

An unusual native tricuspid valve endocarditis caused by *Candida colliculosa*

I. Kaygusuz¹, L. Mulazimoglu², N. Cerikcioglu³, A. Toprak⁴, A. Oktay⁴ and V. Korten^{2,5*}

¹Department of Medicine, ²Department of Infectious Diseases and Clinical Microbiology, ³Department of Microbiology and ⁴Department of Cardiology, Marmara University School of Medicine and ⁵Marmara Üniversitesi Hastanesi; Enfeksiyon Hastalıkları ABD, 81090 Altunizade, Istanbul, Turkey

*Tel/Fax: +90 2163274142 E-mail: korten@turk.net

Candida colliculosa, which grew in blood cultures of a 71-year-old retired man with fever of unknown origin that had lasted for 7 months, in conjunction with transthoracic echocardiography, demonstrating a 20-mm vegetation, superior to the tricuspid valve, herniating into the right atrial cavity. The finding led to the diagnosis of fungal endocarditis. Fluconazole, 600 mg daily, was commenced for 8 days; followed by amphotericin B, 1 mg/kg daily. On the fourth day of the amphotericin B treatment, the patient underwent replacement of the infected tricuspid valve. Even though the initial postoperative period was relatively uncomplicated, the patient died after a gross aspiration on the 67th day of his hospital stay, despite aggressive cardiovascular support and antimicrobial therapy. This is the first report of a native tricuspid valve fungal endocarditis due to *C. colliculosa* or *Torulasporea delbrueckii*, which is not known to be a human pathogen.

Keywords *Candida* spp., fungal endocarditis, native-valve endocarditis

Accepted 20 March 2002

Clin Microbiol Infect 2003; 9: 319–322

INTRODUCTION

Fungal endocarditis, once considered a rare disease, has been reported with increased frequency in the last few decades [1]. During this time, injection-drug abuse, prolonged intravenous hyperalimentation, immunosuppression, intense antibiotic therapy, use of long-term intravenous catheters and use of other intravascular monitoring devices have all become frequent. Pacemaker implantation, cardiac and non-cardiac surgery (in particular, insertion of prosthetic heart valves), rheumatic heart disease and previous bacterial endocarditis have been noted as risk factors for fungal endocarditis. These risk factors and better diagnostic techniques are contributing to the recent increase in the incidence and recognition of fungal endocarditis [1,2]. To our knowledge, we report here the first case of a native tricuspid valve fungal endocarditis due to *Candida colliculosa* in the absence of any listed stem risk factors, except for diabetes mellitus and previous surgery [2].

CASE REPORT

The 71-year-old retired man, recently involved with gardening, was referred to the internal medicine department of the Marmara University Hospital in September 1999 with a history of fever, chills, fatigue, weight loss and night sweats for 7 months. He had a past history of diabetes mellitus for 8 years, controlled by gliclazide, 80 mg bid orally twice daily. He was not an intravenous drug abuser. Two years prior to this admission, he had a skull fracture due to a traffic accident. The patient underwent three cranial surgical procedures following the accident, for the management of postoperative complications (rhinorrhea and pneumoencephalitis) and the operation-related hydrocephalus. Finally, a ventriculoperitoneal shunt was inserted in 1997. A central line was not inserted during the procedures.

On admission, the patient's blood pressure was 110/60 mmHg; fever was 38.3 °C. He was pale, dehydrated and cachectic. Otherwise, the physical

