$P = .017$). There were statistically significant differences between the patients with the CDAD and the carriers in terms of the presence of more than three active medical problems (i.e., requiring treatment in the ICU; 65% vs. 27%; $P = .05$), the presence of more than three underlying diseases (65% vs. 27%; $P = .05$), and longer duration of antibiotic therapy (88% vs. 45%; $P = .02$) (table 1).

A total of 68 stool specimens were positive for *C. difficile,* and 62 of the isolates were preserved for further research. Fifty-nine (95%) of the 62 isolates, evenly distributed in CDAD group and carrier group, were positive for toxins. PCR ribotyping yielded five ribotypes, and the RAPD method yielded seven types. The combination of these two methods generated eight distinctive fingerprints. The most frequently isolated type was type I (isolated from 29 [47%] of 62 patients), which could be isolated from nine (53%) of 17 patients with CDAD and from two (18%) of 11 asymptomatic carriers ($P = .08$). In addition, types II, III, IV, and V were variably associated with diseases. Types VI, VII, and VIII were recovered only from asymptomatic carriers, but the numbers of isolates of these types were small.

Our data show that there was no correlation between genotypes, toxin production, and clinical manifestations of infection. There was no strain-specific difference for asymptomatic carriers vs. patients with CDAD. The predominant type (type I) was variably associated with diseases, and five of eight types were associated with diarrhea. Toxigenic *C. difficile* strains could be isolated both from patients with CDAD and from asymptomatic carriers. Actually, most strains from both groups were toxigenic in vitro. The results of our study also failed to support the belief that the pathogenicity of an isolate depended on strain variation and toxin production. Host factors, especially debilitated status, appear to be important determinants for the clinical expression of CDAD.

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References

1. Pantosti A, Cerquetti M, Gianfrilli PM. Electrophoretic characterization of *Clostridium difficile* strains isolated from antibiotic-associated colitis and other conditions. J Clin Microbiol **1988**;26:540–3.
2. Wren B, Heard SR, Tabaqchali S. Association between production of toxins A and B and types of *Clostridium difficile.* J Clin Pathol **1987**;40:1397–401.
3. McFarland LV, Elmer GW, Stamm WE, Mulligan ME. Correlation of immunoblot type, enterotoxin production, and cytotoxin production with clinical manifestations of *Clostridium difficile* infection in a cohort of hospitalized patients. Infect Immun **1991**;59:2456–62.
4. Gürtler V. Typing of *Clostridium difficile* strains by PCR-amplification of variable length 16S-23S rDNA spacer regions. J Gen Microbiol **1993**; 139:3089–97.
5. Chachaty E, Saulnier P, Martin A, Mario N, Andremont A. Comparison of ribotyping, pulsed-field gel electrophoresis and random amplified polymorphic DNA for typing *Clostridium difficile* strains. FEMS Microbiol Lett **1994**;122:61–8.
6. Onderdonk AB, Allen SD. *Clostridium.* In: Murray PR, Baron EJ, Pfaller MA, Tenover FC, Yolken RH, eds. Manual of clinical microbiology. 6th ed. Washington, DC: American Society for Microbiology, **1995**:574–86.

Right-Sided Pacemaker-Related Endocarditis Due to *Acremonium* Species

Fungal endocarditis is a rare complication of pacemaker placement. We report the successful treatment of disseminated acremonium infection associated with pacemaker-related endocarditis and endophthalmitis in an 80-year-old male patient with no underlying condition.

Three weeks before admission to the hospital, the patient was treated with topical and systemic steroids for an unspecified inflammatory disease of the left eye; he had had a pacemaker in place for 3 years. At admission, the clinical examination was consistent with fungal endophthalmitis and he underwent vitrectomy. After 3 days of incubation, fungal culture (on Sabouraud dextrose and brain-heart infusion agar) yielded *Acremonium* species with the characteristic fine and hyaline septate hyphae, with long awl-shaped phialides producing one-celled oblonged conidia in clusters.

Findings of the rest of the clinical examination were normal; the electrocardiogram, a chest roentgenogram, and a WBC count did not reveal any abnormalities. The erythrocyte sedimentation rate was 16 mm/h, and the level of C-reactive protein was 9 mg/L. Blood cultures (four sets) were sterile. Findings on a transthoracic echocardiogram were normal. The patient received iv amphotericin B therapy (cumulative dose of 1 g).

