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# Endophthalmitis Caused by *Corynebacterium* Species: Clinical Features, Antibiotic Susceptibility, and Treatment Outcomes

**Ajay E. Kuriyan, MD**[1,2,*], **Jayanth Sridhar, MD**[1], **Harry W. Flynn Jr., MD**[1], **Laura C. Huang, MD**[1], **Nicolas A. Yannuzzi, MD**[1], **William E. Smiddy, MD**[1], **Janet L. Davis, MD**[1], **Thomas A. Albini, MD**[1], **Audina M. Berrocal, MD**[1], and **Darlene Miller, D.H.Sc**[1]

[1]Department of Ophthalmology, Bascom Palmer Eye Institute, Miller School of Medicine, University of Miami, Miami, Florida

[2]Department of Ophthalmology, Flaum Eye Institute, University of Rochester Medical Center, Rochester, NY

## Abstract

**Purpose—**To report the clinical features, antibiotic susceptibility profiles, treatment, and visual acuity (VA) outcomes of endophthalmitis caused by *Corynebacterium* species.

**Design—**Retrospective case series.

**Subjects—**Patients with endophthalmitis caused by *Corynebacterium* species.

**Methods—**Microbiology database records were retrospectively reviewed for all patients with endophthalmitis caused by *Corynebacterium* species from January 1, 1990 to December 31, 2012 at a large university referral center. The corresponding clinical records were then reviewed to evaluate the endophthalmitis clinical features and treatment outcomes.

**Main Outcome Measures—**presenting clinical features, visual acuity outcomes, and antibiotic susceptibility patterns.

**Results—**Of 10 patients identified, clinical settings included post-cataract surgery (n = 6), post-penetrating keratoplasty (n = 2), and post-trabeculectomy (n = 2). The mean time from surgical procedure to presentation with endophthalmitis was 6.8 months (range: 1 day to 28 months). All isolates were vancomycin susceptible. Presenting VA ranged from 7/200 to no light perception. Initial treatment strategies were vitreous tap and intravitreal antibiotic injection (n = 5) and pars plana vitrectomy with intravitreal antibiotic injection (n = 5). VA outcomes were ≥ 20/60 in 5 (50%) of 10 patients and ≤ 20/400 in 5 (50%) of 10 patients.

[*]Corresponding Author/Address for Reprints: Ajay E. Kuriyan, MD, 900 NW 17th Street, Miami, FL 33136, Phone: 305-326-6000, Fax: 305-326-6417, ajay.kuriyan@gmail.com.

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**Conclusions—**The most common clinical setting was post-cataract surgery. All isolates were susceptible to vancomycin. Despite prompt treatment with appropriate antibiotics, there were variable visual outcomes.

## INTRODUCTION

Corynebacterium is genus of pleomorphic gram positive bacilli or coccobacilli that is ubiquitous in the environment.[1] Fifty-three Corynebacterium species have been identified as causes of human infections.[2, 3] *Corynebacterium* species are a relatively rare cause of endophthalmitis and accounted for approximately 1% of culture positive acute-onset, post-cataract surgery endophthalmitis cases in the Endophthalmitis Vitrectomy Study.[4]

Although non-diphtheritic *Corynebacterium* (NDC) species were thought to be laboratory contaminants in the past, there are reports of NDC infections, including bacteremia, skin infections, urinary tract infections, endocarditis, osteomyelitis, septic arthritis, peritonitis, brain abscess, meningitis, and infections associated with prosthetic device.[2, 3, 5–20] *Corynebacterium* species are found in the conjunctiva of five to seven percent of healthy adults.[21, 22] Endophthalmitis caused by *Corynebacterium* species was first reported in 1979 and was associated with an intraocular metal foreign body.[23] Since then, there have been several case reports of endophthalmitis caused by *Corynebacterium* species associated with trauma, cataract surgery (acute- and delayed-onset), and endogenous sources.[24–37] *Corynebacterium* species have also been identified in cases of scleral buckle-associated infections.[38–40] The purpose of this study is to report the clinical settings, antibiotic susceptibility profiles, and visual acuity (VA) outcomes in series of culture-proven endophthalmitis due to *Corynebacterium* species in the United States.

