior chamber cultures were obtained from an anterior chamber paracentesis. 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 including 5% sheep blood and chocolate agars. For vitrectomy specimens, 30–50 cc of vitreous washings were filtered using a 0.45- μ m filter. The resultant filter paper was divided into sections and was plated on to different culture media, which typically included chocolate and blood agars. Blood and chocolate agars underwent incubation at 35°C for a period of up to 2 weeks. Additional culture media, including thioglycollate broth, were performed at the discretion of the ophthalmologist performing the culture. All cultures were read and classified by Ocular Microbiology Department staff.

After analyzing microbiology records, the corresponding medical records of these patients were reviewed to ensure clinical course consistent with endophthalmitis. Patient demographics, clinical characteristics, risk factors, treatment strategies, and clinical outcomes were assessed.

Results

Over the 22-year study period, 10 eyes from 10 patients were identified to have positive intraocular cultures for *Klebsiella* species and clinical course consistent with endophthalmitis. three eyes had been reported previously from the same institution by Scott et al¹⁵ and were excluded. In the remaining 7 eyes, cultures were positive for *Klebsiella*

pneumoniae (n=5) or *Klebsiella oxytoca* (n=2, Table 1). Cultures were obtained from vitreous tap (n=4), vitrectomy specimen (n=2), or anterior chamber tap (n=1).

The median patient age was 60 years (range, 31 to 78 years). Median follow-up was 4 months (range, 1 month to 6 years). Endophthalmitis occurred in the clinical setting of penetrating trauma (n=2), post-trabeculectomy (n=1), post-penetrating keratoplasty (n=1), and endogenous (n=3). Two of the three patients with endogenous endophthalmitis were diabetic and had negative systemic workup including blood cultures. The third patient was found to have a liver abscess with positive blood cultures.

Five patients presented with pain. Visual acuity on presentation ranged from 20/60 to light perception (Table 2). Hypopyon was noted in five patients on presentation. Two patients had diffuse vitritis with no view of the posterior segment. One patient was noted to develop a subretinal abscess (Figure 1). One patient presented with orbital cellulitis in addition to endophthalmitis (Figure 2).

Four patients underwent diagnostic vitreous tap with injection of intravitreal antibiotics the same day as presentation. Two patients, with visual acuity of 1/200 and light perception respectively, were evaluated in the evening the day of presentation, received topical fortified antibiotics overnight, and the following morning underwent pars plana vitrectomy with injection of intravitreal antibiotics. One patient status post penetrating trauma underwent anterior chamber tap with injection of intracameral antibiotics during repair of a corneal laceration the same day as presentation. Intraocular antibiotics consisted of vancomycin and ceftazidime for all patients except the one patient post-penetrating keratoplasty who received intravitreal vancomycin and gentamicin. Only the patient with endogenous endophthalmitis with liver abscess received intravitreal corticosteroids.

Initial intraocular cultures were positive for *Klebsiella* species in all patients. All isolates were sensitive to one of the initially administered intraocular antibiotics. The two *Klebsiella oxytoca* isolates were resistant to penicillin but sensitive to gentamicin, ceftazidime, ciprofloxacin, sulfa-trimethoprim, and levofloxacin. All five *Klebsiella pneumoniae* isolates were sensitive to gentamicin, ceftazidime, ciprofloxacin, levofloxacin, and sulfa-trimethoprim. Three of the five *Klebsiella pneumoniae* isolates were resistant to penicillin.