On day 45 of hospitalization, the patient's temperature rose to 39.5°C and he experienced chills; blood cultures yielded *Acremonium* species. Findings on a second transthoracic echocardiogram were normal, but a transesophageal echocardiogram showed a floating mass of ~2 cm in diameter in the right atrium that was surrounding the pacemaker wire. A new course of amphotericin B therapy was started but had to be discontinued after a cumulative dose of only 315 mg because of renal toxicity.

The susceptibility of the *Acremonium* isolate recovered from the eye was tested (P. Troke, Pfizer Clinical Research Department, Sandwich, UK) with use of an agar dilution method and yielded the following MICs: fluconazole, 50 μg/mL; amphotericin B, 31 μg/mL; itraconazole, 3.1 μg/mL; and voriconazole, 0.39 μg/mL. Therapy with voriconazole (200 mg b.i.d. orally, provided by Pfizer) was started, and the patient became afebrile. Twelve days after this treatment was started, the pacemaker and the electrode were surgically removed by right atriotomy (figure 1). Cultures of biopsy specimens from the pacemaker electrode and heart yielded *Acremonium* species. Histopathological examination of the inflammatory tissue adherent to the wire and to the right atrium revealed fungal filaments (hyphae).

The patient received voriconazole (3 mg/kg b.i.d.) intravenously for 7 days after surgery and orally for 5 more weeks. No adverse

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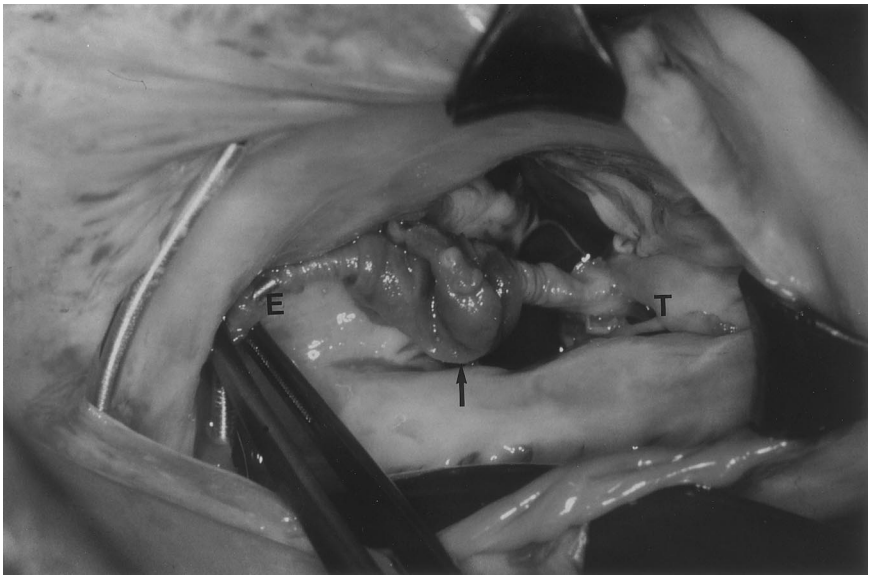

Figure 1. View of the right opened atrium of an 80-year-old man with right-sided pacemaker-related endocarditis due to *Acremonium* species. Note that the electrode (E) is enclosed by a tissue (*arrow*) partially fixed to the right atrium and to the anterior leaflet of the tricuspid valve (T).

event was reported, and the patient left the hospital 10 days after surgery. There were no signs of recurrence of the infection 2 years after the device was removed.

Endocarditis is an uncommon complication of pacemaker placement and is reported in 0.15%–6% of patients [1, 2]; fungal infections are extremely rare in patients with pacemakers, and only a few cases have been reported. The etiologic agents of pacemaker infection include *Candida* species [3, 4], *Aspergillus* species [5, 6], and, in one case, *Petriellidium* (*Pseudallescheria*) species [7]; to our knowledge, we report the first case of pacemaker-related endocarditis due to *Acremonium* species. Invasive infections due to *Acremonium* species can be localized, systemic, or sometimes both [8].

The reported cases of acremonium endophthalmitis were secondary to penetrating injuries, viral or fungal keratitis, or ocular surgery [9]. However, our patient did not report even a minor penetrating injury. In the absence of such an injury, we believe that endophthalmitis was not the site of the primary infection but rather the consequence of a hematologic spread. The filamentous fungus could have contaminated the pacemaker during its placement in 1991.

