Endogenous endophthalmitis caused by *Enterococcus casseliflavus*

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Herein, we report a case of endogenous endophthalmitis caused by *Enterococcus casseliflavus*. The organism was sensitive to gentamicin, vancomycin and chloramphenicol and resistant to cefazolin, ofloxacin, gatifloxacin and ciprofloxacin. The patient was successfully treated with vitrectomy and sensitivity-based intravitreal vancomycin.

**Introduction**

Members of the genus *Enterococcus* are Gram-positive, catalase-negative, facultative anaerobes, seen in pairs, and are frequently isolated from polymicrobial wound infections. *Enterococcus faecalis* (74–90 %) and *Enterococcus faecium* (5–16 %) are the most common species isolated from human infections. Occasionally human infection can be caused by *Enterococcus raffinosus*, *Enterococcus casseliflavus*, *Enterococcus durans* and *Enterococcus avium* (Karmarkar et al., 2004). *E. casseliflavus* has been implicated in a wide variety of infections in humans, especially in immunocompromised hosts (Gascón et al., 2003; Reid et al., 2001), but to the best of our knowledge it has never been reported in patients with endogenous endophthalmitis.

**Case report**

A 20-year-old male, a manual labourer, presented to us with a history of acute onset of deterioration of vision, associated with mild pain and redness in the right eye of 2 days' duration. He had been a known sinusitis patient for the previous 5 years and had a history of a common cold 5 days prior to the presentation. He also had a history of peptic ulcer disease for which he was on medication. There was no history of fever or urinary complaints, prior hospitalization, intravenous drug use or significant trauma to the eye. He was seen by the local ophthalmologist a day prior to the presentation and was started on a topical steroid, prednisolone acetate 1 % twice a day, eye ointment, aciclovir 3 % once daily, and atropine sulfate. On presentation, the right eye had a best corrected visual acuity of perception of light with accurate projection of rays. Anterior segment examination of the right eye revealed 4 + cells, 3 + flare, fibrinous exudates in the pupillary area and a 2 mm hypopyon. There was a hazy view of the lens and no view of the fundus. The left eye had a visual acuity of 20/20, N6, and ocular examination of it was normal. B-scan examination of the right eye showed low to moderate reflective echoes in the vitreous cavity. A clinical impression of endogenous endophthalmitis was made and pars plana vitrectomy with intravitreal antibiotics was advised. Peripheral blood smear, blood and urine cultures and HIV ELISA were also performed. The surgery (pars plana vitrectomy) was performed on the same day and intravitreal vancomycin (1 mg in 0.1 ml) and ceftazidime (2.25 mg in 0.1 ml) were injected at the end of the procedure. A vitreous sample was sent for microbiological evaluation. The patient was started on topical ciprofloxacin (0.3 %) 1 hourly, prednisolone acetate (1 %) 1 hourly, atropine sulfate (1 %) three times daily and oral ciprofloxacin 750 mg twice a day.

Direct microscopic examination of the vitreous showed Gram-positive cocci in pairs. Tiny grey moist colonies were observed on chocolate agar and turbidity was noted in brain heart infusion (BHI) broth as well as in thioglycolate broth after 24 h of incubation. The Gram stain of the colonies on chocolate agar and from BHI and thioglycolate broth revealed Gram-positive cocci in pairs. The Gram-positive cocci were catalase-negative and motile. The organism produced yellow pigment. It was identified as *E. casseliflavus* using mini API ID 32 STREP based on growth in 6.5 % NaCl medium, hydrolysis of bile–aesculin, growth rate at 45 °C, hydrolysis of arginine and acid production from ribose. The isolate identity was further confirmed by 16S rRNA gene sequencing. Sequencing was performed (forward primer, 5’-TTGGAGAGTTTGTCC-TGGCTC-3’; reverse primer, 5’-GGACTAAGGATG-ATCTAA-3’) with fluorescence-labelled dideoxynucleotide terminators using an ABI 3130 XL automated sequencer, following the manufacturer’s instructions (PE Applied
The sequences were analysed and identified using the MEGABLAST search program of the GenBank database. The sequence of the isolate perfectly (100%) matched the sequences of \textit{E. casseliflavus} deposited in GenBank. The sequence of the isolate was deposited in GenBank (accession no. HM007307). Antibiotic susceptibility testing of the isolate was performed using the Kirby–Bauer disc diffusion method. The organism was sensitive to gentamicin, vancomycin and chloramphenicol, resistant to cefazolin, ofloxacin, gatifloxacin and ciprofloxacin, and showed intermediate sensitivity to moxifloxacin.

