Pacemaker Endocarditis Due to Candida albicans: Case Report and Review

Veronique Joly, Nadia Belmatoug, Armelle Leperre, Jerome Robert, Frederique Jault, Claude Carbon, and Patrick Yeni

We describe a case of pacemaker endocarditis due to Candida albicans in a patient who responded favorably to combined surgical and antifungal therapy. Only five cases of candidal pacemaker endocarditis have been reported previously. We review these five cases and discuss the clinical presentation and therapy for this disease in comparison with candidal prosthetic valve endocarditis.

Case Report

A 56-year-old man with a medical history that was unremarkable except for chronic obstructive bronchitis had received a pacemaker in 1991 because of symptomatic sinus dysfunction. In March 1995, infection of the pacemaker pouch led to ablation of the pacemaker; a new one with a ventricular pacemaker lead was implanted in a contralateral site, without the removal of existing intracavitary wires. No pathogen was isolated from pus. On 20 June 1995, the patient became febrile, and oral antibiotic therapy with pristinamycin was initiated. He was admitted to the hospital on 3 July 1995 because of dyspnea and fever that persisted during pristinamycin therapy.

Physical examination detected left basilar crackles without congestive heart failure. A chest roentgenogram showed an infiltrate in the left lower lobe. A pulmonary angiogram demonstrated occlusion of the descending branch of the left pulmonary artery. Blood cultures remained negative. Doppler ultrasonography of the lower extremities did not reveal deep vein thrombosis. Transesophageal echocardiography showed a right atrial mass compatible with a thrombus or a vegetation and no abnormality of the tricuspid, mitral, or aortic valves. The vegetation did not appear to be attached to the pace wires. Pristinamycin therapy was replaced with parenteral antibiotic therapy with vancomycin, cefazidime, and amikacin, and the patient was also treated with heparin. His condition improved clinically, although an elevated temperature of 38°C (which was attributed to the venous toxic effect of vancomycin) was noted. After 2 weeks, therapy was switched to oral fusidic acid and cefixime. Surgical removal of intracavitary wires was performed. On 21 July 1995, the patient underwent right atriotomy, and a vegetation (1 cm in diameter) adjacent to the septum auricularum was found. The vegetation, the three wires, and the pacemaker were removed.

Cultures of the vegetation and the wires were all positive for C. albicans. Furthermore, coagulase-positive staphylococci were isolated from one intracavitary wire, and C. albicans was recovered from the right femoral catheter that had been inserted a few days earlier and removed at the time of surgery. Two cultures of blood obtained 2 days before surgery yielded C. albicans, and the patient was transferred to our institution for management of antifungal therapy.

Laboratory analyses showed the following values: neutrophil count, 10,640/mm³; erythrocyte sedimentation rate (ESR), 82 mm/h; and C-reactive protein level, 104 mg/L. Antibodies to Candida were demonstrated by hemagglutination (titer, 2,560) and counterimmunoelectrophoresis (six arcs). As of 25 July 1995, the patient began receiving treatment with amphotericin B (0.5 mg/[kg·d]) and 5-fluorocytosine (7.5 g/d) for 18 days and then oral fluconazole (400 mg/d). Fungemia persisted as shown by three positive cultures of blood obtained on 27 July 1995. On 3 August 1995, Doppler ultrasonography demonstrated a right femoral vein thrombosis. During treatment, the patient became afebrile and was discharged on 18 August 1995; he continued taking oral fluconazole (200 mg once a day) as well as an anticoagulant. He was then followed up on an outpatient basis.

On 7 December 1995, laboratory studies showed the following values: neutrophil count, 4,128/mm³; ESR, 16 mm/h; and C-reactive protein level, 4 mg/L. The patient was well. Fluconazole therapy was stopped in March 1996 after >7 months of effective treatment. In January 1997, laboratory analyses showed the following: neutrophil count, 3,080/mm³; C-reactive protein level, 3 mg/L; and ESR, 7 mm/h.

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Candida albicans infection with Candida have been reported [9, 10], but there was no evidence of septicemia in these patients.

In our case, the generator pocket could have been the initial site of infection, since 3 months before the onset of endocarditis, the patient had a collection in the pacemaker pouch that remained culture negative and led to the removal of the generator but not the pacing electrodes. However, we cannot exclude the possibility that his initial fever was related to staphylococcal infection and that Candida was an opportunistic pathogen as a result of the selection effect of a prolonged course of antibacterial therapy. The femoral catheter could have possibly been the portal of entry for candidemia. Fungemia persisted 6 days after surgery, whereas Doppler ultrasonography showed right femoral thrombosis (which suggests that the thrombus was infected). The intravascular catheter may have been the source of fungemia or the target of hematogenous seeding from another site. Whatever the mechanism involved in fungal infection, C. albicans—positive cultures of specimens from all sites, including the vegetation, established the diagnosis of fungal endocarditis.

