Case Report

Levofloxacin-resistant-*Streptococcus mitis* endophthalmitis: a unique presentation of bacterial endocarditis

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Endogenous endophthalmitis is a rare complication of infective endocarditis and has been decreasing due to the availability of effective antibiotics. We highlight a case of endogenous endophthalmitis due to levofloxacin-resistant *Streptococcus mitis* presenting as infective endocarditis. Endogenous endophthalmitis should be considered as a manifestation of an underlying systemic disease, especially in patients who present with non-specific signs and symptoms with no obvious source of precipitating infection.

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Case report

An 85-year-old white male, with a medical history significant for hypertension and diabetes mellitus, was referred to our hospital, New York Hospital Queens (NYHQ), for evaluation of positive blood culture results after being treated for endophthalmitis at another hospital. The patient initially reported acute right ocular pain and redness with vision loss initially thought to be glaucoma (Fig. 1). He was evaluated by an ophthalmologist and diagnosed with vitritis and endophthalmitis, and subsequently had an emergent vitrectomy. Intraoperative intravitreal injection of 1 g vancomycin and 400 mg amikacin was given after drainage of the purulent discharge. Blood and vitreous fluid cultures were obtained. The patient was discharged home with a treatment of 750 mg oral levofloxacin daily for a total of 14 days. His vision improved and vitreous fluid cultures contained no organisms despite purulent discharge, while the concomitant blood cultures grew α -haemolytic streptococcus in 2/2 bottles. The patient was then referred to NYHQ to determine if he had subacute bacterial endocarditis. He had been taking levofloxacin for 8 days. Susceptibilities were not available to us on admission.

On presentation to our emergency room, the patient denied fever, chills, malaise, myalgias, shortness of breath, chest pain, diarrhoea, back pain and haematuria. The patient had no recent history of any dental, gastrointestinal or genitourinary procedure. He reported having an old heart murmur. His vital signs were normal, except for a heart rate of 105 beats min⁻¹. The patient remained

afebrile throughout his hospital stay. His right eye was red and inflamed, with normal movement of extra-ocular muscles but decreased visual acuity (20/160). Auscultation of the heart revealed a III/VI holosystolic ejection murmur heard best at the apex. No rash was noted.

Initial blood work showed a normal haemoglobin level of 15.4 g dl⁻¹, a haematocrit level of 46.2 %, an elevated leukocyte count of 14 000 cells μ l⁻¹ (80 % neutrophils, 16 % lymphocytes) and normal renal function. Blood cultures obtained at admission and during his hospital stay resulted in no growth. Urine and sputum cultures remained negative for bacterial growth. Both transthoracic and transoesophageal echocardiography showed a preserved ventricular function without evidence of a thrombus or clots in the ventricles or left atrial appendage, but revealed a 1.4 $\times$ 1.1 cm mobile mass consistent with a vegetation on the posterior leaflet of the mitral valve with moderate mitral regurgitation, confirming the diagnosis of subacute bacterial native valve endocarditis (Fig. 2).

The patient was treated with intravenous ampicillin (2 g every 4 h), and intravenous ceftriaxone (1 g every 12 h), and two doses of intravenous gentamicin (3 mg kg⁻¹) were also administered. On hospital day 4 at NYHQ, which was day 12 post-vitrectomy and post-incubation of the blood cultures, the organism was identified as *Streptococcus mitis* (by Vitek GPI), which was susceptible to penicillin, ceftriaxone and gentamicin, but resistant to levofloxacin. Susceptibility by Etest gave the following MICs (μ g ml⁻¹): penicillin, 0.125, ceftriaxone, 0.19, gentamicin, 0.24 and levofloxacin, 4.0. A peripheral intravenous central catheter was placed in the patient and he was discharged with a total of 6 weeks treatment of intravenous ceftriaxone (1 g every

Abbreviation: NYHQ, New York Hospital Queens.

Fig. 1. Right eye with redness and active inflammation.

12 h) after being evaluated by a thoracic surgeon for a potential need for a mitral valve replacement in case of antibiotic failure. Weekly blood cell count and liver function tests were recommended as an outpatient with close follow up.

