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Case Report

CASE REPORT

Native valve fungal endocarditis caused by *Aspergillus fumigatus*: management dilemma

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Abstract

Fungal endocarditis (FE) accounts for ~50% of the mortality rate associated with predisposing host conditions. Despite optimal therapeutic strategies, the survival rate remains low. FE is mostly caused by *Candida albicans* and *Aspergillus fumigatus*. Previous valvular surgery is the most essential risk factor for Aspergillus endocarditis, which observed in 40–50% of cases. However, native valve FE caused by Aspergillus is uncommon, with only a few reported cases. We hereby report a case of native valve FE caused by *A. fumigatus* with complications following Wegener's disease and prostate cancer. The patient survived after successful management with the combination of surgical and medical therapy. Aspergillus endocarditis is a rare and fatal fungal infection. Despite difficulties in diagnosis and treatment, medical intervention with antifungal therapy and immediate surgical intervention are essential to achieve desirable outcomes.

INTRODUCTION

Fungal endocarditis (FE) is a rare lethal inflammatory disease affecting the endocardium, including the heart valves. Neurological features, such as brain abscess, are known to manifest as complications of infective endocarditis (IE) [1]. Native valve FE caused by Aspergillus is uncommon and only a few cases have been reported in the literature, as it usually occurs in patients who have previously undergone valvular surgery [2]. Herein, we describe a case of native valve FE presented with brain abscess, who was treated successfully with amphotericin B, voriconazole, surgical debridement and mitral valve replacement.

CASE REPORT

A 71-year-old male patient, with a medical history of diabetes, hypertension, coronary artery disease, Wegner's disease and prostate cancer treated with androgen deprivation therapy and radical radiotherapy. He presented with a brain abscess that manifested as a 1-month history of headache, changes in vision, loss of taste and weakness. However, there was no nausea, vomiting, seizure, fever or loss of consciousness. The physical examination was unremarkable. During investigations, brain magnetic resonance image (MRI) showed a right frontal abscess. The patient refused to undergo surgical drainage and

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developed a sudden decrease in vision, but without headache. Subsequently, the patient had sinus tachycardia, facial weakness and slurred speech. The stroke code was activated, followed by an immediate right frontal craniotomy and excision of the brain lesion. However, a culture of the drainage yielded *Aspergillus fumigatus*, and the patient was started on voriconazole. FE was suspected, and the patient was referred to the cardiology department so that the source of the brain abscess could be identified. Later, echocardiography was done and large vegetation was seen on the anterior mitral leaflet. Because of several risk factors, including recent stroke, low platelet count, steroid-induced immunosuppression to treat Wegner's disease and renal impairment, a multidisciplinary meeting was conducted, and finally the cardiac surgeon accepted the case and successfully performed bioprosthetic mitral valve replacement.

Radiographic and laboratory investigations

Two years post-biopsy proven prostatic cancer diagnosis, he presented with hemoptysis, melena, cramps and generalized weakness, with alveolar hemorrhage observed on the chest X-ray. Rheumatology workup was performed and showed positive results for antineutrophil cytoplasmic antibodies (pANCA and cANCA), confirming the diagnosis of Wegener's disease. The patient's diabetes was controlled within normal level, with the highest recorded hemoglobin A1c level being 7.1%.

After 5 months, he presented with neurological manifestations, and MRI of the brain showed a right frontal lobe small abscess with surrounding vasogenic edema (Fig. 1). A biopsy of the brain tissue showed *A. fumigatus*. Three days later, a transthoracic echocardiogram (TTE) was done to diagnose endocarditis based on Duke's criteria and revealed a large 1.7 × 1.7 cm vegetation on the anterior leaflet of the mitral valve (Fig. 2) [3]. Meanwhile, laboratory tests showed a progressive decrease in the platelet count, with the lowest reading of 35 × 10^9/L. Abdominal imaging was performed, revealing no splenomegaly or ascites. Heparin-induced thrombocytopenia was suspected; however, the hematologist excluded this possibility later and suspected it to be due to the systemic disease. The patient was restarted on heparin and there was no decrease in platelet levels.

After 1 month of antifungal therapy, echocardiogram was repeated and showed a slight increase in the vegetation size with a concurrent increase in mitral regurgitation severity. Computed tomography (CT) of the brain was performed and revealed no interval changes.

After surgical debridement and replacement of the mitral valve, tissue culture of the vegetation was obtained and showed isolated *A. fumigatus*. A brain MRI scan was done for comparison with the previous MRI. Fortunately, the right frontal abscess had resolved, yet residual encephalomalacia and hemosiderin deposition were noted. However, the left posterior frontal cortical and subcortical diffusion restriction lesions were significantly improved.