Based on the sensitivity report, topical and systemic ciprofloxacin was discontinued and the patient was started on topical gentamicin 1 hourly while the rest of the treatment was continued. There was no growth from blood and urine cultures and HIV ELISA was negative. The patient showed steady improvement, and at 3 weeks post-operative follow-up, his uncorrected visual acuity improved to 20/100. The topical steroids were tapered at this visit. At one and a half months follow-up, the patient presented with a deterioration in vision, noted for the previous 2 days, associated with pain and redness in the same eye. On examination, he had a visual acuity of hand movement close to the face with accurate projection of rays in the right eye, and the anterior segment showed 3+ cells, 2+ flare and fibrin membrane in the anterior chamber. There was a very hazy view of the fundus and B-scan showed evidence of vitreous echoes of moderate amplitude. A diagnosis of recurrent endophthalmitis was made and the patient underwent vitrectomy with intravitreous vancomycin (1 mg in 0.1 ml) and was started on topical fortified vancomycin and gentamicin along with topical steroids and cycloplegics. The patient was advised to have a course of intravenous gentamicin but refused. During the repeat surgery, vitreous was again sent for microbiological evaluation but the cultures were negative. The patient was kept on close follow-up and given a repeat intravitreal antibiotic (vancomycin 1 mg in 0.1 ml) after a gap of 1 week. He was continued on the same medications, which were tapered after 3 weeks of treatment. At final follow-up visit, 3 months after the last intravitreal injection, the patient had a best corrected visual acuity of 20/60 and near vision of N18. On fundus examination, the media was clear and the retina was attached with pigmented changes at the fovea. An impression of resolved endophthalmitis was made and the patient was advised to follow-up after 3 months.

**Discussion**

\textit{E. casseliflavus} is an uncommon cause of human infection. Though endogenous endophthalmitis due to \textit{Enterococcus} has been reported (Rishi \textit{et al}., 2009), there are no published reports of endogenous endophthalmitis caused by \textit{E. casseliflavus} to our knowledge. There is a report of traumatic endophthalmitis caused by \textit{E. casseliflavus} after horse tail injury (Khurana \textit{et al}., 2009), and there is a report of endogenous endophthalmitis caused by \textit{Enterococcus munditii} (Higashide \textit{et al}., 2005) where the organism was isolated from the vitreous and treatment was vitrectomy along with intravitreal imipenem. In our patient, the portal of entry of the organism is uncertain. Extensive probing of the history revealed that there was a history of common cold, sinusitis and peptic ulcer disease. There was no history of hospitalization or fever or any evidence suggestive of urinary tract infection. The absence of ocular compromise and medical intervention points towards community-acquired enterococcal bacteraemia. In our case, there was no growth in the blood and urine cultures but the organism was isolated from the vitreous. This reflects the difficulty of getting positive blood and urine cultures in cases of endogenous endophthalmitis (Jackson \textit{et al}., 2003). Whether community-acquired enterococcal bacteraemia so fleeting and trivial as to cause no systemic features can cause endogenous endophthalmitis is open to discussion. However, cases of endogenous endophthalmitis with no systemic features have been reported in the literature (Jackson \textit{et al}., 2003). There is evidence in the literature reporting systemic cultures being negative in 20–25% of cases of endogenous endophthalmitis with ocular culture positivity varying from 36% to 73% and this may be the sole source of microbial growth in selected cases (Greenwald \textit{et al}., 1986; Okada \textit{et al}., 1994; Wong \textit{et al}., 2000).

The treatment of choice for endogenous endophthalmitis is systemic antibiotics, and in the early stage of the disease where there is focal chorioretinitis, patients can be managed only by systemic treatment. Systemic treatment has to be given to the patient for several weeks based on the sensitivity report (Lemley & Han, 2007). We advised our patient to take a course of intravenous antibiotics after being admitted to our institute on two occasions, but the patient refused due to personal reasons. This highlights that the treatment of choice in the case of endogenous bacterial endophthalmitis is primarily systemic antibiotics (Jackson \textit{et al}., 2003). Accurate identification of the organism is a must, as our organism was resistant to routinely used antibiotics, notably the fluoroquinolones. However, in this case, the patient developed a recurrence of endophthalmitis, perhaps due to the fact that after the first vitrectomy he was managed with topical antibiotics alone. The suspicion of recurrence of endophthalmitis was purely clinical. Vitrectomy in the case of endophthalmitis is not extensive; it is just core vitrectomy leaving behind the vitreous, which could act as the carrier of infection (Pathengay \textit{et al}., 2005). We were not able to isolate the organism from the second vitreous sample and this is open for discussion. There is evidence in the literature that the yield of positive vitreous culture results is highly variable during initial vitrectomy (Lemley & Han, 2007) and yield might drop further with repeat surgery. This can probably explain the negative culture results from the second vitreous sample from our patient. The final visual outcome in our patient was a significant improvement in visual acuity (20/60). The largest case series of enterococcal endophthalmitis (Rishi \textit{et al}., 2009) reported 26 culture-proven cases of...
E. faecalis, of which only three were because of endogenous endophthalmitis. Twenty-three patients among these 26 needed vitrectomy with intraocular antibiotics and 12 needed repeat intravitreal antibiotics. This case shows us that E. casseliflavus can cause endogenous endophthalmitis, and if diagnosed early and managed appropriately with sensitivity-guided antibacterial therapy, there can be a good visual outcome.

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References