

Surgical Treatment of Native Valve Aspergillus Endocarditis and Fungemic Vascular Complications

Systemic infection with *Aspergillus* is an opportunistic disease that affects mainly immunocompromised hosts, and is associated with a high mortality rate. It typically occurs in patients with several predisposing factors, but *Aspergillus* endocarditis of native valves is rare and experience in diagnosis and treatment is limited. We report a case of native valve endocarditis caused by *Aspergillus*. A 35-yr-old male patient who underwent pericardiocentesis four months previously for pericardial effusion of unknown etiology presented with right leg pain and absence of the right femoral artery pulse. Cardiac echocardiography revealed severe mitral insufficiency with large mobile vegetations, and computed tomographic angiography showed embolic occlusion of both common iliac arteries. We performed mitral valve replacement and thromboembolectomy, and *Aspergillus* was identified as the vegetation. We started intravenous amphotericin B and oral itraconazole, but systemic complications developed including superior mesenteric artery aneurysm and gastrointestinal bleeding. After aggressive management, the patient was discharged 78 days post surgery on oral itraconazole. He was well at 12 months post discharge but died in a traffic accident 13 months after discharge.

Key Words : *Aspergillus*; Endocarditis; Vascular Diseases; Surgery

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INTRODUCTION

Fungal endocarditis is an uncommon occurrence; its incidence was reported as 1.3 to 6% of infective endocarditis cases (1). *Aspergillus* species contributes to approximately 25% of all cases of fungal endocarditis, second to the *Candida* species in frequency. Several conditions predispose patients to *Aspergillus* infections including underlying cardiac abnormalities, prosthetic heart valves, indwelling central venous catheters, prolonged use of broad-spectrum antibiotics, and intravenous drug abuse (1, 2).

We present a case of *Aspergillus* endocarditis of a native valve, presenting as a femoral artery occlusion.

CASE REPORT

A previously healthy 35-yr-old male was admitted with right leg pain. Four months previously, he underwent a pericardiocentesis for a fever and massive pericardial effusion; no organism was found in the pericardial effusion. A precordial systolic murmur was heard during auscultation of the heart, and a right femoral artery pulse was not detected. The transthoracic echocardiography revealed severe mitral insufficiency with large mobile vegetations on the anterior and posterior mitral valve leaflets (Fig. 1A). The computed tomograph-

ic angiography showed an embolic occlusion of both common iliac arteries (Fig. 1B). The patient underwent emergency replacement of the mitral valve with a 29 mm prosthetic mechanical mitral valve (SJM masters series, St. Jude Medical, St. Paul, MN, U.S.A.), and bilateral ilio-femoral artery thromboembolectomy with a Fogarty catheter through both femoral arteries. Gross findings in the surgical field revealed 1.5 × 1.5 cm round irregular vegetations on the middle portions of both mitral valve leaflets. The patient recovered well during the immediate postoperative period. However, a right popliteal artery occlusion was found four day after surgery. We performed a right popliteal artery thrombectomy through a supragenicular approach.

On histology, a fungal lesion showing the characteristic findings of *Aspergillus* was found. Culture of the valvular tissue on Sabouraud dextrose agar confirmed the *Aspergillus* species (Fig. 1C, D). Anti-fungal medication was planned with intravenous amphotericin B for six weeks then oral itraconazole for 12 weeks. Therefore, we started intravenous amphotericin B (5 mg/kg/day).

Forty days after the first operation, the patient complained of abdominal pain. A computed tomography showed multiple aneurysmal changes of the superior mesenteric artery (SMA), splenic artery, hepatic artery and left iliac artery despite amphotericin B treatment (Fig. 2). The patient underwent SMA aneurysmectomy and arterial reconstruction with bovine peri-

