Corynebacterium minutissimum
Bacteremia in an Immunocompetent Host with Cellulitis

Alexander B. Granok,1 Patti Benjamin,2 and Lee S. Garrett3
1Infectious Disease Associates, Foundation Medical Partners, and 2Microbiology Laboratory, Southern New Hampshire Medical Center, Nashua, and 3Hudson Family Practice, Dartmouth-Hitchcock, Hudson, New Hampshire

Since its original description in 1961, Corynebacterium minutissimum, the causative agent of erythrasma, has rarely been associated with extracutaneous disease. We report a case of cellulitis and bacteremia due to C. minutissimum. We discuss the treatment of C. minutissimum infection and describe the clinical settings in which isolation of Corynebacterium species from blood cultures should be considered significant.

Corynebacterium minutissimum is a gram-positive, non–spore-forming, aerobic or facultatively anaerobic bacillus. Its most common association with human disease is the superficial skin infection erythrasma, which typically presents as reddish-brown macular patches involving the intertriginous areas. To date, to our knowledge, there have been 14 cases of C. minutissimum infections that caused conditions other than erythrasma. These include 3 reports of cases of abscess formation. The first of those 3 cases involved a woman with severe, recurrent breast abscesses [1], the second was a postsurgical abscess in a patient who had undergone cervical diskectomy [2], and the third was a costochondral abscess in an HIV-infected patient [3]. Three cases of intravascular catheter–related or fistula-related infection have been reported, as have 2 cases of peritoneal dialysis catheter–related infection [4–7]. Ophthalmologic involvement has occurred in 2 patients; one case stemmed from endocarditis [8, 9], and the other case involved pyelonephritis in an infant with hydronephrosis [10]. Three cases of primary bacteremia have been reviewed, all of which involved patients with underlying hematologic malignancy (chronic myelogenous leukemia, multiple myeloma, and prolymphocytic leukemia) [2, 6, 11]. We describe what is, to our knowledge, the first immunocompetent woman to have C. minutissimum bacteremia with a severe cutaneous infection.

Case report. The patient was a 76-year-old woman who presented to the hospital with a 3- to 4-day history of bilateral leg swelling, erythema, and pain. Although she denied having fever as part of her history, she was in fact febrile (temperature, 39.5°C) at admission to the hospital. Her primary care physician made a diagnosis of bilateral leg cellulitis, and the patient began receiving cefazolin. While receiving this regimen, the patient’s fever improved, but her cellulitis appeared to worsen, with proximal extension and the development of bullous lesions at the leading edge of the cellulitis. Ciprofloxacin was initially added to her regimen, and, the next day, nafcillin and clindamycin were administered as well. Cefazolin was discontinued. She was seen in consultation by both a dermatologist and a podiatrist; both believed that the patient had severe tinea pedis, onychomycosis, and intertriginous candidiasis. Toe nail debridement was performed, and topical gentian violet and a urea-containing cream were prescribed. A sample of the patient’s blood obtained at admission was cultured in a blood culture bottle, and, on the second day of hospitalization, it yielded a gram-positive bacillus (BacT-alert; Organon-Teknika). During the next 24 h, a second blood culture also yielded the same organism. An infectious diseases consultation was requested.

The patient had a medical history remarkable for atrial fibrillation, pneumonia, urinary tract infection, and an episode of lower-extremity cellulitis the year before admission to the hospital. On physical examination, the patient was afebrile. She had pitting edema to the midtibia bilaterally and poorly demarcated, diffuse erythema of the left leg to the midthigh. She had a ruptured bullous lesion (diameter, 9 cm) over her left lateral thigh, which was draining clear, serous fluid, and an unruptured bulla (diameter, 4 cm) over her left medial thigh. In addition, the patient had erythema of her inframammary folds and groin, bilaterally. Her WBC count was 18,500 cells/mm³, with 80% segmented neutrophils. Examination of the patient’s blood cultures revealed short, club-shaped, gram-positive bacilli. The morphology was unchanged on solid media. The organism was identified as a probable non–jeikeium species of Corynebacterium on the basis of its antimicrobial susceptibility pattern [12], and a presumptive identification of C. minutissimum was made (Rapid CB Plus System; Remel).

The patient’s antibiotic regimen was changed to vancomycin (1 g iv “piggyback” [i.e., administration of >1 solution through 1 venipuncture site] q.d.) and azithromycin (500 mg iv pig-
gyback q.d.). The bullous lesion over the left medial thigh was aspirated. The results of Gram staining of the aspirate were negative for microorganisms, and the culture yielded rare coagulase-negative staphylococci in thiol broth only. The results of additional blood cultures were also negative.

The patient remained afebrile, and the erythema of her lower extremities improved. Her blood culture isolate was sent to the New Hampshire Public Health Laboratories (Concord) for further characterization, and it was positively identified as \textit{Corynebacterium minutissimum}. Positive results were obtained for tests for dextrose assimilation (Andrade’s assimilation test), maltose and xylose oxidative fermentation, catalase production, and anaerobic growth. Negative results were obtained for tests for mannitol and fructose assimilation (Andrade’s assimilation test), sucrose oxidative fermentation, esculin, urea, nitrate, and motility (PML Microbiologicals [Warwick, RI]; Binax/TEL [Waterville, ME]). Vancomycin therapy was discontinued, and the patient began to receive azithromycin orally. She completed a 14-day course of azithromycin. She has been healthy on follow-up.

