CASE REPORT

Native aortic valve fungal endocarditis

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SUMMARY

Infective endocarditis is the most common and dangerous form of endovascular infection. Fungal endocarditis especially of native valve is rare with *Candida albicans* being the causative organism in one-fourth of such cases. Diagnosis of such cases is further complicated if blood cultures are sterile, vegetations are not initially seen on echocardiogram and patient presents with non-specific symptoms. We hereby report a patient with native valve fungal endocarditis, treated successfully with voriconazole.

BACKGROUND

Infective endocarditis (IE) is a challenging diagnosis having many presentations ranging from an indolent infection to septicaemia with life-threatening systemic embolisations. We hereby report a case of native aortic valve fungal IE who presented with high-grade fever along with features of septic embolisation (digital gangrene, cutaneous and cerebral infarction) and treated successfully with voriconazole.

CASE PRESENTATION

A 35-year-old man presented with high-grade fever associated with a headache for 10 days, left-sided hemiparesis for 6 days and blurring of vision for 5 days. There was no history of vomiting, seizure and altered sensorium. He had a history of hospitalisation and treatment with intravenous ceftriaxone and artesunate for last 5 days. On examination he was conscious oriented, febrile (temperature 101.6°F) and his vitals were stable. Digital gangrene was present in the left upper and right lower limb (figure 1). Neurological examination revealed bilateral normal pupillary reaction, 4/5 power in both left upper and lower limbs with extensor planter response on left side. Cranial nerve examination was absolutely normal and signs of meningeal irritation were absent. On cardiovascular system examination, a soft diastolic murmur in neo aortic area was heard. Fundus examination revealed Roth's spot in right temporal field (figure 2).

INVESTIGATIONS

Investigations revealed haemoglobin of 10.4 g%, total leucocyte count 10 800/mm³, differential leucocyte count P₇₀L₂₈E₁M₁, platelet count 112 000/mm³, erythrocyte sedimentation rate 42 mm in first hour, random blood sugar 173 mg/dl and normal liver and kidney function tests. Test for malarial parasite was negative. Urine examination revealed 8–10 pus cells, 10–15 RBCs/High Power Field. Blood and stool cultures were sterile. Hepatitis B surface antigen, hepatitis C virus antibody and ELISA for HIV were non-reactive. Antinuclear antibodies test was negative.

Contrast-enhanced CT showed acute infarct in right parieto-occipital lobe (figure 3). Cerebrospinal fluid examination showed 55 cells with differential count of P₁₀L₉₀, protein 37.9 mg/dl, sugar 67.1 mg/dl (blood sugar 158.2 mg/dl) and adenosine deaminase was 4.2 IU/l. Transoesophageal echocardiogram (TOE) confirmed our diagnosis by revealing two large vegetations, mild aortic insufficiency and normal left ventricle. First vegetation was 15 mm×7 mm in size attached to non-coronary cusp and second one was 12 mm×6 mm in size on right coronary cusp (figure 4). Both vegetations were freely mobile and no perivalvular/paravalvular abscess or perforation was seen.

DIFFERENTIAL DIAGNOSIS

- ▶ Complicated malaria
- ▶ Vasculitis

TREATMENT

Initially he was treated with intravenous ceftriaxone, vancomycin and gentamycin for 4 weeks without any significant improvement. Fever persisted and size of vegetations almost remained the same. Meanwhile, his kidney function tests worsened. Considering size of vegetations, negative blood cultures and no response to adequate antibiotics possibility of fungal endocarditis was entertained. Patient was put on oral voriconazole 200 mg twice a day as his serum creatine was 2.6 mg/dl. After 1 week of antifungal therapy his fever subsided and repeat TOE showed single vegetation of 4×1 mm in size. Oral voriconazole 200 mg/day was continued for 4 weeks. After 4 weeks of treatment power in his left upper and lower limbs improved, peripheral embolic manifestations subsided and no vegetations were seen on echocardiography.

OUTCOME AND FOLLOW-UP

The patient was treated successfully with voriconazole and is doing well in follow-up.

