

# Acute-onset postoperative endophthalmitis caused by multidrug-resistant *Klebsiella pneumoniae*

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**Abstract:** The purpose of this paper is to report outcomes of intravitreal imipenem in the treatment of multidrug-resistant *Klebsiella*-related postoperative endophthalmitis. This observational case series consists of three eyes from three patients seen between 2013 and 2014. Multidrug-resistant *Klebsiella pneumoniae* is characterized by a rapid, fulminant course and severe intraocular inflammation. Intravitreal imipenem may be used to treat such infection.

**Keywords:** postoperative endophthalmitis, *Klebsiella pneumoniae*, imipenem, multidrug resistance

## Introduction

Acute-onset postoperative endophthalmitis is characterized by marked inflammation of intraocular fluids and tissues. Gram-negative bacteria are less commonly isolated than Gram-positive bacteria in patients with acute-onset postoperative endophthalmitis. Gram-negative organisms have been isolated in 26%–42% of patients with cataract surgery related to endophthalmitis in developing countries,<sup>1,2</sup> as compared with 5.9%–11.8% in developed countries.<sup>3</sup> The more common Gram-negative organisms causing endophthalmitis include species of *Pseudomonas*, *Haemophilus*, *Proteus*, and *Klebsiella*. There have been reports of multidrug-resistant strains of Gram-negative bacteria being isolated from patients with endophthalmitis.<sup>4</sup> Endophthalmitis caused by *Klebsiella pneumoniae* is associated with generally poor visual outcomes, despite treatment with appropriate antibiotics.<sup>5</sup> Three cases of acute postoperative endophthalmitis due to multidrug-resistant *K. pneumoniae* are reported.

## Case reports

Three patients developed acute-onset endophthalmitis within 1–3 days following cataract surgery (Table 1). All the patients were in good general health and were not known to be suffering from any known systemic illness in the pre and postoperative periods. Presenting visual acuity ranged from 20/50 to light perception. Hypopyon was observed in all patients and corneal infiltrate was observed in two patients who presented with visual acuity of light perception.

One patient underwent vitreous tap with intraocular injection of vancomycin 1 mg/0.1 mL, amikacin 400 µg/0.1 mL, and dexamethasone 400 µg/0.1 mL. The other two patients underwent pars plana vitrectomy with intravitreal injection of the aforementioned antibiotics and dexamethasone. Gram-negative bacilli were isolated and confirmed to be *K. pneumoniae* by Vitek 2 compact (bioMérieux, France). Antibiotic

**Table 1** Intervention and visual outcome of multidrug-resistant *Klebsiella* endophthalmitis

| Case | Eye | Presenting visual acuity | Primary intervention           | Number of intravitreal imipenem injections | Intraocular explantation | Final visual acuity | Outcome       | Follow-up |
|------|-----|--------------------------|--------------------------------|--|--------------------------|---------------------|---------------|-----------|
| 1    | OS  | 20/50                    | Vitreous biopsy + IOAB (V+A)   | 2  | Yes                      | LP, PR inaccurate   | Phthisis      | 7 months  |
| 2    | OS  | LP, PR accurate          | PPV + IOAB (V+A)               | 2  | No                       | LP, PR inaccurate   | Optic atrophy | 4 months  |
| 3    | OD  | LP, PR inaccurate        | PPV + IOL explant + IOAB (V+A) | 2  | Yes                      | NLP                 | Phthisis      | 1 month   |

**Abbreviations:** A, amikacin; IOAB, intraocular antibiotic; IOL, intraocular lens; LP, perception of light; NLP, no perception of light; OD, right eye; OS, left eye; PPV, pars plana vitrectomy; PR, projection of rays; V, vancomycin.

susceptibility testing was determined by the Kirby–Bauer disk diffusion method (Table 2).

All isolates were multidrug resistant (Table 2) and were sensitive to imipenem. The organism that was isolated in case 3 was also found to be sensitive to ceftazidime and colistin.

Clinical deterioration was observed in all patients 2–3 days after initial intervention. Additional procedures in the form of pars plana vitrectomy with intravitreal injection of imipenem 50 µg/0.1 mL were carried out in all patients. Since there was no improvement 2 days after the second intervention, all patients were reinjected with intravitreal imipenem.

