

Candida albicans Endocarditis and a Review of Fungal Endocarditis: Case Report

Ugur Filizcan,¹ Sebnem Cetemen,¹ Yavuz Enç,¹ Mahmut Çakmak,² Onur Göksel,¹ Ergin Eren¹

¹Department of Cardiovascular Surgery,² Department of Cardiology,
Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Center, Istanbul, Turkey

ABSTRACT

Endocarditis due to fungal etiology is rare, but it is the most severe form of infective endocarditis. Fungal endocarditis is commonly complicated by systemic embolizations, and the difficulty in isolating the fungi with routine blood cultures complicates the diagnostic process. In these culture-negative cases of endocarditis, etiologic diagnosis is made with histopathologic examination of the cardiac valve, embolic materials, and systemic ulcers. In this case report, the presented patient with fungal endocarditis and its neurologic complications was treated with a surgical and medical approach.

INTRODUCTION

Fungal endocarditis (FE) is the most severe form of infective endocarditis and has the worst prognosis. Approximately 1.3% to 6% of all endocarditis cases are of fungal origin [Tunkel 1992, Pierrotti 2002]. In the last 2 decades, the increase in the incidence of FE is remarkable. The progress in invasive procedures, increased use of intracardiac prosthetic devices, prolonged use of intravenous catheters, administration of multiple wide-spectrum antibiotics, and immunosuppressive therapies are among the reported risk factors. [Tunkel 1992, Pierrotti 2002, Hauser 2003].

The morbidity and mortality of FE is high (50%) in spite of aggressive treatments. Several studies demonstrate that combined therapy of surgery and medical treatment provides better prognosis in these patients. [Tunkel 1992, Pierrotti 2002, Francisco 2003, Hauser 2003, Zellweger 2003].

This case report presents a patient with fungal endocarditis with neurologic complications; a combined surgical and medical approach was the choice for treatment.

CASE REPORT

A 45-year-old woman was admitted to our cardiac center with symptoms of fatigue, fever, and weight loss. Her medical history revealed that 2 years previously she had undergone a mitral valve replacement with a mechanical prosthesis (mechanical heart valve no. 29; St. Jude Medical, St. Paul, MN, USA). Considering the possibility of infective endocarditis due the prosthetic valve, we performed transthoracic echocardiography, which showed a left atrial mass and vegetations on the mitral prosthesis as well as mechanical valve dysfunction. Blood cultures were taken and intravenous (IV) ceftriaxone and gentamycin and oral rifampicin were given. Within hours, because of a worsening state of heart failure and dysfunctional prosthetic mitral valve, the patient was taken to surgery.

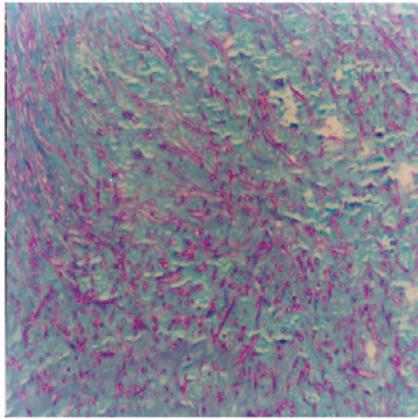
Intraoperatively, free-moving spheric multiple masses in the left atrium and large vegetations organized on the mitral annulus were seen. The infected prosthetic valve was explanted and another mechanical prosthesis (no. 29, St. Jude Medical) was implanted. Samples of the masses and vegetations were sent for bacteriologic and pathologic investigation.

Blood cultures taken previously revealed methicillin- and ceftriaxone-sensitive coagulase-negative *Staphylococcus aureus*. Initial antibiotherapy was continued. Unfortunately, the patient did not do well during hospitalization, and her initial complaints were sustained during her clinical observation.

Microscopy of intraoperatively taken samples revealed *Candida albicans* hyphae (Figure). Antibiotherapy was changed to IV teicoplanin and amphotericin B and oral rifampicin. The patient's fever resolved, but she began to show changes in mental status and persistent headache. She was examined by a certified clinical neurologist, and a suspected subarachnoid hemorrhage was confirmed with a cranial computed axial tomographic (CAT) scan. A control cranial CAT scan 4 days later showed tetraventricular hydrocephalus. The patient was transferred to the neurosurgery department when cardiac and hemodynamic stability was established, but she suffered progressive deterioration of her neurologic status. External ventricular drainage was applied in the neurosurgery department. Her cerebral digital subtraction angiography showed reduced contrast flow in her right middle cerebral artery trunk, a finding that was considered a sign of postoc-

Received May 14, 2004; accepted May 20, 2004.

Address correspondence and reprint requests to: Sebnem Cetemen, Sekerevler Evler B 22 Kucukbakkalkoy Yolu, Icerenkoy, Istanbul, Turkey; 9-0-532-3421701 (e-mail: sebnemal@yahoo.com).



Microscopy of intraoperatively taken tissue samples reveals *Candida albicans* hyphae.

clusive recanalization. Fortunately, the patient then showed progressive recovery in her neurologic status, regaining normal cooperative and orientation skills.

DISCUSSION

The first report of fungus species as the infective agents after a mitral valve replacement was by Newman and Cordell in 1964. Afterward, reports of many cases of fungal endocarditis were published [Hauser 2003]. This type of endocarditis is a rare but important infection with high mortality that affects mainly younger patients (average age, 44.5 years) [Tunkel 1992, Pierrotti 2002, Hauser 2003]. The common infectious agents are the yeast species *Candida albicans* (60%-67%) and filamentous *Aspergillus fumigatus* [Pierrotti 2002, Hauser 2003]. Patients infected with *C. albicans* have been reported to have a better prognosis than those infected with *A. fumigatus* [Durack 1994, Hogevis 1996].

