Management of multi drug resistant endogenous *Klebsiella pneumoniae* endophthalmitis with intravitreal and systemic colistin

Mohit Dogra, Mansi Sharma, Deeksha Katoch, Mangat Dogra

We report a case of a 35-year-old male with a pancreatic pseudocyst, who developed bilateral endogenous endophthalmitis, 4 days after surgical drainage of the pseudocyst. Bacterial cultures of the pancreatic drain fluid and the vitreous tap showed the growth of *Klebsiella pneumoniae*. The cultured organism was resistant to all the tested antibiotics except colistin. Intravenous colistin was instituted and three injections of intravitreal colistin were given in the left eye of the patient. Complete resolution of infection was seen and visual acuity of 6/6 was regained in both eyes, which was maintained at 4-month follow-up.

Key words: Endogenous endophthalmitis, intravitreal colistin, *Klebsiella pneumoniae*

Endogenous endophthalmitis (EE) is a vision-threatening intraocular infection that results from hematogenous spread of microorganisms to the eye from a distant focus. Risk factors for the development of EE include recent hospitalization, diabetes mellitus, immunosuppression, malignancy, human immunodeficiency virus infection, intravenous drug abuse, and indwelling catheters.[1]

Liver and pancreatic abscesses have been noted to be associated with EE, especially those caused by Gram-negative rods such as *Klebsiella pneumoniae* (KP).[1,2] EE is seen in about 9% patients of KP-associated pancreatitis in Asia.[2] Diagnosis is often delayed and these patients have dismal outcomes, with 80%–89% having poor vision and 25%–41% needing evisceration.[3,4] We present the successful management of a patient with multidrug-resistant (MDR) KP endophthalmitis, secondary to an infected pancreatic pseudocyst with intravitreal and intravenous colistin.

Case Report

A 35-year-old male was referred to the ophthalmology services from the gastroenterology department for complaints of sudden, painless diminution of vision in the left eye with fever of 2 days' duration. He was a diagnosed case of alcohol-related necrotizing pancreatitis with a pancreatic pseudocyst and had undergone drainage of the same, 4 days ago.

He had a best-corrected visual acuity (BCVA) of 5/60 in the left eye (LE) and 6/6 in the right eye (RE). Ocular examination of the LE revealed the presence of 2+ cells and flare in the anterior chamber. Fundus of the LE revealed vitreous cells, Media clarity Grade 2, and multiple, yellowish, well-defined vitreous and retinal exudates in the macula [Fig. 1]. Anterior segment examination of the RE was unremarkable. Fundus examination revealed no vitreous cells, Media clarity Grade 1, and three distinct faint yellow intraretinal lesions in the macula. A clinical diagnosis of bilateral EE was made and the patient's LE was subjected to a vitreous tap. Vitreous was sent for Gram-stain, potassium hydroxide mount, and bacterial and fungal cultures. The patient received intravitreal vancomycin (1.0 mg/0.1 mL) and ceftazidime (2.25 mg/0.1 mL) in the LE along with topical 0.5% moxifloxacin, steroids, and cycloplegics.

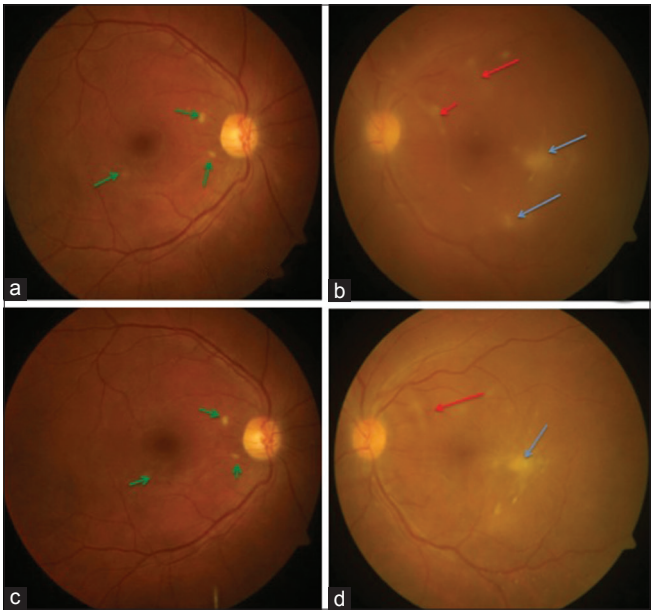

Figure 1: Fundus photographs of both eyes (a) Right eye at presentation showing Media clarity Grade 1 with three discrete intraretinal yellowish infiltrates (green arrows). (b) Left eye at presentation showing Media clarity Grade 2 with vitreous exudates (red arrows) and multiple yellowish-white retinal infiltrates (blue arrows). (c) Right eye at 4 months showing healing intraretinal infiltrates (green arrows). (d) Left eye at 4 months showing Media clarity Grade 1 with resolved vitreous infiltrates with detaching posterior hyaloid (red arrow) and fibrosed retinal infiltrate, temporal to fovea (blue arrow)