The patient initially treated with anterior chamber tap and intracameral antibiotics, one patient initially treated with vitreous tap and injection, and one patient initially treated with pars plana vitrectomy demonstrated clinical improvement and did not require further intraocular treatment. Final visual acuity in these three patients was 20/25, 20/60, and 20/70, respectively. One patient who underwent initial vitreous tap and injection showed no clinical improvement. This patient underwent subsequent pars plana vitrectomy 3 days after presentation with no evidence of persistent infection on repeat vitreous culture and had a good post-operative result with final visual acuity of 20/70. Two patients who underwent initial vitreous tap and injection developed panophthalmitis and underwent evisceration and enucleation, respectively, within one week of presentation with the evisceration specimen culture showing persistent infection. One patient who underwent initial pars plana vitrectomy demonstrated clinical worsening and eventually underwent enucleation 1 month

after presentation for the blind painful eye. All three patients undergoing evisceration or enucleation had endogenous endophthalmitis. Two of these patients received systemic antibiotics. One patient, a diabetic woman with multiple myeloma, received intravenous ceftazidime for 14 days. The patient with the liver abscess received intravenous ceftriaxone for 7 days and oral gatifloxacin for 14 days concurrently with resolution of orbital cellulitis and the liver abscess.

Discussion

Klebsiella-specific virulence factors contribute to the organism's propensity for ocular involvement. *Klebsiella* species possess a polysaccharide capsule with specific capsular serotypes conferring resistance to phagocytosis by neutrophils.²⁰ Specifically, *Klebsiella pneumoniae* serotypes K1 and K2 have increased virulence and decreased susceptibility to intracellular destruction by neutrophils than other *Klebsiella* serotypes. This ability to avoid phagocytosis among K1 and K2 serotypes has been demonstrated to be enhanced in diabetes mellitus patients with poor glycemic control.²¹ In fact, diabetes mellitus is a significant risk factor for endogenous endophthalmitis caused by *Klebsiella* as well as a poor visual prognostic factor in patients with ocular involvement.^{5,8,22} Two of the three patients in the current series with endogenous endophthalmitis were diabetic and had poor visual outcomes. Other known risk factors for ocular involvement include systemic immunocompromise, disseminated intravascular coagulation, and delayed treatment of systemic *Klebsiella* bacteremia.⁴

The high incidence of endogenous endophthalmitis caused by *Klebsiella* in Asia is at least partially attributed to the relatively high incidence of *Klebsiella* bacteremia in the Asian population, although genetic susceptibility has been suggested as a contributing factor as well.⁵ In recent years it has been recognized that the K1 and K2 serotypes of *Klebsiella pneumoniae* constitute the majority of endogenous endophthalmitis cases in Asia, representing a significant public health challenge.²³

In contrast, only a small number of cases of endophthalmitis caused by *Klebsiella*, endogenous or non-endogenous, have been reported in the USA.¹⁴⁻¹⁹ Chen and Adelman²⁴ reported *Klebsiella* species growth in only 3.1% of all vitreous samples reviewed over a 21 year period at a large tertiary referral center in New England. Okada et al²⁵ and Schiedler et al²⁶ independently reported large domestic series of endogenous endophthalmitis with an incidence of endophthalmitis caused by *Klebsiella* of 3.6% and 5%, respectively. Of note, none of the cases in the 'Endophthalmitis Vitrectomy Study' were due to *Klebsiella* species.²⁷

In the largest prior series from the USA, five patients were seen at the same institution as patients in the current series¹⁵. In that series, one patient had endogenous endophthalmitis and underwent enucleation, similar to the results found for the endogenous cases in the current series. Visual acuity ranged from 20/60 to light perception in the remaining cases. *Klebsiella* isolates in that series were sensitive to aminoglycosides, 3rd-generation cephalosporins, 2nd, 3rd, and 4th generation fluoroquinolones, and sulfa-trimethoprim. This prior sensitivity profile is essentially identical to the sensitivity data in the current series. By

contrast, there appears to be a worldwide increase, primarily reported in Asia, of *Klebsiella pneumoniae* species with variable resistance to 3rd-generation cephalosporins and fluoroquinolones.²⁸