examination was unremarkable. He gave a history of fever of unknown origin, investigated in different hospitals without leading to a diagnosis. The laboratory evaluations revealed: erythrocyte sedimentation rate, 110 mm/h; hemoglobin, 11.6 g/L; leukocytes, 3×10^9 /L; platelets, 88×10^9 /L; fasting blood glucose level, 140 mg/dL; purified protein derivative test (-); antinuclear antibody (-); C-reactive protein (+++); rheumatoid factor (+++). The chest X-ray was normal. The urine analysis revealed microscopic hematuria with granular casts. Thorax tomography showed hilar calcific lymphadenopathy, and abdominal tomography showed splenomegaly. Fundoscopic evaluation was unremarkable. The cerebrospinal fluid examination and cranial tomography were normal, and no shunt infection was diagnosed. Two sets of blood cultures obtained on admission grew a *Candida* species, initially giving inconclusive results with API ID 32C (Biomerieux, Marcy-l'Etoile, France), but later identified as *C. colliculosa* in the Fungus Testing Laboratory of Texas Health Science Center, San Antonio, Texas, USA. The yeast identification was derived from: classic Wickerham fermentations, API 20X AUX (Biomerieux); temperature studies; cycloheximide testing; and dalmau plates. Transthoracic echocardiography demonstrated a 20-mm vegetation, superior to the tricuspid valve, that had herniated into the right atrial cavity with moderate regurgitation. Intravenous fluconazole therapy was initiated at a dosage of 600 mg daily. The next six sets of blood cultures also grew a *Candida* species. On the eighth day of fluconazole treatment, the patient developed sudden chest pain, cough and tachypnea. The chest X-ray showed an infiltration at the middle zone of the right lung with central cavitation. A perfusion lung scan suggested pulmonary embolism. Since the patient was still febrile and an embolus occurred, therapy was switched to amphotericin B, 1 mg/kg per day, on the eighth day of fluconazole treatment, despite in vitro susceptibility of the isolate to fluconazole (minimum inhibitory concentration (MIC): 4 mg/L) [3]. After obtaining consent from his family, on the fourth day of amphotericin B treatment the patient underwent replacement of the infected tricuspid valve. The patient tolerated the procedure well, and the initial postoperative period was uncomplicated. Cultures of the vegetation also grew a *Candida* species with in vitro sensitivity to amphotericin B (MIC: 1 mg/L) [3]. Twelve days after surgery, the

patient developed complete atrioventricular block, and an epicardial pacemaker was inserted. Two weeks after the initiation of the antifungal treatment, on the second day after the valve replacement surgery, the follow-up blood cultures were negative. The patient's fever recurred 19 days after surgery, with purulent sputum production. Parenteral antibiotic therapy with sulbactam-cefoperazone was initiated for hospital-acquired pneumonia due to *Acinetobacter calcoaceticus* identified from growth in deep tracheal aspirate ($> 10^6$ CFU/mL). The patient responded to the treatment. On the 60th day after admission, he developed a sudden gross aspiration, apnea and convulsions, and laboratory analysis showed an increase in serum levels of creatinine up to 5.1 mg/dL after a total use of 1775 mg of amphotericin B desoxycholate, and 400 mg of liposomal amphotericin B. The cranial tomography was normal. The patient died on the 67th hospital day due to nosocomial sepsis, despite aggressive cardiovascular support and antimicrobial therapy. Permission for a post-mortem examination was not granted.

DISCUSSION

The incidence of infective endocarditis caused by fungi has undergone a striking increase in the past decade. Fungal endocarditis occurs principally in a setting of previous valve surgery, after the prolonged intravenous administration of broad-spectrum antibiotics, and rheumatic heart disease [2]. It is an extremely rare occurrence in patients with normal cardiac valves [1]. Open-heart cardiac surgery is the most frequent underlying factor for these patients.

This is the first report of endocarditis due to *C. colliculosa* or *Torulaspora delbrueckii*, formerly *Torulopsis colliculosa*. *C. colliculosa* is not known to be a human pathogen. This yeast is found in grapes, grape juice, sour figs, sorghum brandy, cucumber brine, soil, wine, bark of trees, sheep's milk, rodents, and dairy products [4–6]. The patient in this report had interests in gardening and in producing his own dairy products. Both gardening and consumption or production of dairy products can be risk factors for the acquisition of *C. colliculosa* infection. There are no human cases of this pathogen in the literature to our knowledge. This is also the first reported case of native valve *C. colliculosa* endocarditis in a patient without a previous history of abnormal valves or heart murmur.

Patients with fungal endocarditis usually have a symptom complex indistinguishable from those of bacterial endocarditis. Fever, non-specific systemic symptoms and congestive heart failure are common. Multiple large arterial emboli occur more frequently than in bacterial endocarditis [7]. Common laboratory findings are non-characteristic. Emboli to large vessels are characteristic features of fungal endocarditis, and major emboli occur in 68% of cases [1,2], as seen in our patient while he was under fluconazole treatment. Metastatic abscesses represent another frequent complication.

The specific diagnosis of candida endocarditis is usually made when blood cultures are positive for *Candida* spp. The most common pathogens are *C. albicans*, non-*albicans* species of *Candida*, and *Aspergillus* species [2].