Course of management

The prostate cancer was treated with radical radiotherapy for 49 days and androgen deprivation therapy with leuprorelin every 3 months for 2 years. The patient's latest prostate-specific antigen level was 0.02 ng/ml and an abdominal and pelvis CT was unremarkable.

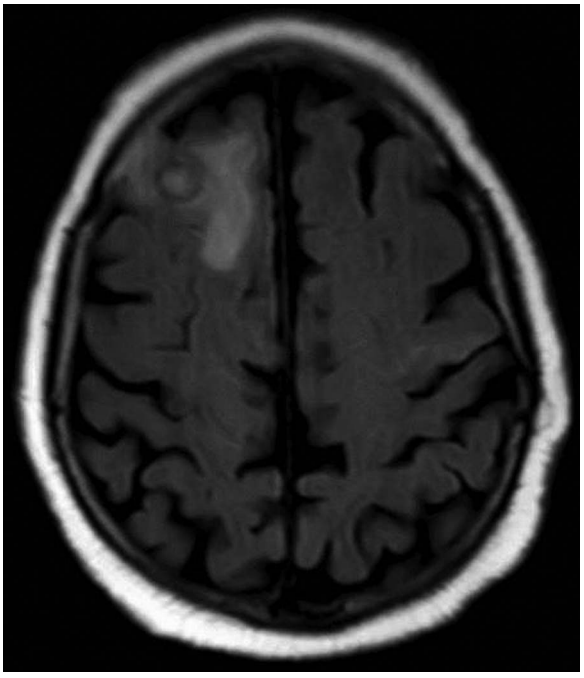

Figure 1: MRI of the brain showed a small abscess in the right frontal lobe with surrounding vasogenic edema.

Manifestations of Wegener's disease and worsening hemoptysis (200–250 ml) with difficulty in breathing were treated with 12 units of fresh frozen plasma and 3 units of packed red blood cells after the activation of the critical care response team. Furthermore, the patient was intubated and investigated with bronchoscopy, and some improvements were noticed. Subsequently, cyclophosphamide, prednisone and antibiotics (meropenem, vancomycin, azithromycin and caspofungin) were started while mesna was administered intravenously (i.v.). Variable doses of oral cyclophosphamide were administered following the discontinuation of i.v. cyclophosphamide accompanied by adjustable doses of oral prednisone depending on the severity of the clinical symptoms. Furthermore, plasmapheresis was initiated once daily for 3 days and subsequently every other day for another three sessions.

Brain abscess was managed by right frontal craniotomy and excision of the brain lesion. After the identification of *A. fumigatus*, antifungal therapy was initiated with a combination of oral voriconazole for >4 months and amphotericin B for 2 months. Voriconazole was continued for 1 year as secondary prophylaxis and the patient was not discharged.

Although the echocardiogram showed a large vegetation, the surgical removal was delayed due to the patient's multiple comorbidities. Because of the recent craniotomy (11 months prior) and other comorbidities, the surgery was not urgent (Supplementary Table A1). Despite the high risk, successful resection of the native mitral valve with a thorough debridement of the vegetation was achieved. Subsequently, the patient received a 29-mm Magna mitral bioprosthetic valve (Fig. 3). After adequate reperfusion, the cardiopulmonary bypass was weaned off. The aortic cross-clamp was removed after left atrium closure.

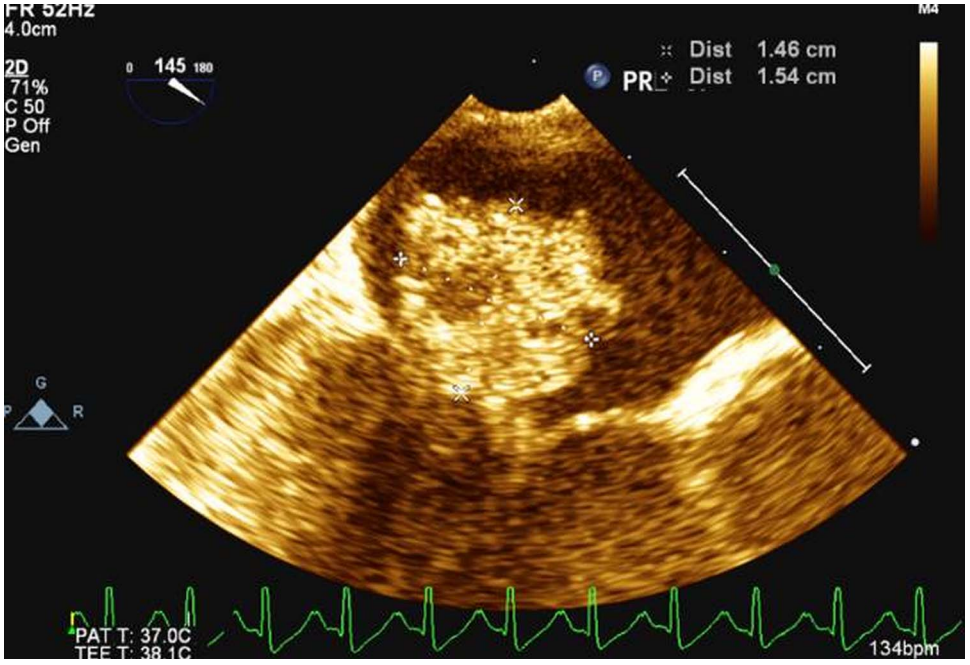

Figure 2: Preoperative 2D TTE showing large vegetation on the anterior mitral valve leaflet.