Although patients usually do not survive an episode of fungal pacemaker-related endocarditis, a recent case was reported in which a 56-year-old man with pacemaker-related endocarditis due to candida infection survived after undergoing surgery and receiving treatment with antifungal agents [3]. In the other four cases of fungal pacemaker-related endocarditis reported, the outcome was fatal [4–7]. Right-sided endocarditis has been diagnosed with use of the transesophageal echocardiogram after two transthoracic approaches. Transesophageal echocardiography is significantly more sensitive than transthoracic echocardiography for the recognition of vegetations and paravalvular abscesses [10] in patients with infectious endocarditis. However, this series includes mostly patients with aortic and mitral endocarditis.

The antimicrobial treatment for acremonium infections is not yet well defined because of the rarity of this infection [8]. In our case, susceptibility testing of our isolate suggested resistance in vitro to amphotericin B; on the other hand, this test showed that the MIC of voriconazole was low. Although the MIC results should be cautiously interpreted because of a lack of standardized methodology for susceptibility testing of filamentous fungi, treatment with amphotericin B was clinically unsatisfactory. Our patient was cured by surgery combined with voriconazole treatment, and there were no signs of recurrence of the infection at a 2-year follow-up visit.

This case report is important for three reasons: (1) our case of pacemaker-related fungal endocarditis is rare, (2) to our knowledge, we report the first case of pacemaker-related endocarditis due to *Acremonium* species, and (3) our patient survived an episode of fungal pacemaker-related endocarditis.

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References

1. Phibbs B, Marriott HJL. Complications of permanent transvenous pacing. N Engl J Med **1985**;312:1428–32.
2. Kugener H, Rey JL, Tribuilloy C, et al. Endocardites infectieuses sur sondes de stimulation permanentes: intérêt de l'échocardiographie et revue de la littérature. Ann Cardiol Angeiol (Paris) **1993**;42:331–8.
3. Wilson HA Jr, Downes TR, Julian JS, White WL, Haponik EF. Candida endocarditis: a treatable form of pacemaker infection. Chest **1993**;103: 283–4.
4. Davis JM, Moss AJ, Schenk EA. Tricuspid candida endocarditis complicating a permanently implanted transvenous pacemaker. Am Heart J **1969**; 77:818–21.
5. Kramer L, Rojas-Corona RR, Sheff D, Eisenberg ES. Disseminated aspergillosis and pacemaker endocarditis. PACE Pacing Clin Electrophysiol **1985**;8:225–9.
6. Moorman JR, Steenbergen C, Durack DT. Aspergillus infection of a permanent ventricular pacing lead. PACE Pacing Clin Electrophysiol **1984**; 7:361–6.

7. Davis WA, Isner JM, Bracey AW, Roberts WC, Garagusi VF. Disseminated Petriellidium boydii and pacemaker endocarditis. Am J Med **1980**; 69:929–32.
8. Fincher R-M, Fisher JF, Lovell RD, Newman CL, Espinel-Ingroff A, Shadomy HJ. Infection due to the fungus Acremonium (Cephalosporium). Medicine (Baltimore) **1991**; 70:398–409.
9. Culbertson WW, Mandelbaum S. Exogenous fungal endophthalmitis. Ophthalmology **1988**; 95:19–30.
10. Birmingham GD, Rahko PS, Ballantyne F. Improved detection of infective endocarditis with transesophageal echocardiography. Am Heart J **1992**; 123:774–81.

Pleural Empyema Due to *Clostridium difficile* and *Clostridium cadaveris*

Pleuropulmonary infections with clostridial species, usually *Clostridium perfringens,* have been reported occasionally [1]. We describe a patient with a bronchogenic cyst who developed pleuropulmonary empyema due to *Clostridium difficile* and *Clostridium cadaveris* after surgical removal of the cyst.

A 33-year-old male pig farmer had had a bronchogenic cyst in the upper lobe of the left lung for ~8 years. Because the cyst was enlarging, segmental resection was performed on 31 January 1996. On the sixth postoperative day, the patient developed fever with leukocytosis (leukocyte count, 17,700 cells/mm^3). A chest radiograph revealed pleural effusion on the left side. Foul-smelling fluid was obtained via transthoracic puncture on 11 February.