## MATERIALS AND METHODS

The study protocol for a retrospective review of medical and microbiology records for all patients treated at the Bascom Palmer Eye Institute with vitreous fluid culture-proven endophthalmitis caused by *Corynebacterium* species between January 1, 1990 and December 31, 2012 was approved by the Institutional Review Board of the University of Miami Miller School of Medicine Medical Sciences Subcommittee for the Protection of Human Subjects. Vitreous cultures were obtained either at the time of vitreous tap and inject or during vitrectomy as previously described.[41, 42] All vitreous fluid samples were plated on 5% sheep blood and chocolate agars, which were incubated at 35°C f or a period of up to 2 weeks. Additional culture media, including thioglycollate broth, were inoculated at the discretion of the ophthalmologist performing the culture. All cultures were read and classified using standard culturing techniques by Ocular Microbiology Department staff. Patients who only grew *Corynebacterium* isolates in thioglycollate broth, but not other culture media, did not meet the criteria for a positive culture and were excluded from the study.

The medical records were retrospectively reviewed for all patients with vitreous fluid culture-proven endophthalmitis caused by *Corynebacterium* species during the study period to ensure clinical course consistent with endophthalmitis. Patient demographics, clinical

characteristics, risk factors, treatment strategies, and clinical outcomes were assessed. The treatment strategies were determined by the individual treating physicians and did not follow a standardized protocol.

## RESULTS

### Patient demographics and clinical settings

Endophthalmitis caused by *Corynebacterium* species was identified in 10 eyes of 10 patients. The demographics and clinical setting for each case is summarized in Table 1. Of the 10 cases, six (60%) were male and five (50%) were right eyes. Mean age at presentation was 79 years (median: 79 years, range: 66 to 90 years). Clinical settings included six post-cataract surgery (60%), two post-penetrating keratoplasty (PKP, 20%), and two bleb-associated (20%) cases. The mean time from surgical procedure to presentation with endophthalmitis was 6.8 months (median: 19 days, range: 1 day to 28 months). One of the post-cataract surgery cases occurred 14 days after a laser capsulotomy procedure was performed for a dense posterior capsule plaque, eight months after the initial cataract surgery. One of the post-cataract surgery cases was due to a dehisced wound. One of the bleb-associated cases occurred one day after a bleb needling procedure was performed, seven years after the initial trabeculectomy surgery.

### Microbiology and antibiotic resistance

*Corynebacterium* species was identified in vitreous samples in all (100%) of the 10 patients, six cultures (60%) were monomicrobial and four cultures (40%) were polymicrobial. The antibiotic susceptibilities of the *Corynebacterium* isolates are summarized in Table 2. All of the 10 isolates were susceptible to vancomycin. All tested isolates were susceptible to ceftazidime (2 of 2), imipenem (2 of 2), and penicillin (8 of 8). There was a high rate of susceptibility to gentamicin (6 of 7, 86%) and sulfamethoxazole/trimethoprim (6 of 8, 75%). Among the fluoroquinolones tested, isolates were more susceptible to ciprofloxacin (6 of 8, 75%) compared to gatifloxacin (1 of 2, 50%) and moxifloxacin (1 of 2, 50%). There was poor susceptibility to oxacillin (1 of 5, 20%).

### Clinical presentation and management

The initial and subsequent clinical management of patients are summarized in Table 3. The presenting VA was count fingers in three (30%), light perception (LP) in two (20%), hand motion (HM) in two (20%), 1 to 7/200 in two (20%), and no light perception (NLP) in one (10%) of 10 patients. Pain was present in seven (70%) of 10 patients. The mean intraocular pressure (IOP) was 18 mmHg (median: 16, range: 8 to 33). A hypopyon was present in 8 (80%) of 10 patients. A view of the posterior pole was unobtainable in all of the patients due to severe anterior and posterior segment inflammation and media opacities.

Initial treatment consisted of a vitreous tap and intravitreal antibiotics in five (50%) of 10 patients and pars plana vitrectomy (PPV) and intravitreal antibiotics in five (50%). One (10%) of 10 patients underwent a PPV and intravitreal antibiotic injection six days after initial treatment (vitreous tap and injection of antibiotics) due to persistent vitreous opacities, increased height of the hypopyon, and persistent pain.

