

Fatal aortitis: a complication of aspergillus endocarditis following coronary artery bypass graft surgery

M Esmailzadeh, MMPeighambari, M Parsaee, AJ Khamooshi, SS Hosseini

Shaheed Rajaei Cardiovascular Medical and Research Center, Tehran, Iran.

The most common fungal organism to cause endocarditis is *Candida* which is followed by *Aspergillus*. *Aspergillus* endocarditis can occur in either the native or prosthetic heart valves, usually occurring post operatively after cardiac surgery on implanted valves. The usual route of infection for invasive aspergillosis is through inhalation of organism into the lungs. Diagnosis is difficult because blood culture usually remains negative even with extensive disease. Long term survival is limited even with surgical intervention.

Herein, we present a 49-year-old man with previous history of coronary artery bypass graft and aortic valve endocarditis which was diagnosed as *Aspergillus* endocarditis after the valve surgery. Unfortunately the patient died because of late occurrence of progressive aortic invasion caused by *Candida* and *Enterococci*.

Key words: Aspergillosis, Coronary artery bypass graft, Endocarditis, Complication

Introduction

The most common fungal organism to cause endocarditis is *Candida* with 62%, which is followed by *aspergillus* at 18%¹. *Aspergillus* is a hyaline mold that is the etiologic agent responsible not only for invasive aspergillosis but also a variety of noninvasive or semi-invasive conditions². The organism is found in solid, water, food, air and is particularly common in decaying vegetation². The inoculate for establishing infection is not known, but it is apparent that hosts with normal pulmonary defenses very rarely develop disease despite daily exposure to the organism's airborne conidia, arising from food stuffs². In contrast patients with decreased host immunity show increasing susceptibility to the organism². The usual route of infection

for invasive aspergillosis is through inhalation of *aspergillus* conidia into the lungs, although other routes of exposure such as inhalation of aerosols contaminated with *aspergillus* conidia have been suggested². Although less common, invasive infection may also follow local tissue invasion such as through surgical wounds or contaminated intravenous catheters leading to cutaneous infection. *Aspergillus* endocarditis can occur in either native or prosthetic heart valves. *Aspergillus* endocarditis usually occurs post- operatively after cardiac surgery on implanted valves. Diagnosis is difficult because blood culture usually remains negative despite extensive disease³. Even with surgical intervention, long term survival is limited.

Case Report:

A 49 year-old-man was referred to our institution because of 3 months fever, dyspnea, malaise, left leg pain, anorexia, and weight loss.

Correspondence:

Maryam Esmailzadeh,
Shaheed Rajaei Cardiovascular Medical and Research Center, Vali-Asr Ave. Adjacent to Mellat Park, Tehran, Iran.
email: m_eszadeh@yahoo.com, meszadeh@rhc.ac.ir

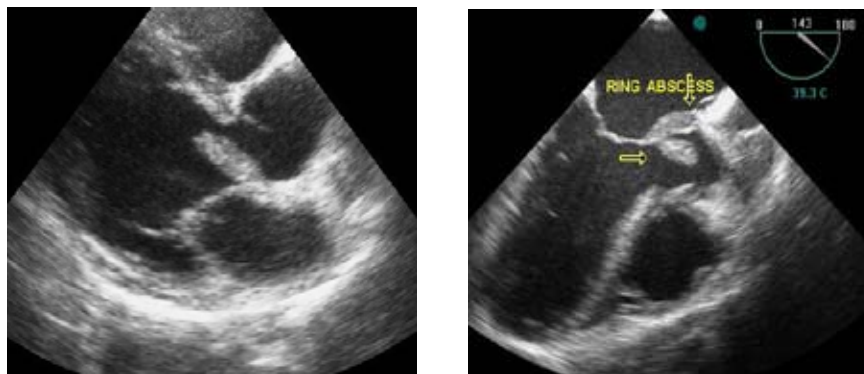


Figure 1. Left, transthoracic parasternal long-axis view showing very large smooth surface bulky vegetation on left coronary cusp of Aortic valve. Right, transesophageal long-axis view showing large vegetation and ring abscess (arrows).

He had a history of tooth extraction almost 1 month before the presentation and coronary artery bypass grafting (CABG) 2.5 years ago and twice recent vascular surgery for arterial emboli in another center.

On physical examination, there was tachycardia (HR=105), low grade fever (38°C), holo-diastolic murmur along the left sternal border, paresthesia and absence of the left lower extremity arterial pulse. But there were no peripheral signs of endocarditis.