Discussion

Endogenous endophthalmitis or metastatic endophthalmitis is usually associated with Gram-positive cocci, predominantly *Streptococcus pneumoniae* and *Staphylococcus aureus*, and Gram-negative bacilli, most commonly *Escherichia coli* (Karchmer, 2008; Wilson *et al.*, 2001). Endogenous endophthalmitis occurs when organisms reach the eye haematogenously and cross the blood–ocular barrier causing inflammation of intraocular tissues. Endogenous endophthalmitis accounts for only 2–6% of all cases of endophthalmitis, and is most commonly seen in patients with underlying conditions including diabetes, like our patient, cardiac disease, malignancy and immunocompromised states (Koul & Philipson, 1989; Shrader *et al.*, 1990; Stonecipher *et al.*, 1994).

Fig. 2. Transthoracic echocardiogram image showing the 1.4×1.1 cm vegetation. The vegetation is indicated by an arrow.

Endogenous endophthalmitis as the initial presentation of infective endocarditis is uncommon. It represents an embolic phenomenon of infective endocarditis and high clinical suspicion is necessary in patients who present with endophthalmitis. Endogenous endophthalmitis secondary to *S. mitis* is rare, with there being only one documented case of endogenous endophthalmitis, in a 3-year-old female who was hospitalized for possible retinoblastoma (Harrison & Bateman, 1997). However, the source of infection was not identified. The patient was appropriately treated with intravenous vancomycin until she developed a drug-related rash and antibiotic therapy was changed to intravenous cefotaxime; she was treated for a total of 14 days. Her visual acuity improved and optic nerve oedema resolved over time.

In our case, *S. mitis*, an α -haemolytic Gram-positive coccus belonging to the viridans streptococcus group, was recovered in 2/2 blood culture bottles. Viridans streptococci are commonly found in the oropharynx, gastrointestinal tract, skin and female genital tract, and are documented to be the third most frequent cause of bacterial endocarditis. *S. mitis* is considered to have low virulence and pathogenicity but may cause life-threatening infections, particularly endocarditis and meningitis (Pelletier & Petersdorf, 1977; Kutlu *et al.*, 2008). Patients presenting with subacute bacterial endocarditis usually have an indolent start with non-specific signs and symptoms; ocular findings without fever can be the only herald symptoms, as in our patient's presentation. Subacute bacterial endocarditis is in the differential diagnosis of fever of unknown origin and, therefore, the physician must always consider endophthalmitis as a manifestation of subacute bacterial endocarditis.

Our patient presented with endogenous endophthalmitis with blood cultures positive for *S. mitis*, in the setting of mitral valve endocarditis as the presumed source of infection. The patient initially improved whilst receiving levofloxacin treatment, most likely due to the vitrectomy and initial intraoperative intravitreal antibiotics administered, since blood cultures revealed levofloxacin-resistant *S. mitis* with an MIC of 4 $\mu\text{g ml}^{-1}$.

Quinolone resistance in viridans streptococci is a recognized phenomenon, and can be due to efflux pumps and/or mutations in the quinolone-resistance-determining regions (QRDRs) (Schmitz *et al.*, 2001). The mechanism of levofloxacin resistance in this isolate of *S. mitis* was not elucidated but was most likely due to the acquisition of QRDRs from other bacteria. This patient was discharged with empiric levofloxacin therapy after the first hospital visit but blood cultures then grew levofloxacin-resistant *S. mitis*.

Our patient was then given 6 weeks of intravenous ceftriaxone therapy based on the 2005 treatment guidelines of the American Heart Association for patients with native-valve endocarditis caused by viridans streptococcal isolates with a penicillin MIC of >0.12 to $<0.5 \mu\text{g ml}^{-1}$ (Baddour *et al.*, 2005). The full recovery of our patient, including

resolution of the endophthalmitis, recovery of vision and an absence of mitral valve vegetations, assessed by transoesophageal echocardiography, after completion of 6 weeks of antibiotic treatment, suggests that the endogenous endophthalmitis was an embolic manifestation of infective endocarditis.

In conclusion, patients should be followed after discharge, especially after prescribing empiric antibacterial therapy, and adjustment of the antibiotics should be made after final identification and antibiogram susceptibility are obtained. Endogenous endophthalmitis should be considered as a manifestation of subacute bacterial endocarditis, even in patients who present with non-specific signs and symptoms and no obvious source of precipitating infection.

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