Candidal pacemaker endocarditis (which is a right-sided infection) should be considered a form of fungal prosthetic valve endocarditis even though most cases of prosthetic valve endocarditis are left-sided (table 2). Ten percent of all cases of prosthetic valve endocarditis are due to Candida species. The risk factors for candidal prosthetic valve endocarditis are central venous catheters, prior therapy with antibacterial agents, and recent cardiothoracic surgery; these risk factors should also be considered as risk factors for candidal pacemaker endocarditis. C. albicans is the most common fungal pathogen involved in prosthetic valve endocarditis [11].

In a recent review of 18 cases of candidal prosthetic valve endocarditis [12], infection was always left-sided. Sixty-seven percent of the patients presented with the sudden onset of symptoms, and blood cultures were positive for all patients. The mortality rate was 54%. The incidence of embolization in cases of fungal prosthetic valve endocarditis has been reported to range from 41% to 70% [13]. Our case had several features in common with cases of candidal prosthetic valve endocarditis,
including positive blood cultures, an embolus during the course of the disease, and a large-sized vegetation. The association of persistent fever, a vegetation on a foreign body, and previous embolization prompted us to remove all the wires.

Management pacemaker-associated endocarditis due to bacteria remains controversial because of a lack of prospective studies comparing medical treatment with the combination of intensive antibiotic therapy and electrode removal. Leaving wires in the setting of infection may favor the failure of antibiotic therapy. On the other hand, removing the electrode is not always simple: intravenous traction done by an interventional cardiologist may be associated with complications such as a tear of the tricuspid valve, and removal by cardiotomy is associated with morbidity and mortality. When the results of the different reported studies were pooled [5], there was a significant advantage of combined surgery and medical treatment over medical treatment alone. That analysis did not specify whether the nature of the pathogen affects the absolute need for electrode removal. The severity of candidemia in the presence of intravascular devices results from the properties of the Candida species. Candida species can adhere to various plastics, which favors their colonization of foreign intravascular and, in particular, intracardiac materials. C. albicans mediates a platelet aggregation response, and platelets facilitate germ tube formation [14].

Since candidal pacemaker endocarditis remains uncommon, no therapeutic recommendations can be drawn from the few reported cases. However, the value of removing infected materials is highly suggested by the recommendations established for candidal infections of indwelling venous catheters or prosthetic valves. Different studies show that removing catheters is advocated in cases of central venous catheter–associated candidemia [15–17]. In cases of candidal prosthetic valve endocarditis, the combination of valve replacement and antifungal therapy has become the standard approach to treatment [18–20]. Delay in valve replacement increases the risk of emboli. Amphotericin B is the drug of choice, at least during the initial phase of therapy. We have shown that amphotericin B is clearly more effective than fluconazole as treatment of experimental left-sided C. albicans endocarditis [21]. In the present case, we used the combination of amphotericin B and 5-fluorocytosine, which has been shown to be more effective than amphotericin B alone as treatment for infections due to Cryptococcus [22] as well as Candida [23, 24]. Successful therapy with antifungal agents alone has been reported in some cases of candidal prosthetic valve endocarditis [25, 26] (providing that the drugs could be administered for a prolonged period), but these results must be confirmed. Furthermore, relapse may occur late after the end of therapy. In our case, the decision to remove intravascular wires on the basis of persistent fever allowed us to control the infection rapidly and easily.

In conclusion, candidal pacemaker endocarditis remains rare. This disease shares with candidal prosthetic valve endocarditis features that should help in its diagnosis. As in other candidal intravascular device infections, early aggressive combined surgical and medical therapy is advocated. This infection may represent one of the most severe forms of pacemaker endocarditis.

Acknowledgment

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References


Table 2. Distinct features of candidal pacemaker endocarditis and candidal prosthetic valve endocarditis.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Pacemaker</th>
<th>Prosthetic valve</th>
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<tbody>
<tr>
<td>Site of endocarditis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency*</td>
<td>&lt;.5%</td>
<td>10%</td>
</tr>
<tr>
<td>Side</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>Emboli</td>
<td>Pulmonary</td>
<td>Peripheral</td>
</tr>
<tr>
<td>Blood cultures</td>
<td>Usually positive</td>
<td>Usually positive</td>
</tr>
<tr>
<td>Candida species</td>
<td>C. albicans, &gt;80% of cases</td>
<td>C. albicans, 50%</td>
</tr>
<tr>
<td>Treatment</td>
<td>Combined medical and surgical therapy</td>
<td>Combined medical and surgical therapy</td>
</tr>
</tbody>
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* No. of candidal infections/total no. of infections.