The electrocardiogram related sinus tachycardia with first degree AV block and inverted T waves in left precordial leads. Lab data disclosed mild normochromic-normocytic anemia (hemoglobin=9.5g/dl), leukocytosis (WBC=13700) polymorphonucleosis (78 %), eosinophil (8%), increased erythrocyte sedi-

mentation rate (ESR) up to 105 and C reactive protein (CRP) more than 90 mg/lit. Urine analysis, liver and renal function tests were normal. Serologic tests for HBS antigen, HCV antibody, and HIV antibody were negative. Results of all blood cultures were negative. Chest CT scan was normal. Doppler sonography of lower extremities arteries showed bilateral occlusion or high grade stenosis of superficial femoral artery which seemed to be chronic because of the presence of abundant collaterals.

Transthoracic echocardiography (TTE) followed by transesophageal echocardiography (TEE) revealed moderately enlarged left ventricle (LV) with subnormal ejection fraction (EF=50%) very large (25 x 18 mm) bulky smooth surface mobile vegetation on the non-coronary aortic cusp with ring abscess formation

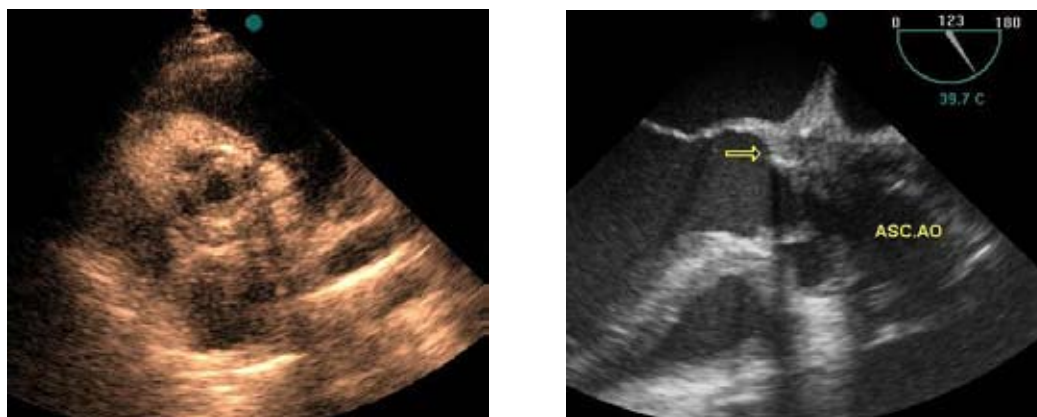


Figure 2: Left, transthoracic parasternal short-axis view exhibiting much thickened aortic bioprosthesis leaflets with significant obstruction secondary to commissural fusion. Right, transesophageal long-axis view of aortic valve and ascending aorta revealing severe obliteration and obstruction of ascending aorta by multiple bulky vegetations (arrow).

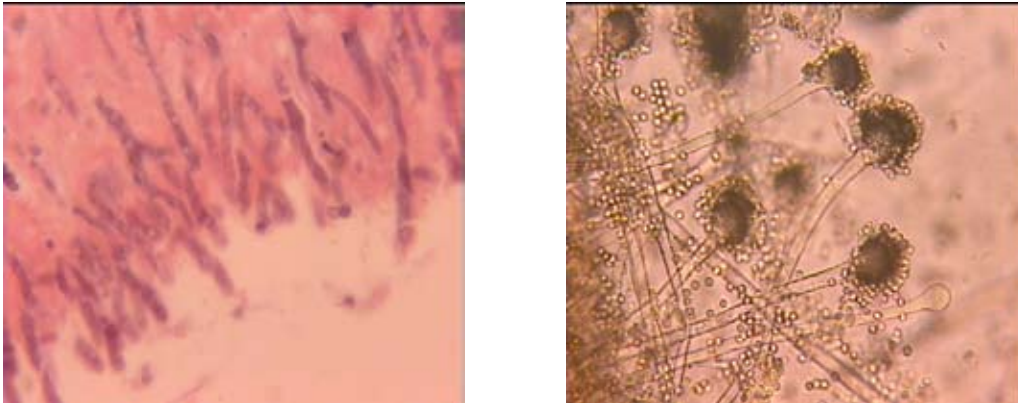


Figure 3: Left, microscopic section of aortic valve vegetation (H& E staining x400) consisting of acute-angle branching septate hyphae. Fungal elements consistent with *Aspergillus* Spp. Right, septate hyphae with acute-angle-branching and numerous fruiting bodies (wet-mount smear from cultured specimen).

on posterior side of aortic root(Fig.1) and severe aortic regurgitation secondary to flail aortic valve. Coronary CT angiography showed patent grafts.