DISCUSSION

This case report illustrates an unusual native aortic valve fungal endocarditis in an immunocompetent patient. He was diagnosed to have endocarditis by using modified Duke criteria¹ on the basis of one major criterion (vegetations on echocardiogram) and three minor criteria (fever, vascular and immunological phenomenon). Because of large vegetations, culture negativity and unresponsive to intravenous antibiotics possibility of fungal endocarditis was considered.

Incidence of predisposing rheumatic heart disease, congenital heart disease and the proportion

To cite: Chaudhary SC, Sawlani KK, Arora R, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2012-007144

Figure 1 Clinical photograph showing digital gangrene in the left hand and the right foot. Septic infarcts in left hand are also seen.

of patients who are aware that they have a heart disease predisposing them to IE has decreased significantly. However incidence of endocarditis in patients with no predisposing heart disease is increasing considerably.² *Staphylococcus aureus* is the more common cause of infection in patients without and *Streptococcus viridians* in patients with predisposing heart disease. Fungi cause less than 10% of cases of IE, with native valve fungal endocarditis being even less common. Approximately one-fourth of such cases are caused by *Candida albicans*. It is usually seen in patients with valvular diseases, intravenous drug use, indwelling vascular lines or immunocompromised states. Diagnosis of such cases is usually difficult because blood cultures remains negative in 25–31% cases of IE, especially in patients with prior antimicrobial therapy, right-sided endocarditis, fastidious organism or fungi such as *C. albicans*.³

TOE is preferred over transthoracic echocardiography for diagnosis because of increased sensitivity (90–100%) for detecting leaflet vegetations and perforations, as well as superior precision for defining perivalvular extension in the presence of a myocardial abscess. A negative TOE has an important clinical impact on the diagnosis of endocarditis with a high negative-predictive value ranging from 86% to 97%. Negative TOE virtually rules out the diagnosis of IE.⁴

Systemic embolisation is very frequent, complicating 22–50% of cases of IE. Emboli often involve major arterial beds including lungs, coronary arteries, spleen, bowel and extremities. Up to 65% of embolic events involve the central nervous system and more than 90% of central nervous system emboli lodge in the distribution of the middle cerebral artery.^{1–5} The highest incidence of embolic complications is seen with mitral and aortic valve infections in IE due to *S. aureus*, *Candida species*,

HACEK and *Abiotrophia organisms*. Emboli can occur before diagnosis, during therapy, or after therapy is completed, although most emboli occur within the first 2–4 weeks of antimicrobial therapy. The risk of embolism is highest in mitral vegetations >1 cm in diameter (anterior>posterior leaflet).¹ In another study, the effect of vegetation size on embolic potential was specific to the infecting organism, with large vegetations independently predicting embolic events only in setting of streptococcal IE. In contrast staphylococcal or fungal IE appears to carry a high risk of embolisation that is independent of vegetation size. The number of vegetations, the number of valve involved and vegetations characteristics (eg, lack of calcification) also predict embolic complication.⁶ Vegetations >1 cm are usually either due to *S. aureus* or fungal infections.

Amphotericin-B is a fungicidal medication that has historically been considered gold standard for fungal endocarditis; however, it fails to penetrate well into vegetations and has many side effects which can result in premature discontinuation. Our patient had deranged renal function which enforced us to use oral voriconazole, which previously has been used for treatment of fungal endocarditis either alone or in combination. Voriconazole is a broad spectrum antifungal agent acts by inhibiting the synthesis of ergosterol in the fungal cell membrane.⁷

Figure 2 Fundus examination showing Roth's spot in right temporal field.

Figure 3 CT brain showing acute infarct in the temporo-occipital region.

Figure 4 Transesophageal echocardiographic picture of aortic valve of showing vegetations attached to right and non-coronary cusps.

Learning points

- ▶ Native valve endocarditis is increasing recently; high index of clinical suspicion is required for diagnosis.
- ▶ Previous use of antibiotics is the most important cause of culture negative endocarditis, the possibility of fungal endocarditis should be considered in such a scenario.
- ▶ Voriconazole can be used as an alternative therapeutic option to amphotericin-B, especially in patients with renal dysfunction.

Competing interests None.

Patient consent Obtained.

Provenance and peer review None.

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