\textbf{Discussion.} \textit{Corynebacterium} species have long been classified as skin contaminants, or “colonizers.” Not surprisingly, clinicians often disregard blood cultures that yield these organisms. This is likely an appropriate course of action when there is a single, isolated positive culture. In an older review, Van Scoy et al. [13] suggested that ∼10% of blood culture contaminants were diphtheroids. Multiple positive blood cultures, when performed in an appropriate manner, are more indicative of true bacteremia.

With the decrease in diphtheria transmission, nondiphtherial \textit{Corynebacterium} species are assuming a greater significance in clinical medicine. The increasing size of the immunocompromised population and the more common use of intravascular access devices have likely contributed to this phenomenon. During trial VIII of the International Antimicrobial Therapy Cooperative Group of the European Organization for Research and Treatment of Cancer (1989–1991), 5% of the gram-positive organisms that caused bacteremia were \textit{Corynebacterium} species [14]. Although the majority of serious infections have been attributed to \textit{Corynebacterium jeikeium}, other species now recognized as pathogens include \textit{Corynebacterium urealyticum} (formerly \textit{Corynebacterium group D2}) and \textit{Corynebacterium striatum}, among others [15]. At our institution (Southern New Hampshire Medical Center [Nashua], a community teaching hospital licensed for 188 beds), there have been 16 blood cultures positive for diphtheroids during the period of December 2000 to December 2001. Of these, 3 were positive in >1 set. Two infections were related to intravascular access devices (1 with \textit{Corynebacterium confluens} and 1 with a \textit{Corynebacterium} species that was not \textit{C. jeikeium}), and the third was in the patient described in this report.

Although it remains unproven that our patient’s cellulitis was in fact caused by \textit{C. minutissimum}, it seems highly probable, given the coexistent bacteremia. Another possibility is that severe skin damage from her cellulitis allowed \textit{C. minutissimum} to cross what would normally be an intact epithelial barrier. Unfortunately, the patient’s skin was not subjected to Wood’s lamp examination (a potentially useful diagnostic test) before treatment with antimicrobials, although the typical coral-red fluorescence described for erythrasma is not seen universally [16]. Although the intertriginous spaces could have been involved with erythrasma, her antecubital fossae appeared normal, and the cellulitic area certainly did not have the appearance characteristic of that disorder. All previous patients with \textit{C. minutissimum} bacteremia had either an indwelling intravenous access device in place, were immunosuppressed, or had endocarditis [2, 4–7, 9, 11]. Our patient had none of these conditions, and thus adds to the situations in which \textit{C. minutissimum} bacteremia can be seen.

Erythrasma has historically been treated with erythromycin (250 mg by mouth q.i.d. for 14 days). For invasive disease, treatment regimens reported in the literature have included β-lactams (both penicillins and cephalosporins), aminoglycosides, trimethoprim-sulfamethoxazole, erythromycin, and vancomycin. Our patient experienced clinical improvement while receiving vancomycin and azithromycin. In their 1993 review of the National Institutes of Health experience with identification and susceptibility testing of various \textit{Corynebacterium} species, Williams et al. [15] reported the results of antibiotic susceptibility testing that involved the microdilution technique. Twenty-one isolates of \textit{C. minutissimum} were tested. All strains tested were susceptible to vancomycin, and 90% were susceptible to imipenem and cefotetan. Seventy-six percent of the isolates were susceptible to ampicillin and ciprofloxacin, whereas the rate of erythromycin susceptibility was actually quite low (28%). Nearly all of these isolates were recovered from blood samples or were related to intravascular catheter use. In a study by Soriano et al. [17], the antimicrobial susceptibility of 20 strains of \textit{C. minutissimum} was determined using the agar dilution method [17]. Again, there was uniform susceptibility to vancomycin (MIC$_{90}$ 0.5 μg/mL [range, 0.25–0.5 μg/mL]) for all strains. The penicillins and cephalosporins had similarly high MIC$_{90}$ values in this study (MIC$_{90}$ of ampicillin, 32 μg/mL; MIC$_{90}$ of cefuroxime, >256 μg/mL), as did erythromycin (MIC$_{90}$ >256 μg/mL [range, 0.03 to >256 μg/mL]). The sources of these isolates were not specifically reported. Finally, Lagrou et al. [18] reported their findings for \textit{Corynebacterium} species during a 6-month period at a large teaching hospital in Belgium [18]. Nine strains of \textit{C. minutissimum} underwent antibiotic susceptibility testing, although only 2 strains were believed to be directly associated with infection. Their data suggested that resistance was not...
quite as widespread: 56% of isolates were susceptible to ampicillin and 78% were susceptible to erythromycin. The National Committee for Clinical Laboratory Standards does not report susceptibility criteria for Corynebacterium species [19]. In general, reports in the literature have identified breakpoints on the basis of attainable blood levels of the antibiotic in question. However, because data linking MIC results to clinical outcomes are lacking for these organisms, susceptibility data generated in the microbiology laboratory should be interpreted with caution. It would appear, however, that either the rates of antibiotic resistance among nondiphtherial Corynebacterium species are increasing, or that invasive strains tend to be of a more resistant nature (this particular aspect of Corynebacterium genetics has not been the object of investigation). Therefore, there may be clinical grounds to treat patients who have invasive disease with agents such as vancomycin. It is our feeling that infections with nondiphtherial Corynebacterium species will continue to increase in frequency, and this increase in the number of clinical isolates will eventually prompt the adoption of uniform clinical standards regarding antimicrobial susceptibility testing and treatment.

Acknowledgments

We thank Nancy Taylor of the Clinical Microbiology Unit, New Hampshire Public Health Laboratories (Concord), for technical support, and Janis Silver, for assistance in conducting our literature search.

References