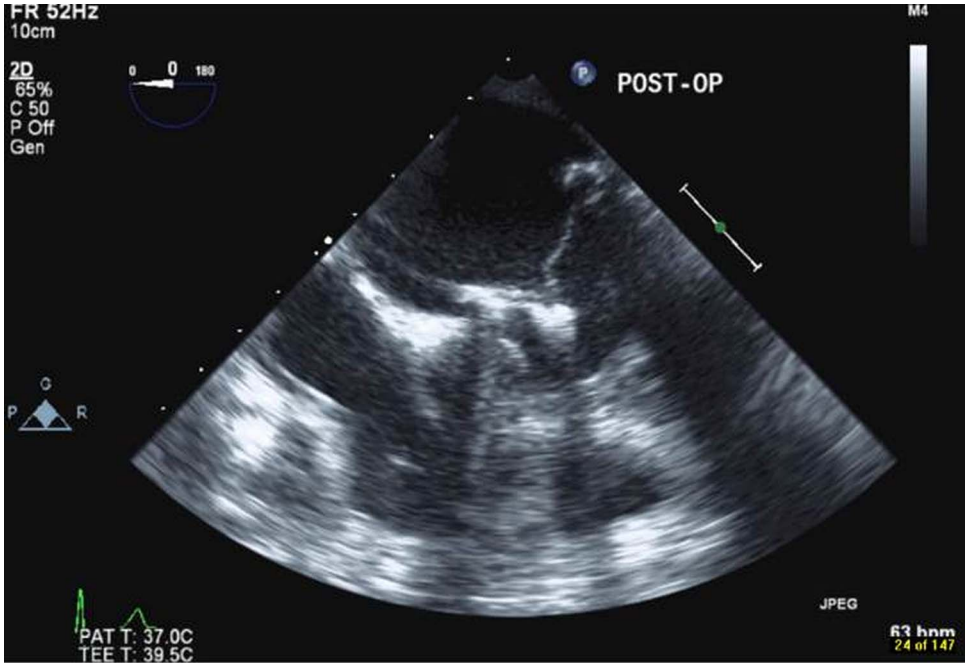

Figure 3: Postoperative TTE with a 29-mm bioprosthetic mitral valve.

Outcome and follow-up

A year post-cardiac surgery, the patient is asymptomatic, still on oral voriconazole and doing well.

DISCUSSION

Aspergillus endocarditis is rare and often associated with an obvious predisposition, mostly prior cardiac surgery, which was found in 40–50% of patients [2]. Its rarity accounts for the limited experience in its diagnosis and treatment [4]. Therefore, native valve FE caused by Aspergillus is unusual [5]. Up to 50% of patients with IE developed systemic embolization as a complication [6], including brain abscess [1]. The good clinical outcome and prognosis of such a condition requires well-developed medical and surgical skills attributed to the high morbidity and mortality rate associated with the insult [7].

Early diagnosis is very crucial for better outcomes in Aspergillus endocarditis. Generally, diagnosis can be made by echocardiography and multiple blood cultures and/or biopsies

[4]. Additionally, the diagnosis of Aspergillus endocarditis can be challenging as the blood culture usually appears negative, despite the presence of vegetation on echocardiography. Only 4–30% of Aspergillus endocarditis cases show positive blood cultures [8]. In our patient, the inflammatory process and IE might have led to the development of Wegner's granulomatosis as an autoimmune reaction [9].

Currently, new non-culture methods have been developed to detect the presence of fungus in the blood. These include mannan antigen and antibody tests, 1,3-β-D-glucan test, polymerase chain reaction (PCR), real-time PCR targets and next-generation sequencing [10]. However, despite the advancements in molecular technology and imaging studies, the course of this condition and delayed clinical recognition remain obstacles.

Aspergillus endocarditis is a rare and fatal fungal infection. Despite the difficulties in diagnosis and treatment, medical intervention with antifungal therapy and immediate surgical intervention are essential to achieve desirable outcomes.

SUPPLEMENTARY DATA

Supplementary data are available at *OMCREP* online.

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