Vancomycin was used initially for intravitreal antibiotic treatment in all patients. Nine (90%) of 10 patients received intravitreal ceftazidime initially. Additionally, 9 (90%) of 10 patients were treated with intravitreal dexamethasone as part of their initial treatment. All patients were started on topical antibiotic drops: 9 (90%) of 10 on fortified vancomycin (50 mg/ml) and a second antibiotic (fortified tobramycin (14 mg/ml), fortified gentamicin (14 mg/ml), fortified ceftazidime (50 mg/ml), moxifloxacin, or polymyxin B/trimethoprim) and one (10%) of 10 patients on fortified gentamicin alone. A topical steroid drop was started within 48 hours of the initial treatment in all 10 patients.

### Clinical outcomes

Clinical outcomes are summarized in Table 3. Enucleation was performed due to blind painful eyes in two (20%) of 10 patients. The VA outcome was 20/60 or better in five (50%) of 10 patients and 20/400 or worse in 5 (50%) of 10 patients (including the two enucleated eyes). The mean follow-up period was 11.5 months (range: 7 months, range: 1 day to 42 months).

## DISCUSSION

The current study demonstrates that there are variable VA outcomes in patients with endophthalmitis due to *Corynebacterium* species, despite prompt and appropriate intravitreal antibiotic treatment. Although there have been reports of vancomycin resistance in *Corynebacterium* species isolates from non-ocular infections, all of the isolates in the current series were sensitive to vancomycin.[43, 44] All of the isolates tested were sensitive to imipenem and 75% (6 of 8) were sensitive to ciprofloxacin, the antibiotics used in the reported cases of vancomycin-resistant *Corynebacterium* species.

The susceptibility pattern of the isolates in our study is similar to those reported by Joseph *et al.* in a series of 16 cases of endophthalmitis caused by *Corynebacterium* in India.[45] In that report, which excluded polymicrobial cases, all of the isolates were susceptible to vancomycin, and as in our study, there was a high rate of susceptibility to cirpofloxacin (Table 4).[45] A notable difference, however, is the high rate of susceptibility to ceftazidime (2 of 2, 100%) in the current series, compared to the Joseph *et al.* study (1 or 10, 10%).

Susceptibility of all *Corynebacterium* isolates to vancomycin is consistent with most studies on endophthalmitis; a study by Gentile *et. al.* found that among 727 gram-positive isolates, all but two (E*nterococcus faecium* and *Nocardia exalbida,* 99.7%) were susceptible to vancomycin.[28] A high rate of gram-positive susceptibility to third generation cephalosporins (147 of 156, 94.2%) was also noted in the Gentile *et. al.* study, similar to susceptibility of *Corynebacterium* isolates in the current study (2 of 2, 100%).[28] The current study demonstrated similar rates of *Corynebacterium* susceptibility to ciprofloxacin (6 of 8, 75%) as other gram-positive isolates (331 of 466, 71%).[28] There was a higher rate of gentamicin sensitivity among *Corynebacterium* isolates (6 of 7, 86%) in the current study compared to gram positive isolates (448 of 599, 74.8%) in the Gentile *et. al.* study.[28]

The most common etiology in the current series is post-cataract surgery, compared to trauma in the Joseph *et al.* series.[45] In the current series, only one (10%) of 10 patients presented ≤

7 days after the associated surgery. One patient developed endophthalmitis 14 days after a laser capsulotomy procedure performed eight months after cataract surgery. Corynebacterium has been previously described to be associated with endophthalmitis after YAG capsulotomy and has been demonstrated to stay sequestered within the capsular bag and even form a capsular hypopyon.[31, 32, 35] None of the patients in the current series required intraocular lens removal or capsulectomy, which is commonly required when treating endophthalmitis caused by *Propionbacterium acnes*, the most common cause of delayed-onset endophthalmitis.[46] Although persistently positive vitreous cultures in endophthalmitis caused by *Corynebacterium* species have been reported, there were no cases of persistently positive vitreous cultures in the current series.[47]

Six of (60%) of 10 patients with endophthalmitis due to *Corynebacterium* species in the current series had VA outcomes ≥ 20/400. The Joseph *et al*. series also had similarly favorable visual outcomes with 11 (69%) of 16 patients achieving VA outcomes ≥ 20/400.[45] In contrast, only 59 (14%) of 420 in the Endophthalmitis Vitrectomy Study with VA outcomes ≥ 5/200. This suggests that *Corynebacterium* species are less virulent than other organisms.