Diagnosis of endocarditis due to *Candida* species is commonly delayed because of the difficulty of isolating the organism in blood cultures. In culture-negative endocarditis cases, diagnosis is possible with histopathologic investigation of the explanted valve, peripheral emboli, or systemic ulcers [Tunkel 1992, Muehrcke 1995]. As in our case, fungal superinfection in the presence of a bacterial infection may complicate diagnosis and proper therapy. Persistence of fever and worsening general status in spite of appropriate treatment, and peripheral embolization as well as presence of large vegetations or perivalvular aggressive invasion evident during echocardiography or intraoperatively should arouse the suspicion of a fungal infection [Muehrcke 1995, Pierrotti 2002]. The appropriate treatment approach to fungal endocarditis is surgery combined with prompt use of amphotericin B [Muehrcke 1995, Pierrotti 2002, Hauser 2003]. Surgery should include careful inspection and resection of perivalvular vegetations on explanation of the valve. Some authors advocate flushing of the surgical field with amphotericin-B solution [Francisco 2003, Hauser 2003]. Medical therapy consists of amphotericin B as the only first-line medication, although it has a low penetra-

tion rate into tissues and an even lower penetration rate into fungal vegetations [Tunkel 1992, Francisco 2003, Hauser 2003]. Surgery is, therefore, inevitable.

As Osler defined his renowned triad (fever, cardiac murmur, and hemiplegia), severe neurologic complications due to infective endocarditis have been reported. Thirty percent of patients develop neurologic complications during the disease [Kantner 1991, Hargrave 2003]. Risk factors for such complications are the type of infectious agent (54% consist of staphylococci) and the location (embolization to the central nervous system vasculature is more common in mitral than aortic disease). Embolic phenomena due to large valvular vegetations are also common in cases with fungal endocarditis [Salgado 1987, Kantner 1991, Hargrave 2003].

Diagnosis of complications related to nervous system involvement is possible with CAT or magnetic resonance imaging scans, and the presence of intracranial mycotic aneurysms may be confirmed with cerebral angiography [Salgado 1987, Kantner 1991].

Neurologic complications of infective endocarditis are as follows: stroke (6%-31% of patients, most commonly affecting the middle cerebral artery area, as in our case); infectious (mycotic) aneurysms (15% of patients, mostly extracranial origin: proximal aorta 25%, visceral arteries 24%, and extremity arteries 22%; only 15% of mycotic aneurysms are of intracranial origin); intracranial hemorrhage (usually focal subarachnoid hemorrhage, 3%-7% of patients with neurologic complications); abscess formation of the meningeal processes (15% of all patients with infective endocarditis, more common with staphylococcal or pneumococcal disease); seizures (11% of patients, usually embolic etiology); nonfocal symptoms and encephalopathy (due to ischemia following microemboli); immune complex vasculitis (late proliferative endarteritis, thrombotic occlusion, and stroke). In patients with fungal endocarditis, changes in consciousness and persistent headache must alert us to possible neurologic complications. Because of large vegetations, there is a high risk of neurologic embolic events [Kantner 1991, Hargrave 2003].

CONCLUSIONS

Indications for surgery in infective endocarditis, as modified by the American College of Cardiology/American Heart Association, are valvular regurgitation with severe heart failure, tachycardia accompanying aortic regurgitation and early mitral valve closure, fungal infections, annular or aortic abscess formation, sinus or aortic true or false aneurysms, valvular dysfunction, and intractable infections in spite of antibiotherapy for 7 to 10 days. Presence of fungal infection is, by itself, an indication for surgery.

Optimal timing for surgery is before hemodynamic deterioration and perivalvular progression of the infection.

REFERENCES

- Durack DT, Lukes AS, Bright DK. 1994. New criteria for diagnosis of infective endocarditis: utilization of specific findings. Duke Endocarditis service. *Am J Med* 96:200-9.
- Hargrave K, Kothari MJ. 2003. Neurological sequelae of infectious

- endocarditis. eMedicine. Available at: <http://www.emedicine.com/neuro/topic264.htm>. Accessed June 3, 2004.
- Hauser M, Hess J, Belohradsky BH. 2003. Treatment of candida albicans endocarditis. *Infection* 31:125-7.
- Hogevik H, Alestig K. 1996. Fungal endocarditis, a report on seven cases and a brief review. *Infection* 24:17-21.
- Kanter MC, Hart RG. 1991. Neurologic complications of infective endocarditis. *Neurology* 41(7):1015-20.
- Moreno-Martinez FL, Lopez FH, Bermudez R, Lagomasino A, Lastayo R, Lopez-Bernal OJ. 2003. A case report of fungal mitral valve endocarditis. *MedGenMed* 5(1):9.
- Muehrcke DD, Lytle B, Cosgrove D. 1995. Surgical and long-term antifungal therapy for fungal prosthetic valve endocarditis. *Ann Thorac Surg* 60:538-43.
- Salgado AV, Furlan AJ, Keys RF. 1987. Mycotic aneurysms, subarachnoid haemorrhage and indications for cerebral angiography in infective endocarditis. *Stroke* 18:1057-67.
- Pierrotti LC, Baddour LM. 2002. Fungal endocarditis, 1995-2000. *Chest* 122:302-10.
- Tunkel AR, Kaye D. 1992. Endocarditis with negative blood cultures. *N Engl J Med* 326:1215-7.
- Zellweger C, Zimmerli S. 2003. Candida albicans endocarditis. A rare disease with serious complications. *Dtsch Med Wochenschr* 128(19): 1048-50.