Culture of the material yielded two anaerobic gram-positive spore-forming rods with different colony morphologies and odors. With use of the API 20A system (bioMérieux, Marcy l'Etoile, France) and gas chromatography, the isolates were identified as *C. difficile* and *C. cadaveris* (the identity of the latter isolate was confirmed by Dr. M. McTeague, Wadsworth Anaerobe Laboratory, Los Angeles). The *C. difficile* strain produced cytotoxin B. The Etest (AB BIODISK, Solna, Sweden) showed that both organisms were susceptible to amoxicillin/clavulanate and metronidazole. Therapy with iv amoxicillin/clavulanate (1,000/200 mg t.i.d.) was started on 11 February.

On 19 February, the patient developed a bronchopleural fistula. A second thoracotomy was performed on 21 February. The rest of the left lung was found to be necrotic, and pneumonectomy was performed. Intravenous metronidazole (500 mg t.i.d.) was added to the patient's regimen of amoxicillin/clavulanate. Cultures of fluid from the thoracic drain were repeatedly negative after antimicrobial therapy was initiated. The drain was removed on 1 March, antibiotic therapy was stopped, and the patient was discharged from the hospital.

Four days later, he returned to the hospital with fever and pain on the left side of the thorax. A chest radiograph revealed a normal pleural cavity but enlarged cardiac contours. An echocardiogram revealed a 5-cm pericardial effusion. A third thoracotomy with pericardiotomy was performed on 25 March for debridement followed by drainage and daily rinsing with 5% povidone-iodine. Culture of the pleural fluid yielded only *C. cadaveris;* the isolate was susceptible in vitro to amoxicillin/clavulanate and metronidazole. The pericardial fluid was sterile. The patient again received the intravenous combination of amoxicillin/clavulanate (1,000/200 mg q4h) and metronidazole (500 mg t.i.d.). Follow-up cultures of fluid from the drain were all sterile. Therapy with metronidazole was stopped on 12 April, and the drain was removed 1 week later. Therapy with amoxicillin/clavulanate was continued until 26 May (during the last 2 weeks, amoxicillin/clavulanate was administered orally at a dosage of 500/125 mg t.i.d.). A CT scan showed no signs of abscesses. The leukocyte count was 8,200/mm^3. No β-lactamase production was detected in the *C. cadaveris* isolate. The patient was discharged from the hospital in good clinical condition with a prescription for oral amoxicillin (500 mg q.i.d.). As of this writing (3 months later), he is clinically stable.

Few cases of pleural infection with *C. difficile* have been reported [2, 3]. *C. cadaveris* is not known to produce a toxin and is considered to be nonpathogenic for humans and laboratory animals [4]. However, *C. cadaveris* bacteremia (in two immunocompromised patients) and *C. cadaveris*–associated spontaneous bacterial peritonitis have been described [5, 6]. Aspiration of aerosol from animal material while handling dead piglets seems to be a logical explanation for our patient's pulmonary infection. The severity of his infection with two anaerobic organisms that are both considered to be of little pathogenic importance, with destruction of a whole lung despite adequate antimicrobial therapy, is remarkable.

We believe that the *C. cadaveris* isolate persisted after 4 weeks of therapy because of its capacity to sporulate. The persistence of *C. cadaveris* despite adequate therapy was not described in the three previously mentioned case reports [5, 6]; those patients all died of complications during hospitalization, which obscured the possible role of *C. cadaveris.* We conclude that the pathogenicity of *C. cadaveris* needs further study.

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References

1. Bekemeyer WB. Clostridial infections of the lungs and pleura. South Med J **1986**; 79:1393–7.
2. Smith LDS, King EO. Occurrence of *Clostridium difficile* in infections of man. J Bacteriol **1962**; 84:65–7.
3. Simpson AJH, Das SS, Tabaqchali S. Nosocomial empyema caused by *Clostridium difficile.* J Clin Pathol **1996**; 49:172–3.
4. Willis AT. Characteristics of the pathogenic and related clostridia. In: Willia AT, ed. Anaerobic bacteriology: clinical and laboratory practice. Boston: Butterworths, **1977**:111–66.
5. Gucalp R, Motyl M, Carlisle P, Dutcher J, Fuks J, Wiernik PH. *Clostridium cadaveris* bacteremia in the immunocompromised host. Med Pediatr Oncol **1993**; 21:70–2.
6. Herman R, Goldman IS, Bronzo R, McKinley MJ. *Clostridium cadaveris:* an unusual cause of spontaneous bacterial peritonitis. Am J Gastroenterol **1992**; 87:140–2.

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