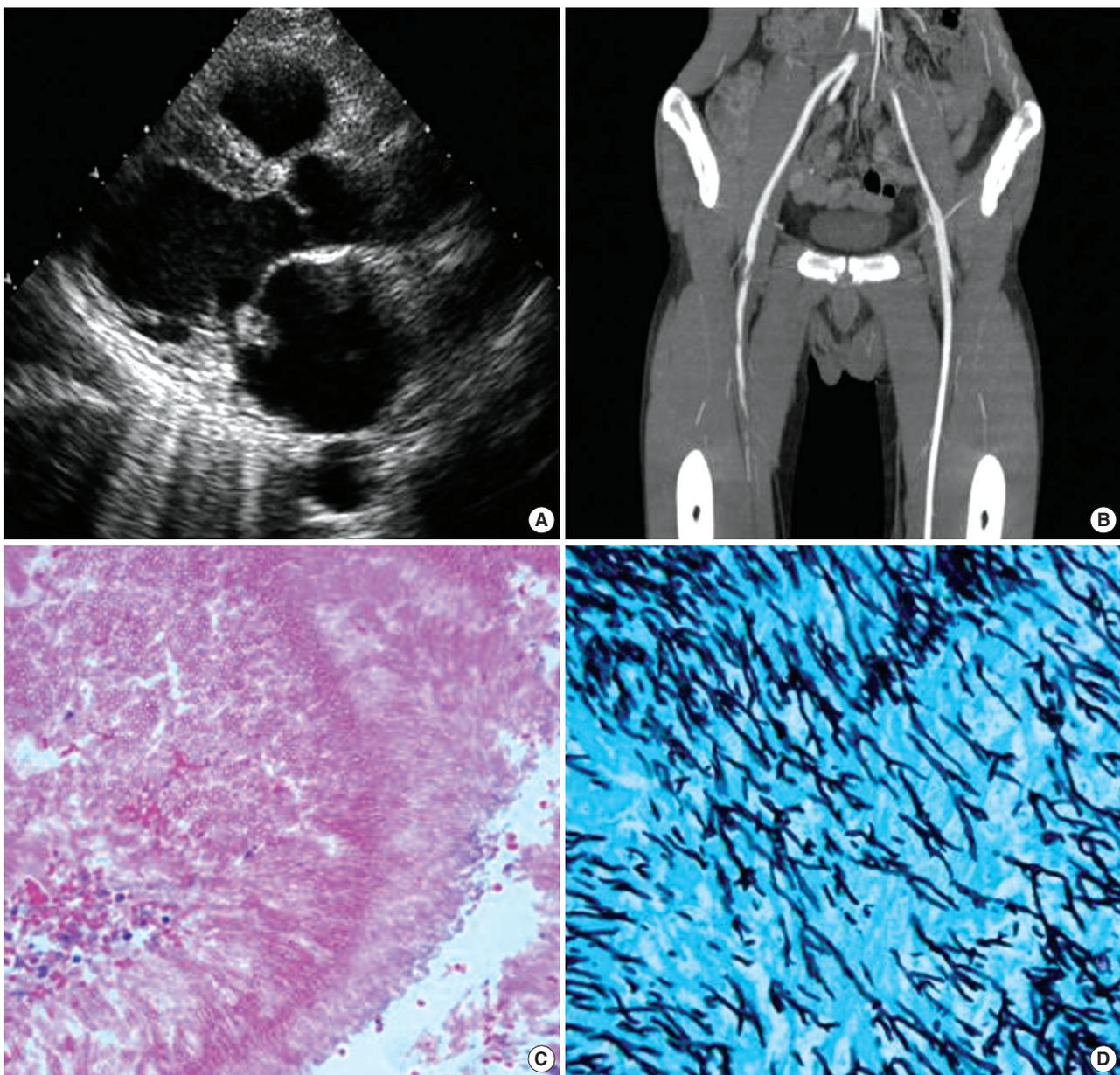


Fig. 1. (A) Preoperative cardiac 2-D echocardiography. This shows large mobile vegetations of the anterior leaflet of the mitral valve. The estimated size of vegetation was 1.2×1 cm. (B) Preoperative computed tomographic angiography shows focal occlusion of the iliac bifurcation and the right femoral artery. (C, D) Histological findings of vegetation of the mitral valve (C, H&E stain $\times 400$; D, GMS stain $\times 400$). Note the septate hyphae consistent with *Aspergillus*.

cardium, and left iliac artery repair. Concomitant thromboembolectomy was performed because of the bilateral internal iliac artery occlusions. Amphotericin B was changed to oral itraconazole (800 mg/day) at 6 weeks after the first operation.

Fifty-eight days after the first operation, the patient had hematochezia, and had a colonoscopy that revealed multifocal intestinal bleeding. He recovered after massive transfusion and supportive care. The patient was discharged 78 days after surgery on oral itraconazole and warfarin. On follow-up, the itraconazole was discontinued 10 weeks later. He was alive and

doing well 12 months later without recurrence. Unfortunately, he died in a traffic accident 13 months after discharge.

DISCUSSION

Aspergillus is a ubiquitous mold capable of causing several diseases in both healthy humans and immunocompromised hosts. *Aspergillus* species endocarditis is an ominous condition and its prevalence is increasing in the hospital population.

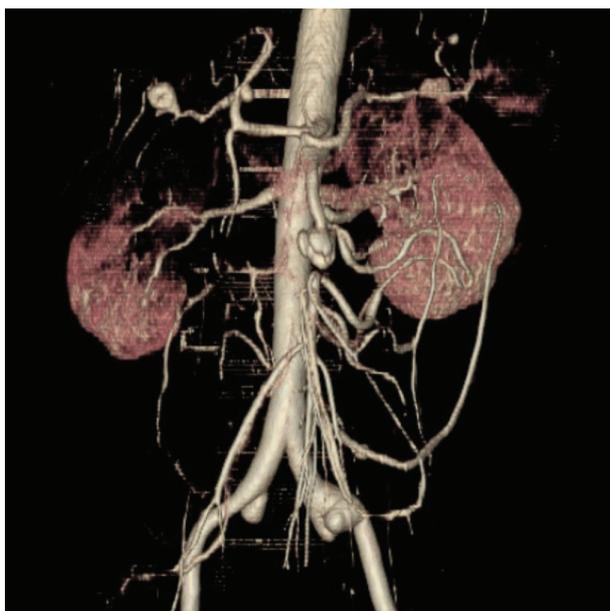


Fig. 2. 3-D reconstruction of the computed tomographic angiography at 40 days after the first operation. This shows multiple aneurysmal of the aorta, such as the superior mesenteric artery, splenic artery, left iliac artery.