Several reported series have demonstrated extremely poor visual acuity outcomes with high rates of enucleation or evisceration in cases of endogenous endophthalmitis caused by *Klebsiella* despite adequate treatment. In a large series of endogenous cases, final visual acuity of 4/200 or worse was reported in 77.5% of eyes and 26.8% of eyes ultimately had evisceration¹⁰. In addition, Yang et al¹³ reported final visual acuity of light perception or worse in 89% of study eyes with 41% undergoing evisceration or enucleation and patients with hypopyon having significantly worse outcomes. *Klebsiella pneumoniae* has been shown in vitro to induce a significant pro-inflammatory response in human retinal pigmented epithelium, likely contributing to the rapid progression and poor prognosis of associated endophthalmitis.²⁹ Similar inflammatory response has been shown in animal models for *Klebsiella oxytoca*.³⁰ In concordance with the Asian studies, all three patients in the current series with endogenous endophthalmitis ultimately underwent evisceration or enucleation. In contrast, the other four patients all had final visual acuity of 20/70 or better. Only case reports and small cases series have described outcomes of non-endogenous *Klebsiella* endophthalmitis with variable results.^{14,31} It is unclear why there was a substantial difference in the outcomes between endogenous and non-endogenous cases in the current series. The authors hypothesize that only more virulent serotypes, such as the K1 and K2 *Klebsiella pneumoniae* serotypes, are able to break through the blood-retinal barrier and produce endogenous endophthalmitis whereas any serotype, regardless of virulence, may gain access to the eye either after trauma or surgical manipulation. Thus, endogenous cases may progress much faster and result in poorer visual outcomes.

It has been proposed that early vitrectomy may be preferred in endogenous cases given the fulminant nature of these infections. Yoon et al¹² reported 10 eyes, 8 of which underwent vitrectomy within one week of onset of symptoms. At final follow-up no eyes were enucleated, 5 eyes had count fingers vision or better, and the retina was attached in all cases. Similarly, Yarnig et al³² reported a patient with bilateral endogenous *Klebsiella pneumoniae* endophthalmitis who underwent vitrectomy in one eye with improved visual outcome compared to the fellow eye. It is hypothesized that surgical intervention aids in the clearance of purulent material and the penetration of intravitreal antibiotics.

In conclusion, endophthalmitis caused by *Klebsiella* is an increasingly prevalent entity both worldwide and in the USA. In endogenous cases it is associated with poorest outcomes and high rates of evisceration or enucleation.

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Summary Statement: A 22-year retrospective review of patients with endophthalmitis caused by *Klebsiella* species at a large tertiary academic center is presented. This report demonstrates the poorest visual outcomes in endogenous cases.