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Advanced Eye Centre, PGIMER, Chandigarh, India

Correspondence to: Dr. Deeksha Katoch, Advanced Eye Center, PGIMER, Sector 12, Chandigarh, India. E-mail: doc_deeksha@yahoo.com

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The gastroenterologist sent pus from the pancreatic drain for bacterial and fungal cultures. Bacterial culture of vitreous tap and pus from the drain showed growth of KP. Kirby–Bauer's disc diffusion method was used for obtaining antibiotic sensitivity and it revealed resistance to ciprofloxacin, gentamicin, ceftazidime, and imipenem, but sensitivity to colistin. Intravenous colistin 2 million IU, three times a day, and 0.1 mg/0.1 ml of intravitreal colistin (1000 IU/0.1 ml) along with intravitreal dexamethasone (0.4 mg/0.1 ml) were administered in the LE. As the visual acuity in the RE was 6/6, this eye was kept under observation.

Visual acuity in the LE improved to 6/36 and vitreous exudates decreased, 2 days after the intravitreal injection. As there was improvement, intravitreal colistin and dexamethasone were repeated in the LE at day 4 and day 8. Intravenous colistin was continued for 10 days, following which the patient was discharged. He was followed up weekly thereafter. The LE showed excellent response with anterior chamber and vitreous cells, showing complete resolution and Media clarity improving to Grade 1 at 1 month. BCVA improved to 6/9 in the LE and remained 6/6 in the RE with complete resolution of inflammation in both eyes. The patient was maintaining the aforementioned status in both eyes at 4-month follow-up.

Discussion

KP is the most common cause of bacterial EE in Asian countries in patients with liver and pancreatic disease.[2,4] MDR strains of KP are increasingly been implicated as causes of pancreatitis.[5] MDR strains of *Klebsiella* species carry plasmids that confer resistance to multiple classes of antibiotics, including cephalosporins, aminoglycosides, and tetracyclines. This warrants treatment with unconventional antimicrobials – colistin, polymyxin B, and tigecycline.[5,6] Our patient had a pancreatic pseudocyst infected with MDR KP which led to EE. The organism was sensitive only to colistin, and hence the patient was treated with intravenous colistin. As the LE of the patient had significant vitreous and retinal infiltrates, intravitreal colistin was administered.

Two case series citing the use of intravitreal colistin exist in literature. Samant and Ramugade reported successful use of intravitreal colistin for the management of MDR *Pseudomonas aeruginosa* endophthalmitis after cataract surgery in eight patients. All of the eyes could be salvaged.[7] Taneja *et al*. also reported successful use of intravitreal colistin combined with multiple vitrectomies for managing postendothelial keratoplasty endophthalmitis due to MDR KP.[8] Intravenous colistin has been shown to have poor ocular penetration in rabbits, with concentrations in the aqueous and vitreous not reaching therapeutically relevant levels after intravenous administration.[9] Hence, we decided to augment systemic colistin with intravitreal colistin. The concentration of intravitreal colistin (0.1 mg/0.1 ml) was the same as was used in the aforementioned studies. Colistin is used for treating infections caused by MDR bacteria including *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and KP. It exerts its bactericidal effect by damaging bacterial cell membranes and promoting extracellular leakage of cellular proteins leading to cell death.[6,9]

Poor outcomes are reported in patients with *Klebsiella* EE, with evisceration needed in up to 41%.[3,4] The role of early vitrectomy has been advocated, and Yoon *et al*. reported successful outcomes in these patients with early vitrectomy, with none of the eyes requiring evisceration.[10]

Conclusion

In our case of bilateral EE due to MDR KP, managed with intravenous and intravitreal colistin, successful anatomic and functional outcome was achieved without the need of vitrectomy. Hence, with the increase in the incidence of drug resistance, unconventional antibiotics should be considered for endophthalmitis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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