Several blood cultures were obtained, the empiric treatment with vancomycin and ceftriaxon was started. The patient was taken to the operating room for elective aortic valve replacement (AVR) on day three to decrease the major embolic rate. Since homograft valve was not available, the aortic valve was replaced by a mechanical bileaflet valve. A large mass with smooth surface was found on non-coronary cusp of aortic valve.

Histopathologic examination of the excised

valve demonstrated acute infective endocarditis with fungal elements consistent with *aspergillus* Spp (Fig.3).

Immediate treatment with, amphotericin B (1mg/kg) was started.

One week after valve replacement the post operative TEE showed pseudoaneurysm formation of intervalvular fibrosa and normal prosthetic aortic valve function. The posterior aortic root was thickened but no typical vegetation could be seen. However, the patient continued to be febrile with elevated ESR and CRP. On day 28 the second post operative TEE was done which showed multiple vegetations on the aortic valve prosthesis and inside the

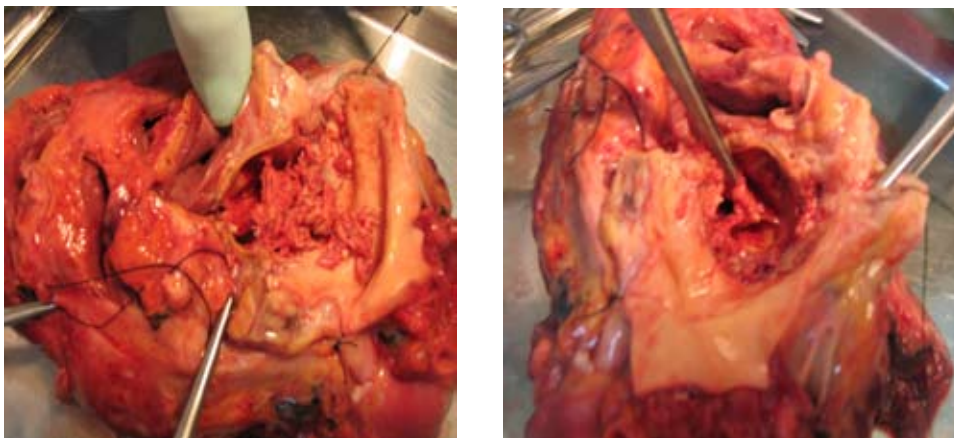


Figure 4: Left, post mortem examination showed significant thickening of aortic bioprosthesis, Right, aortic lumen had been filled by fragile and soft pieces of vegetations.

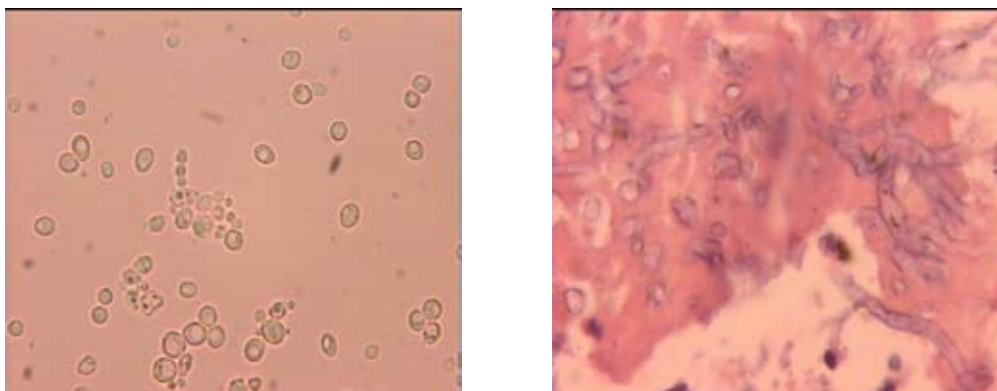


Figure 5: Left, microscopic examination of bulky vegetation in aortic root obtained at autopsy (H&E staining x400). Fungal elements consistent with *Candida* SPP. Right, numerous yeast forms with budding (wet-mount smear from cultured specimen).

ascending aorta. On day 32 repeat operation was done by which mechanical valve was removed and replaced by a porcine free style valve with mini root replacement.

Tissue culture resulted in isolation of coagulase negative staphylococcus and aspergillus SPP, for which vancomycin and rifampin were added to antifungal regimen. The patient remained febrile despite antimicrobial and antifungal therapy.