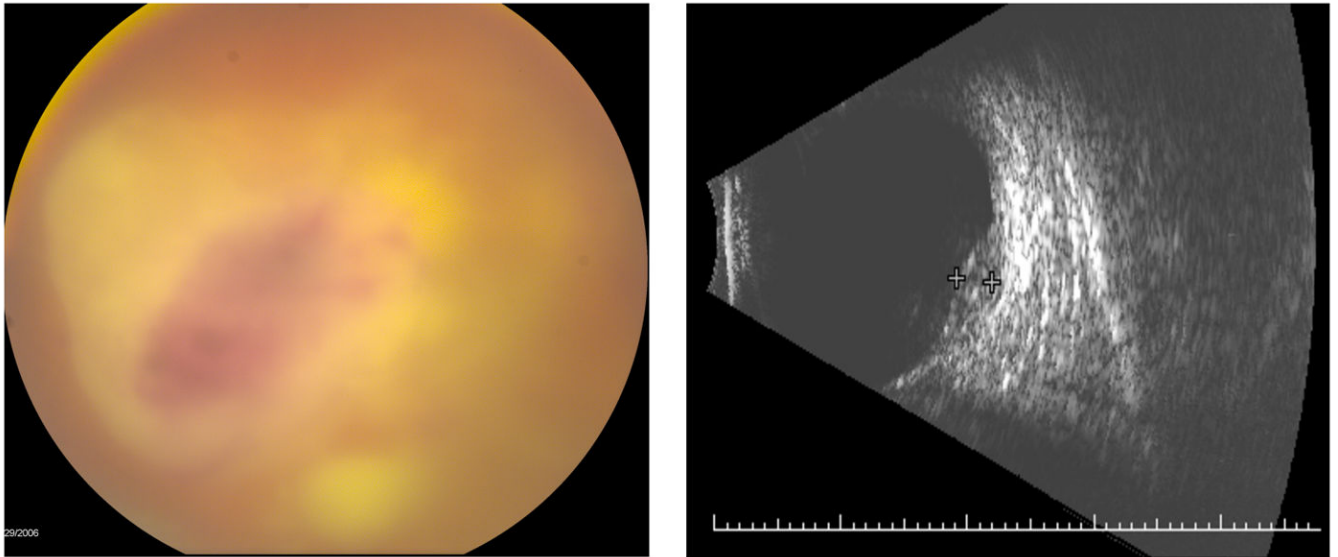


Figure 1.

Patient 2 was a 58 year-old woman with history of diabetes mellitus and recent localized cellulitis on the arm who presented with pain and 1/200 visual acuity in the right eye. Posterior segment examination revealed a hazy view with moderately dense vitritis obscuring a subretinal abscess (left). B-Scan ultrasonography confirmed the subretinal abscess adjacent to the optic nerve (right). The patient underwent pars plana vitrectomy with intravitreal injection of antibiotics. Vitreous specimen culture grew *Klebsiella pneumoniae*. One month after presentation the patient was enucleated for blind, painful eye.

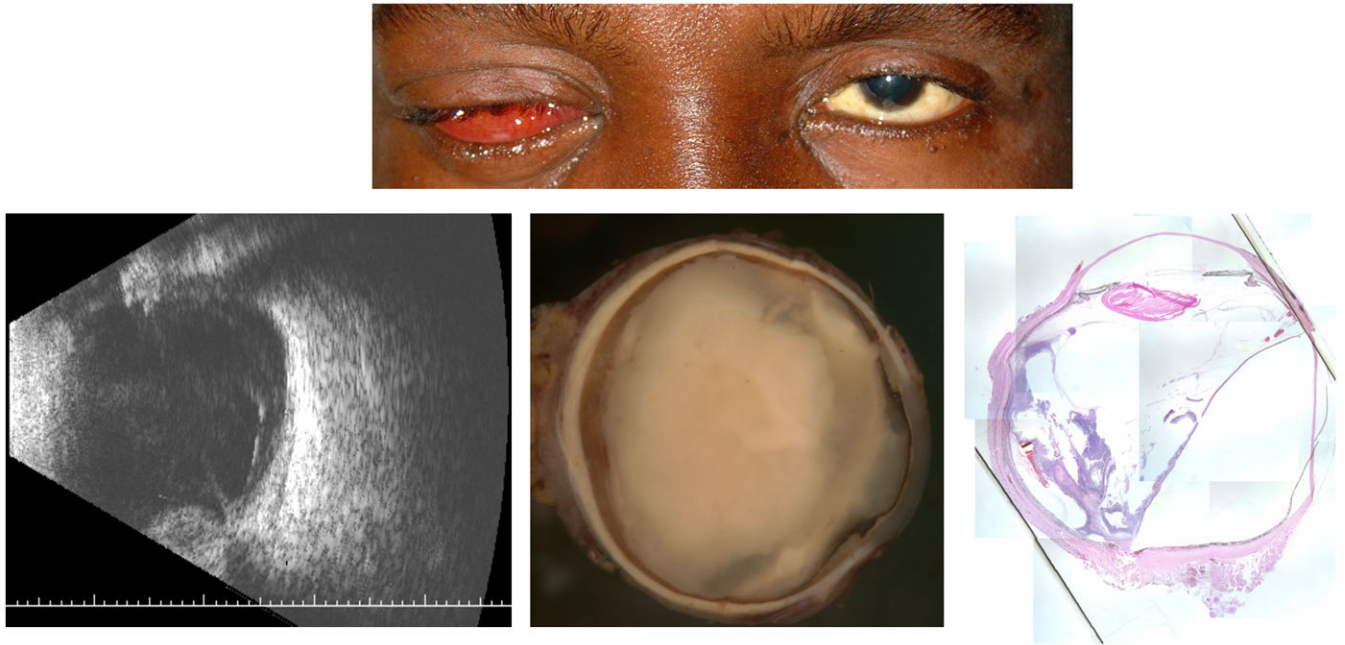


Figure 2.