In general, treatment of fungal endocarditis requires a combined medical and surgical approach [2,7]. After 1–2 weeks of amphotericin B therapy at full dosages, surgery should probably be performed. Candida endocarditis is associated with a low survival rate, approximately 25%, if early valve replacement is not performed. With surgery, it reaches about 60% [1]. Patients with peripheral emboli were more likely to undergo surgical intervention, but there are rare cases treated with antifungals alone [7–10]. Our patient was offered valve replacement after bulky vegetations were detected, but surgery could be performed only after his family agreed on the 13th day of antifungal treatment, and unfortunately after the embolus occurred.

Isolated native tricuspid valve endocarditis has rarely been described in the absence of intravenous drug use, intracardiac catheters, or cardiac anomalies as presented in our patient. However, *Candida* spp. were found as the third most common cause of isolated tricuspid valve endocarditis in non-addicted patients, after *Staphylococcus* and *Streptococcus* spp. [11]. Ellis et al. [2] reviewed the literature for fungal endocarditis between 1965 and 1995, and underlined the importance of a high index of suspicion for the diagnosis of fungal endocarditis for middle-aged men with pre-existing major stem risk factors. They recommended the use of antigen and antibody detection systems in addition to the conventional diagnostic approach for the diagnosis of high-risk patients. Early use of the combination of high doses of antifungal treatment and valve replacement was necessary for optimal success [2].

This patient showed that *C. colliculosa* can cause isolated right-sided endocarditis in a host without previously well-described stem risk factors for this condition. The portal of entry of *C. colliculosa* is not clear in this patient. The role of gardening, the role of dairy products and whether diabetes mellitus poses a risk factor for *C. colliculosa* infection remain undetermined. Though the optimal approach to fungal endocarditis remains controversial, the recommendations made by Ellis et al. [2] might enhance the diagnosis and management of fungal endocarditis.

ACKNOWLEDGMENTS

We thank Dr M. A. Pfaller and Dr M. G. Rinaldi for their help in further identification of the patient's *Candida* isolate.

REFERENCES

1. Rubinstein E, Lang R. Fungal endocarditis. *Eur Heart J* 1995; 16(suppl B): 84–9.
2. Ellis ME, Al-Abdely H, Sandridge A, Greer W, Ventura W. Fungal endocarditis: evidence in the world literature, 1965–95. *Clin Infect Dis* 2001; 32: 50–62.
3. National Committee for Clinical Laboratory Standards. *Reference method for broth dilution antifungal susceptibility testing of yeasts*. Approved standard M27-A. Wayne, Pa: National Committee for Clinical Laboratory Standards, 1997.
4. Barnett JA, Payne RW, Yarrow D. *Torulaspora delbrueckii*. In: Barnett JA, Payne RW, Yarrow D., eds. *Yeasts characteristics and identification*, 2nd edn. Cambridge: Cambridge University Press, 1990: 647–8.
5. Andrighetto C, Psomas E, Tzanetakis N, Suzzi G, Lombardi A. Randomly amplified polymorphic DNA (RAPD) PCR for the identification of yeasts isolated from dairy products. *Lett Appl Microbiol* 2000; 30: 5–9.
6. Romano P, Ricciardi A, Salzano G, Suzzi G. Yeast from water buffalo mozzarella, a traditional cheese of the Mediterranean area. *Int J Food Microbiol* 2001; 69: 45–51.
7. Hernandez JA. Candidal mitral endocarditis and long-term treatment with fluconazole in a patient with human immunodeficiency virus infection. *Clin Infect Dis* 1992; 15: 1062–3.
8. Nguyen MH, Nguyen ML, Yu VL. *Candida* prosthetic valve endocarditis. Prospective study of six cases and review of the literature. *Clin Infect Dis* 1996; 22: 262–7.

9. Baddour LM. Long-term suppressive therapy for *Candida parapsilosis* induced prosthetic valve endocarditis. *Mayo Clin Proc* 1995; 70: 773–5.
10. Thadur RK, Skelcy KM, Kahn RG. Successful treatment of *Candida* prosthetic valve endocarditis with a combination of fluconazole and amphotericin B. *Crit Care Med* 1994; 22: 712–74.
11. Nandakamur R, Raju G. Isolated tricuspid valve endocarditis in nonaddicted patients: a diagnostic challenge. *Am J Med Sci* 1997; 314(3): 207–12.