Intravitreal linezolid in the management of vancomycin-resistant enterococcal endophthalmitis

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ARTICLE INFO

Keywords:
Intravitreal
Linezolid
Vancomycin-resistant enterococcus
Endophthalmitis

ABSTRACT

Purpose: Linezolid is a synthetic antibiotic, the first of the oxazolidinone class, used for the treatment of infections caused by multi-resistant bacteria including Streptococcus, methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE). We report on a case of endophthalmitis caused by vancomycin-resistant Enterococcus faecium treated with intravitreal linezolid. It has proved efficacious in animal models but its safety in humans is not fully known.

Observations: An 84-year-old man who had phacoemulsification surgery and anterior chamber intraocular lens due to posterior capsule rent. Visual acuity (VA) following surgery was 6/24 uncorrected. The following week he developed signs of endophthalmitis, characterized by corneal infiltration and keratic precipitates, with anterior chamber and vitreous haze. Cultures yielded no growth, while repeated treatments with intravitreal vancomycin, ceftazidime, and amphotericin B did not control the infection. Vitrectomy was performed twice during the patient’s course, with intravitreal amikacin injection after the second vitrectomy, but poor control of the endophthalmitis persisted. After several weeks of limited response to treatments, the diagnosis was finally made using Giemsa stain of direct smear which showed characteristic morphology of Enterococcus faecium. Linezolid, one of the oxazolidinones, was initially given in oral form 600 mg BID for three weeks, but did not prove efficacious. Subsequently, intravitreal linezolid 200 mcg in 0.1ml was injected, which cleared the vitreous and cornea infection within a week. However, there was a residual exudative detachment of the retina in the posterior pole, leaving the patient with a final vision of hand movement.

Conclusion and importance: Vancomycin-resistant enterococcus is a rare cause of endophthalmitis. Intravitreal linezolid is an effective treatment, but the subsequent exudative retinal detachment may have been related to this novel therapy.

1. Introduction

The incidence of endophthalmitis after cataract and other intraocular surgeries varies from country to country and from hospital to hospital. Over the years, protocols have been developed to manage this condition, which depend on a successful vitreous tap and positive culture and sensitivity to guide treatment. Most of the common causative organisms are sensitive to broad-spectrum antibiotics; combination vancomycin (for gram positive organisms) and ceftazidime or amikacin (for gram negative organisms) are often the first line drugs. In many cases, this usually suffices. But in some cases, there is poor response to this combination. In a series of endophthalmitis cases by Gentile et al., 99.7% of gram-positive bacteria were susceptible to vancomycin.

We encountered a case in which a patient developed endophthalmitis after a complicated phacoemulsification procedure (posterior capsule rent) in which an anterior chamber intraocular lens (ACIOL) was placed. The endophthalmitis did not respond to the standard intravitreal vancomycin, ceftazidime and amphotericin B. In addition, the cultures came back negative, and we had to resort to a direct smear and KOH test to make a diagnosis. The direct smear showed a gram positive diplococcoid forms with a pale bisection, identifying Enterococcus faecium. This report details our encounter with this patient, and management with intravitreal linezolid, a synthetic antibiotic in the oxazolidinone class used for the infections with multi-resistant bacteria.

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https://doi.org/10.1016/j.ajoc.2020.100974

Received 30 June 2020; Received in revised form 4 September 2020; Accepted 10 September 2020
Available online 17 October 2020

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2. Case report

An 84-year-old man underwent phacoemulsification OD for moderate cataract using a clear corneal incision; the case was complicated by posterior capsule rent, and consequently, an ACIOL was placed. He was seen a week later with lacrimation and corneal edema and corneal infiltration with keratic precipitates, with anterior chamber and vitreous haze. There was no retinal reflex with indirect ophthalmoscopy. On the suspicion of endophthalmitis, a vitreous tap was obtained followed by intravitreal vancomycin 1mg and ceftazidime 2mg, both in 0.1 ml. The day after the injection, there was lid edema, conjunctival hyperemia, and corneal edema and striae, with worsened inflammatory reaction in the anterior chamber. Unfortunately, no growth was shown on vitreous cultures after 48 hours.

On the eleventh day post-operation, the corneal decompensation worsened. We repeated intravitreal vancomycin and ceftazidime, gave subconjunctival depomedrol (0.5ml containing 20 mg of methyl) and placed a bandage soft contact lens to manage the superficial corneal disease. On the fourteenth post-operative day, with no improvement, amphotericin B injection was given intravitreally on the suspicion that this might be a fungal endophthalmitis. Oral fluconazole 200mg BID was also introduced. On post-operative day 16, still without significant improvement, the decision was made to perform three-port posterior vitrectomy, with repeat vancomycin injection, obtaining another sample for microscopy, culture and sensitivity. At the end of the procedure, a clear view of the retina was obtained. However, on the day following the vitrectomy, the vitreous was seen to be filled with new greyish flocculent material, also involving the anterior chamber. We again gave intravitreal amphotericin B and ceftazidime. Nevertheless, the eye did not improve. The AC became increasingly filled with exudates. A second vitrectomy was carried out post-operative day 20 with amikacin injected intravitreally. The vitreous cultures came back again with ‘no growth’; however, we had reserved a sample for potassium hydroxide (KOH) test for fungal hyphae and for gram stain characteristics. The KOH prep can describe hyphate forms and can give indication of gram polarity. The KOH prep suggested that we were dealing with Gram-positive organisms, although we still had no identification as to the specific organism. A direct Gram stain showed Gram-positive diplococci with a pale connecting band in between, which were identified as Enterococcus faecium.

Our further research indicated that some strains of this organism were vancomycin resistant (so-called vancomycin-resistant enterococci or VRE) which were only susceptible to certain antibiotics such as...
3. Discussion

The first case report of endophthalmitis with VRE (Enterooccus faecium) was by Bains et al. In addition to intravitreal vancomycin and amikacin, they administered intravenous linezolid 600 mg BID but stopped short of administering the medication into the vitreous. The literature suggests that oral linezolid 600 mg BID is capable of crossing the blood retina barrier. We found the patient had developed a detachment of the retina confined to the posterior pole centered on the macula, confirmed by OCT (Fig. 1). We felt this was an exudative detachment limited to the posterior pole. We gave bevacizumab injection but there was no improvement. At ongoing follow-up, the serous detachment persists. This lack of response to Bevacizumab has been commented on by Chung et al.

3. Funding

None.

3. Declaration of competing interest

None.

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