Patient 1 was a 43-year-old man with no past medical history who presented with pain, chemosis, and finger count vision in the right eye (top). Posterior segment examination revealed dense vitritis with no view in the right eye. Initial B-scan ultrasonography confirmed no evidence of retinal detachment. The patient underwent vitreous tap and injection of intravitreal antibiotics. Vitreous culture grew *Klebsiella pneumoniae*. Systemic workup revealed positive blood cultures for *Klebsiella pneumoniae* and large liver abscess. The patient clinically worsened and repeat B-scan ultrasonography revealed a bullous retinal detachment and evidence of panophthalmitis (bottom left). The patient underwent enucleation one week after presentation (bottom center). Histopathologic examination with hematoxylin and eosin at 1.25x magnification revealed a subretinal inflammatory collection underlying the detachment (bottom right).

Table 1
Endophthalmitis caused by *Klebsiella* species: Clinical Characteristics, Initial Treatment Strategies, and Outcomes

Patient	Demographics	Etiology	Organism (source)	Presenting VA	Initial Treatment	Clinical Improvement	Follow-up (months)	Last VA
1	43 year-old man diagnosed with liver abscess after ocular presentation	Endogenous	<i>K. pneumoniae</i> (vitreous tap)	2/200	Vitreous tap/injection	No	1	enucleated
2	58 year-old woman with history of DM and recent spider bite and cellulitis on arm	Endogenous	<i>K. pneumoniae</i> (PPV specimen)	1/200	PPV with intravitreal injection	No	4	enucleated
3	60 year-old woman with history of multiple myeloma on chemotherapy and DM	Endogenous	<i>K. pneumoniae</i> (vitreous tap)	Light perception	Vitreous tap/injection	No	20	eviscerated
4	60 year-old man status post penetrating trauma with retained IOFB (glass)	Penetrating Trauma	<i>K. pneumoniae</i> (PPV specimen)	Light perception	PPV with intravitreal injection	Yes	2	20/60
5	31 year-old woman status post penetrating trauma	Penetrating Trauma	<i>K. oxytoca</i> (anterior chamber tap)	20/60	Anterior chamber tap/injection*	Yes	4	20/25
6	78 year-old man status post PK/IOL exchange	Post-operative	<i>K. oxytoca</i> (vitreous tap)	Hand movements	Vitreous tap/injection	Yes	83	20/70
7	67 year-old woman with history of trabeculectomy 7 months prior	Bleb-related	<i>K. pneumoniae</i> (vitreous tap)	Hand movements	Vitreous tap/injection	No+	76	20/70

DM: diabetes mellitus; IOFB: intraocular foreign body; PPV: pars plana vitrectomy; PK: penetrating keratoplasty; IOL: intraocular lens; VA: Snellen visual acuity; Last VA: visual acuity at last follow-up examination

* Patient 5 underwent repair of corneal laceration simultaneously

+ Patient 7 subsequently underwent pars plana vitrectomy

Table 2
Initial Treatment Strategies and Outcomes of Patients with Endophthalmitis caused by *Klebsiella* species

Patient	Presenting VA	Initial Treatment	Clinical Improvement	Follow-up (months)	Last VA
1	2/200	Vitreous tap/injection	No	1	enucleated
2	1/200	PPV with intravitreal injection	No	4	enucleated
3	Light perception	Vitreous tap/injection	No	20	eviscerated
4	Light perception	PPV with intravitreal injection	Yes	2	20/60
5	20/60	Anterior chamber tap/injection*	Yes	4	20/25
6	Hand movements	Vitreous tap/injection	Yes	83	20/70
7	Hand movements	Vitreous tap/injection	No+	76	20/70

VA: Snellen visual acuity; Last VA: visual acuity at last follow-up examination; PPV: pars plana vitrectomy

* Patient 5 underwent repair of corneal laceration simultaneously

+ Patient 7 subsequently underwent pars plana vitrectomy