Repeat TEE 7 weeks after the second surgery showed extensive invasion of the bioprosthetic aortic valve and aortic root by vegetation resulting in moderate valve stenosis with significant intramural and intraluminal invasion

(Fig.2), severely decreased LV systolic function (EF=25-30%) in favor of infective, hypersensitivity and or drug-induced myocarditis.

Varicomazole a new antifungal agent was prescribed and the patient scheduled for Bentall operation with homograft valve but unfortunately he developed acute severe chest pain followed by asystole cardiac arrest. Full cardiopulmonary resuscitation was carried out without success. On post mortem examination there was extensive thickness of bioprosthetic valve leaflets with ring abscess. The aortic lumen had been filled by fragile and soft creamy pieces (vegetations), resulting in coronary artery ostial obstruction (Fig. 4). However, since

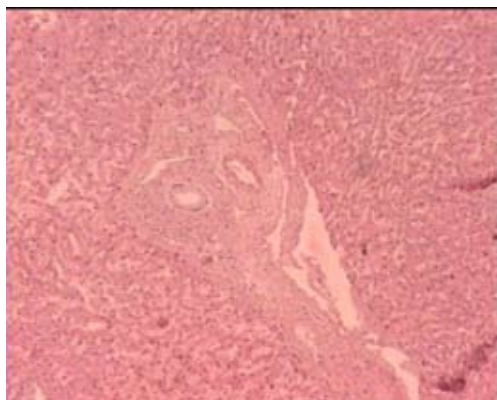


Figure 6: Section of liver showing fibrous expansion of portal spaces, on macroscopic examination centrilobular hemorrhagic necrosis, bile pigment deposition in intracanalicular ducts, and sinusoidal congestion were noted.

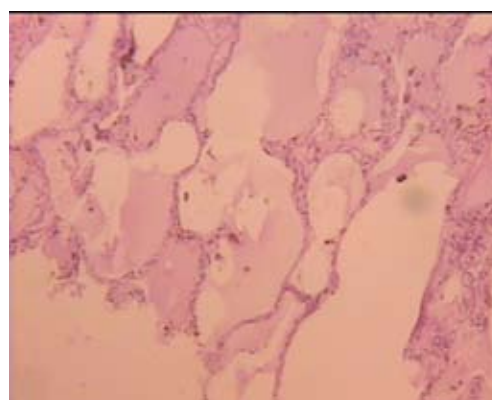


Figure 7: Section of lung demonstrating edema fluid in alveoli and hemosiderin-laden macrophages (CHF cells).

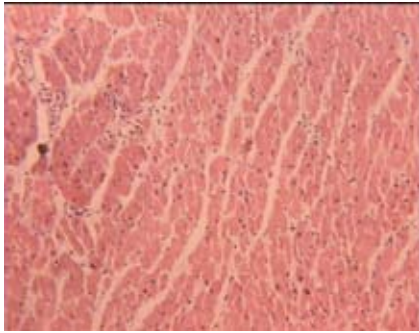


Figure 8: Microscopic section of myocardium showing unremarkable myocytes, mild interstitial chronic inflammatory cell infiltrates and edema.

the patient died within 12 hours of the chest pain episode, the histological findings of myocardial infarction could not be seen (Fig.6). The histological findings of liver and lung also were unremarkable (Fig.7,8). Microscopic examination showed pseudohyphae and yeast consistent with candida Spp (Fig. 5). Enterococci also were isolated from tissue culture of ring abscess.

Discussion

Aspergillus is a ubiquitous mold and also the most common laboratory contaminant. In healthy individuals with a normally functioning immune system, the body is usually able to clear aspergillus effectively. However, in the debilitated state or in immunocompromised hosts, aspergillus can cause opportunistic infections, colonizing aspergillosis, invasive aspergillosis or aspergillus endocarditis. Aspergillus endocarditis usually occurs post-operatively after cardiac surgery on implanted valves, but is rarely present in native heart valves.

Aspergillus endocarditis is mostly an opportunistic infection⁴. Interestingly, none of the patients with aspergillus endocarditis after cardiac surgery were immunocompromised. Sanches-Recalde et al reported eight patients with cardiac aspergillosis after AVR or CABG,

who were not immunocompromised⁵. This was consistent with our case that was not immunocompromised and did not receive long-term antibiotic treatment. Supheinous vein graft rupture due to aspergillus necrotizing vasculitis in an immunocompetent host was reported by Jutta Draganou et al⁶. This suggested that the most important alteration of host defense was probably due to the surgical procedure itself⁵. Aspergillus is a primary infection secondary to aortic surgical damage after cannulation for cardiopulmonary bypass. Aspergillus is common after aortotomy for AVR or CABG. Surgical trauma of aortotomy could damage the aortic valve, which would be contaminated by airborne fungal spores and initiating an inflammatory response⁵. In view of the fact that aspergillus not reported after mitral valve surgery⁵, the source of infection probably located at the supracoronary sinus level, distal to blood flow from the heart.