There was a higher rate of polymicrobial cases in the current series (4 of 10, 40%), compared to the Endophthalmitis Vitrectomy Study (27 of 291, 9%)[4] All of the polymicrobial cases occurred in post-cataract surgery patients. Growth of Corynebacterium in multiple plates in these patients demonstrates that bacteria were not merely contaminants. On culture and smear, mycobacteria may be confused for *Corynebacterium* and may require subsequent DNA analysis.[48] Of note, DNA sequencing was not required to identify any of the isolates in this series. A study by Uehara and colleagues demonstrated that *Corynebacterium* species was able to inhibit colonization of nasal cavities by Staphylococcus aureus through bacterial interference.[49,50] Bacterial interference is a term used to describe the antagonism between bacterial species during the process of nutrient acquisition and surface colonization.[49] Bacterial interference may have contributed to VA outcomes ≥ 20/400 in three (75%) of four polymicrobial cases.

The limitations of the current study include its retrospective design, relatively small number of patients, and use of positive vitreous cultures using standard culture techniques as the inclusion criteria for the study, which could potentially have excluded cases with false negative cultures. The use of polymerase chain reaction-based identification methods for *Corynebacterium* species have been described, but were not used in this study.[20] Despite these limitations, this study provides important prognostic and antibiotic resistance data for endophthalmitis caused by *Corynebacterium* species.

In conclusion, despite prompt treatment with intravitreal vancomycin, patients in the current study had variable VA outcomes. *Corynebacterium* species can cause a delayed-onset endophthalmitis. The antibiotic susceptibility data from the current study further supports continued use of vancomycin.

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**Table 1**

Clinical features of patients with endophthalmitis caused by *Corynebacterium* species.

| No. | Age | Clinical Setting | Time After Surgery | Organism | Polymicrobial | Other organism |
|---|---|---|---|---|---|---|
| 1 | 75 | Phaco/IOL (uncomplicated) | 21 days | Coryne species | No | N/A |
| 2 | 90 | Phaco/IOL (uncomplicated) | 9 days | Coryne species | No | N/A |
| 3 | 73 | Phaco/IOL (complicated with RLF) | 15months | Coryne xerors | Yes | *Staph. epidermidus* |
| 4 | 85 | Phaco/IOL (complicated with wound dehiscence) | 8 days | Coryne xerosis | Yes | *Staph. Aureus* * |
| 5 | 81 | ECCE (uncomplicated) | 17 days | Coryne species | Yes | *Strep. Veridans* |
| 6 | 74 | ECCE (uncomplicated)/YAG capsulotomy | 8months/14 days | Coryne minutissimum | Yes | *Staph. haemolyticus* |
| 7 | 88 | Penetrating Keratoplasty | 22months | Coryne pseudodiphtheriticum | No | N/A |
| 8 | 66 | Penetrating Keratoplasty | 1 month | Coryne macginleyi | No | N/A |
| 9 | 81 | Trabeculectomy with 5-FU | 28months | Coryne species | No | N/A |
| 10 | 77 | Trabeculectomy/Needling of bleb | 7 years/1 day | Coryne species | No | N/A |

5-FU = 5-fluorouricil, *Coryne* = *Corynebacterium*, ECCE = extracapsular cataract extraction, IOL = intraocular lens, N/A = non-applicable, Phaco = phacoemulsification, RLF = retained lens fragment, *Staph* = *Staphylococcus*, *Strep* = *Streptococcus*, YAG = Yttrium aluminium garnet,

* This isolate was methicillin-resistant.