Men are more commonly affected than are women with a peak incidence during the third to fourth decades of life (1, 3). Numerous risk factors have been identified in the pathogenesis of *Aspergillus* endocarditis. Previous valvular surgery is the most important risk factor, and was reported in 40% to 50% of patients diagnosed with *Aspergillus* endocarditis (1, 2).

Aspergillus endocarditis of native valves is rare and experience in diagnosis and treatment is limited (1, 4). Only 28 cases of *Aspergillus* endocarditis were found in a MEDLINE search from 1995 to 2006, and the mortality rate was reported to be higher than 90% despite aggressive surgical and antifungal therapies (1). In most cases, predisposing factors were found including underlying cardiac conditions, prosthetic cardiac devices, central venous catheters, and previous antibiotic treatment. In 3.4% of cases with fungal endocarditis, no predisposing factor was reported (1). In this case, the patient underwent pericardiocentesis for pericardial effusion, but we could not find any predisposing factors.

Because of the ubiquitous nature of the organism, establishing a definitive diagnosis of disease caused by *Aspergillus* is difficult (5). The *Aspergillus* species is very rarely isolated from blood culture. Many cases are diagnosed on surgical specimens or at autopsy. Recently, antigen detection methods and the polymerase chain reaction have been developed to improve the diagnosis of invasive *Aspergillosis* (6). Echocardiography is a very important diagnostic modality for *Aspergillus* endocarditis. The vegetations in *Aspergillus* endocarditis are large and highly mobile and peripheral embolization is common in early stage disease (1). In this case, the patient presented

with iliac artery occlusions and with large mobile vegetations of the mitral valve.

The optimum therapy in patients with *Aspergillus* endocarditis remains unclear. In general, the largest databases for *Aspergillosis* treatment include amphotericin B and various surgical modalities (5). In this case, we used a combination of amphotericin B, itraconazole and aggressive surgical treatment, but severe disseminated fungemia reappeared unexpectedly during the early postoperative period with a SMA aneurysm and peripheral artery embolic occlusions. These complications may have been due to delay of antifungal treatment after surgery and dissemination by cardiopulmonary bypass before antifungal therapy was started. Relapsing fungal endocarditis is a complication seen in as many as 30 to 40% of patients who have fungal endocarditis and who survive to complete short-term therapy (7). Thus, all patients who survive long enough to complete acute treatment are potential candidates for long-term suppressive antifungal therapy (1, 3, 8).

Aspergillus endocarditis is rare and there is limited experience with its diagnosis and treatment. Native valve *Aspergillus* endocarditis is uniformly fatal without immediate and extensive surgical intervention combined with prolonged antifungal therapy.

REFERENCES

- Pierrotti LC, Baddour LM. *Fungal endocarditis 1995-2000*. *Chest* 2002; 122: 302-10.
- Ellis ME, Al-Abdely H, Sandridge A, Greer W, Ventura W. *Fungal endocarditis: evidence in the world literature, 1965-1995*. *Clin Infect Dis* 2001; 32: 50-62.
- El-Hamamsy I, Durrleman N, Stevens LM, Perrault LP, Carrier M. *Aspergillus endocarditis after cardiac surgery*. *Ann Thorac Surg* 2005; 80: 359-64.
- Gumbo T, Taeye A, Mawhorter S, McHenry MC, Lytle BH, Cosgrove DM, Gordon SM. *Aspergillus valve endocarditis in patients without prior cardiac surgery*. *Medicine (Baltimore)* 2000; 79: 261-8.
- Stevens DA, Kan VL, Judson MA, Dummer S, Denning DW, Bennett JE, Walsh TJ, Patterson TF, Pankey GA. *Practice guidelines for diseases caused by Aspergillus*. *Infectious Diseases Society of America. Clin Infect Dis* 2000; 30: 696-709.
- McCracken D, Barnes R, Poynton C, White PL, Isik N, Cook D. *Polymerase chain reaction aids in the diagnosis of an unusual case of Aspergillus niger endocarditis in a patient with acute myeloid leukemia*. *J Infect* 2003; 47: 344-7.
- Fernandez-Guerrero ML, Verdejo C, Azofra J, de Gorgolas M. *Hospital-acquired infectious endocarditis not associated with cardiac surgery: an emerging problem*. *Clin Infect Dis* 1995; 20: 16-23.
- Kotanidou AN, Zakynthinos E, Andrianakis I, Zervakis D, Kokotsakis I, Argyrakos T, Argiropoulou A, Margariti G, Douzinas E. *Aspergillus endocarditis in a native valve after amphotericin B treatment*. *Ann Thorac Surg* 2004; 78: 1453-5.