Interestingly, males' predominated in all of the previously reviewed cases. This may be explained by female hormones playing a protective role as estradiol was described as an inhibitor of aspergillus growth in vitro. However, the roles played by gender as a risk factor for aspergillosis is controversial, due to limited number of cases and because coronary and aortic valve surgery are more prevalent in males than in females. Our patient underwent cardiac surgery (CABG) 2.5 years ago in another medical center with another reported case of post surgical aspergillus endocarditis in the same center. In a study by Sanchez-Recalde et al. high concentration of aspergillus were found in the ventilation system and on the surgical unit floor 5. In one study aspergillosis began 4 to 24 months after surgery⁵. Our patient had a delayed presentation of 27

months after cardiac surgery. *Aspergillus* cardiovascular infection presents as endocarditis with clinical manifestations similar to other fungal cardiovascular infections. Blood cultures are typically negative in aspergillosis³. In our patient the results of all blood cultures were negative, leading to delayed diagnosis and playing an important role in patient's death. In addition, prolonged latency from surgery to clinical onset was at least partly responsible for fatal outcome. The management of fungal endocarditis required aggressive medical and surgical approaches. Prompt therapy with high doses of amphotericin B is indicated². After 1 to 2 weeks of full dose amphotericin B therapy, surgery might reduce the potential infectious load and the recurrences of this disseminating disease². Therefore early diagnosis and immediate medical treatment before surgery may improve the poor survival. Although in our patient, the accurate diagnosis of *aspergillus* endocarditis was made after surgery, the inability to reduce the infectious load by antifungal therapy before surgery may account for a potential cause of disease progression.

Echocardiography is a rapid and reliable diagnostic tool for early detection of vegetation on heart valves, and might have changed the fatal outcome⁴. *Aspergillus* endocarditis results in large bulky vegetation with a greater tendency for valvular insufficiency, destruction of adjacent tissue, and embolization⁴. The vegetation starts at the lines of closure, and extends

into the adjacent areas of the valve leaflet and chordae tendinae⁴.

The postmortem isolation of candida and enterococci from aortic wall tissue culture may be secondary to long-lasting hospitalization, partial immunosuppression secondary to prolonged multiple antimicrobial treatment and drug-resistance resulting from nosocomial infection.

TEE and as needed other imaging techniques such as CT scan, and MRI should be considered in patients with prolonged fever and negative blood culture after open-heart surgery involving significant aortic valve or wall damage irrespective of the postoperative period⁵.

Survival rate in patients increased approximately 40% with improved diagnostic techniques and subsequent initiation of rapid combined medical and surgical treatments².

Conclusion

Aspergillus endocarditis is a dismal complication typically found after valve or coronary surgery. Echocardiography is a reliable diagnostic tool for early detection of fungal endocarditis and its complications. Persistent or recurrent fever with elevated ESR and CRP are strong predictors of ongoing infection and development of complication. We recommend close monitoring of the integrity and regular maintenance of the air-filtration system, and particulate counts as a preventive strategy against this fatal entity.

References

- 1 Barbara Knollman-Ritschel, LT, MC, USNR. Pathology Cases for Diagnosis Case 97-01: *Aspergillus* Endocarditis on a Native Heart Valve: August 1997
- 2 Mandell's Principles and Practices of Infectious Diseases. Elsevier Inc 2005; 4: 2958-2970.
- 3 El-Hamamsy I, Durrleman N, Stevens LM; et al. Carrier M. *Aspergillus* endocarditis after cardiac surgery. *Ann Thorac Surg* 2005; 80(1): 359-364
- 4 Alvarez JR, Quiroga JS, Taboada CR, et al. Cardiac *Aspergillus* with Pedunculated Mass in Left Ventricle. *Tex Heart Inst J* 2004; 31(4): 439-441.
- 5 Sanchez-Recalde A, Mate I, Merino JL, et al. *Aspergillus* aortitis after cardiac surgery. *J Am Coll Cardiol* 2003; 41(1): 152-156.
- 6 Draganou J, Michael Klein H, Ghosizad A, et al. Rupture of a Saphenous Vein Coronary Artery Bypass Graft Due to *Aspergillus* Necrotizing Vasculitis. *Ann Thorac Surg* 2005; 80: 724-726.