At last follow-up, visual acuity was poor in all the patients, there was light perception in two patients, and no light perception in the third patient. Phthisis bulbi occurred in two patients (Table 1).

**Table 2** Antibiotic susceptibility patterns of *Klebsiella pneumoniae* isolates

| Antibiotic      | Susceptibility result |        |        |
|-----------------|-----------------------|--------|--------|
|                 | Case 1                | Case 2 | Case 3 |
| Amikacin        | R                     | R      | R      |
| Chloramphenicol | R                     | R      | R      |
| Ciprofloxacin   | R                     | R      | R      |
| Gatifloxacin    | R                     | R      | R      |
| Moxifloxacin    | R                     | R      | R      |
| Levofloxacin    | R                     | R      | R      |
| Ceftazidime     | R                     | R      | S      |
| Ceftriaxone     | R                     | R      | R      |
| Ceftizoxime     | I                     | R      | R      |
| Imipenem        | S                     | S      | S      |
| Azithromycin    | I                     | I      | R      |
| Co-trimoxazole  | R                     | R      | R      |
| Colistin        | R                     | R      | S      |
| Tetracycline    | R                     | R      | R      |
| Erythromycin    | R                     | R      | R      |
| Gentamicin      | R                     | R      | R      |
| Neomycin        | I                     | I      | I      |

**Abbreviations:** I, intermediate; R, resistant; S, sensitive.

## Discussion

Multidrug resistance is defined as acquired nonsusceptibility to at least one agent in three or more antimicrobial categories.<sup>6</sup> Incidences of multidrug-resistant Gram-negative bacilli have been increasing in tertiary care hospitals.<sup>7</sup> It was reported that 5.2% of microbiological isolates from endophthalmitis patients were multidrug resistant, and 78.6% of those isolates were Gram-negative bacteria.<sup>4</sup>

The various mechanisms contributing to virulence of *K. pneumoniae* are the presence of capsular K1/K2 serotypes, hypermucoviscosity, and the presence of the *magA* gene and the *bla*<sub>NDM-1</sub> gene, which is a carbapenemase β-lactamase.<sup>7–9</sup> These bacteria can be resistant to all currently available antimicrobial agents or remain susceptible only to older, potentially more toxic agents such as the polymyxins, leaving limited and suboptimal options for treatment.<sup>6</sup>

Intravitreal imipenem has been studied previously in rabbit eyes and has been reported to be nontoxic to retina.<sup>10</sup> It acts by inhibiting cell wall synthesis of various Gram-positive and Gram-negative bacteria. It is stable to hydrolysis by the common plasmid-mediated β-lactamases produced by various bacteria and lacks cross-resistance with penicillins and third-generation cephalosporins.<sup>11</sup> One case series reported use of intravitreal imipenem in the treatment of endophthalmitis caused by *Acinetobacter baumannii*. The authors reported that despite the use of multiple intravitreal injections of imipenem, the visual outcomes were poor.<sup>12</sup> Based on reported antimicrobial sensitivity, 50 µg/0.1 mL intravitreal imipenem was utilized in all patients in the current series.

*K. pneumoniae* has been commonly associated with endogenous endophthalmitis. In reported series, most patients have poor visual outcome despite appropriate antibiotic therapy, and the outcomes are usually phthisis and blindness.<sup>5,13</sup> This may be attributed to the highly virulent organism as well as to delayed recognition of antibiotic resistance and susceptibility. The outcome of patients in the current case

series was either phthisis or blindness, even after the best possible treatment.

## Author contributions

Shekhar Sanghi carried out the data collection and drafted the manuscript. Avinash Pathengay is one of the treating physicians and also carried out correction of the manuscript. Animesh Jindal, Vishal Raval, Sameera Nayak, and Abhishek Bawdekar are the other treating physicians. Savitri Sharma was the microbiologist. Harry W Flynn Jr corrected the manuscript. All authors contributed toward data analysis, drafting and revising the paper and agree to be accountable for all aspects of the work.

## Disclosure

The authors report no conflicts of interest in this work.

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