**Table 2**

*Corynebacterium* species antibiotic susceptibility.

| Antibiotic | Number of Isolates Tested | Susceptible Isolates (%) |
|---|---|---|
| **Vancomycin** | 10 | 10 (100) |
| **Gentamicin** | 7 | 6 (86) |
| **Clindamycin** | 5 | 3 (60) |
| **Sulfamethoxazole/Trimethoprim** | 8 | 6 (75) |
| **Beta-Lactams** | | |
| Penicillin | 8 | 8 (100) |
| Oxacillin | 5 | 1 (20) |
| Ceftazidime | 2 | 2 (100) |
| Imipenem | 3 | 3 (100) |
| **Fluoroquinolones** | | |
| Ciprofloxacin | 8 | 6 (75) |
| Gatifloxacin | 2 | 1 (50) |
| Moxifloxacin | 2 | 1 (50) |

**Table 3**

Presentation, treatment strategies, and outcomes of patients with endophthalmitis caused by *Corynebacterium*.

| No | Pre- infection VA | Initial VA | IOP | Initial Tx | Initial Intravitreal Injection(s) | Additional Tx (Days After Initial Tx) | Additional Intravitreal Injections | Last VA | Follow-up Time |
|---|---|---|---|---|---|---|---|---|---|
| 1 | UK | CF | 14 | T+I | VANC + CTZ + DEX | None | None | 20/40 | 12 mos |
| 2 | 20/40 | 1/200 | 22 | T+I | VANC + CTZ + DEX | PPV (6) | VANC + CTZ | 20/60 | 9 mos |
| 3 | UK | 7/200 | 16 | PPV | VANC + CTZ + DEX | None | None | 20/20 | 4 mos |
| 4 | UK | LP | - | T+I | VANC + CTZ + DEX | Enuc (17) | None | Enuc | 42 mos |
| 5 | UK | HM | 14 | PPV | VANC + CTZ + DEX | None | None | 20/40 | 30 mos |
| 6 | 20/80 | CF | 8 | PPV | VANC + DEX | None | None | 20/400 | 1 day |
| 7 | NLP | NLP | - | T+I | VANC + CTZ + DEX | Enuc (44) | None | Enuc | 2 mos |
| 8 | 20/50 | CF | 16 | T+I | VANC + CTZ | None | None | CF | 10 mos |
| 9 | 6/200 | LP | - | PPV | VANC + CTZ + DEX | None | None | 5/200 | 5 mos |
| 10 | 20/30 | HM | 33 | PPV | VANC + CTZ + DEX | None | None | 20/30 | 1 mos |

CF = count fingers, CTZ = ceftazidime, DEX = dexamethasone, Enuc = enucleation, HM = hand motion, LP = light perception, mos = months, NLP = no light perception, No. = number, PPV = pars plana vitrectomy, T + I = vitreous tap + intravitreal injection, Tx = treatment, VAN = vancomycin, VA = visual acuity, UK = unknown.

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## Table 4

Comparison of Endophthalmitis due to *Corynebacterium* species studies

| | Current Study | Joseph *et al*.LV Prasad Eye Institute[45] |
|---|---|---|
| **Antibiotic** | **No. of Patients (%)** | **No. of Patients (%)** |
| **Clinical setting** | | |
| Post-cataract surgery | 6 (60%) | 5 (31%) |
| Post-PKP surgery | 2 (20%) | 1 (6%) |
| Post-Glaucoma procedures | 2 (20%) | - |
| Trauma | - | 10 (63%) |
| **Initial treatment** | | |
| Vitreous tap + antibiotics | 5 (50%) | - |
| PPV + antibiotics | 5 (50%) | 16[a] (100%) |
| **Presenting VA** | | |
| LP or Worse | 3 (30%) | 7 (44%) |
| HM or Better | 7 (70%) | 9 (56%) |
| **Final VA** | | |
| ≥20/400 | 6 (60%) | 11 (69%) |
| <20/400 | 4 (40%) | 5 (31%) |
| **Antibiotic Susceptibility** | | |
| Vancomycin | 10/10 (100%) | 16/16 (100%) |
| Gentamicin | 6/7 (86%) | 11/14 (79%) |
| Ceftazidime | 2/2 (100%) | 1/10 (10%) |
| Fluoroquinolones | | |
| Ciprofloxacin | 6/8 (75%) | 12/16 (75%) |
| Gatifloxacin | 1/2 (50%) | 15/16 (94%) |
| Moxifloxacin | 1/2 (50%) | 7/9 (78%) |

HM = hand motion, LP = light perception, PKP = penetrating keratoplasty, No. = number, PPV = pars plana vitrectomy, VA = visual acuity, UK = unknown**,**

[a]Includes nine patients treated with PPV and intravitreal antibiotics as well as seven patients treated with pars plana lensectomy along with pars plana vitrectomy and intravitreal antibiotics.