

# A Spontaneous Joint Infection with *Corynebacterium striatum*<sup>∇</sup>

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***Corynebacterium striatum* is a ubiquitous saprophyte with the potential to cause bacteremia in immunocompromised patients. Until now, spontaneous infection of a natural joint has not been reported. When phenotyping failed, gene sequencing was used to identify the species. The isolate demonstrated high-level resistance to most antibiotics.**

## CASE REPORT

An 87-year-old man with a history of osteoarthritis and advanced heart failure presented with complaints of aching lower extremities and pain in the left knee with weight bearing. Four days earlier, he had fallen while transferring from chair to bed. On inspection, he appeared chronically ill. The lower extremities were swollen and erythematous below the knees. Shallow venostasis ulcers over the shins showed no signs of localized infection. A moderate-size, cool effusion could be felt around the left knee, and tenderness was present along the medial joint line. The skin around the knee was intact, without breaks. Crepitus was present with flexion, and pain developed beyond 90°. Ligaments were stable, and a radiograph showed no fracture. A sample of clear synovial fluid was found to have a high concentration of inflammatory cells without crystals. Gram staining and culture after 5 days on standard media were negative, as were blood cultures after 5 days. The patient had been admitted, and treatment begun with 1 g of cefazolin administered intravenously every 6 h along with intravenous furosemide. Over 4 days, his edema and erythema diminished; however, he could not bear weight on the left knee. He was discharged with a presumed traumatic effusion to a skilled nursing facility for rehabilitation, where he completed 6 more days of 500 mg of cefazolin administered orally four times a day.

Twenty days later, he returned with fever, dyspnea at rest, and pulmonary infiltrates. A culture of respiratory secretions grew *Streptococcus pneumoniae*. Blood cultures drawn after the administration of levofloxacin were negative after 5 days. It was noted that he had never regained the ability to bear weight on his left knee. Magnetic resonance imaging revealed a persistent effusion and a faint line of increased signal at the apex of the posterior medial meniscus, suggesting an incomplete meniscal tear. A sample of cloudy synovial fluid contained high concentrations of neutrophils without crystals. Twenty-four hours later, “diphtheroids” were recovered in pure culture. This result was thought to indicate skin contamination. After 3 days of treatment with 500 mg of levofloxacin given orally with

intravenous furosemide, the fever and dyspnea had resolved but the knee remained swollen and painful. Another sample of cloudy synovial fluid drawn 9 days later contained high concentrations of segmented neutrophils and grew *Corynebacterium* sp. in a pure culture within 24 h.

Infusion of 1 g of vancomycin every 24 h was initiated (full dose based on renal function), and the patient underwent laparoscopic exploration and drainage the same day. A large volume of purulent fluid was evacuated, and the joint space was flushed with 6 liters of bacitracin. A small tear of the posterior pole of the medial meniscus was repaired. Synovial fluid sampled at the time of surgery contained “gram-positive bacilli in palisades.” *Corynebacterium* sp. was identified in pure culture within 24 h. After 2 weeks of treatment, he resumed walking short distances and the effusion decreased.

**Identification.** The isolate was cultivated on 5% sheep blood tryptic soy agar plates incubated at 35°C in 5% CO<sub>2</sub>. Within 24 h, 2-mm cream-colored nonhemolytic colonies were seen. Samples incubated at 35°C for 4 weeks on brucella agar fortified with 5% sheep blood, hemin, and vitamin K under anaerobic conditions grew no other organisms. An attempt at identification with API Coryne (bioMérieux, Lyon, France) returned 76% similarity to *Corynebacterium macginleyi* and 19% similarity to *C. striatum*-*C. amycolatum* (ATCC 6940 type strain). The API Coryne profile number was 0100105, indicating catalase activity and fermentation of both glucose and sucrose. The strain did not demonstrate oxidase or pyrazinamidase activity or reduction of nitrate. The match with API Coryne was deemed poor and likely to require additional reagents not available at our microbiology laboratory. A separate attempt at identification by fatty acid methyl ester analysis (Sherlock MIDI, Newark, DE) returned similarities of 58% to *C. minutissimum*, 55% to *C. glucuronolyticum*, and 44% to *C. striatum*. A repeat analysis returned 62% similarity to *C. afermentans*, 54% similarity to *C. minutissimum*, and 50% similarity to *C. striatum*. Ultimately, the strain was evaluated by a sequence analysis of the first 500 bp of the 16S rRNA gene (Microbial ID, Newark, DE). The strain exhibited 100% homology to *C. striatum* type strain ATCC 6940. The next closest matches were *C. minutissimum* and *C. macginleyi*, both with 95.4% genetic homology.

**Susceptibility testing.** Susceptibilities were measured by both disk diffusion and the E test (AB Biodisk, Piscataway, NJ). All samples were cultured on Mueller-Hinton agar sup-

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TABLE 1. Resistance profile of organism isolated

Agent(s) tested	MIC <sub>90</sub> <sup>a</sup> (μg/dl)	Ring diam (mm)
Vancomycin		25
Linezolid		32
Erythromycin		11
Clindamycin		0
Levofloxacin		0
Tetracycline		0
Trimethoprim-sulfamethoxazole		0
Penicillin	4	
Cefotaxime	24	

<sup>a</sup> MIC for 90% or isolated tested based on Clinical and Laboratory Standards Institute breakpoints for alpha-hemolytic *Streptococcus* (3).

plemented with sheep blood and incubated at 35°C in ambient atmosphere for 24 h. Our methods were in accord with recently published standards (3). Disk diffusion plates demonstrated the strain's resistance to tetracycline, levofloxacin, trimethoprim-sulfamethoxazole, clindamycin, and erythromycin (Table 1). E-test strips indicated the strain's resistance to penicillin and ceftazidime (Table 1). Breakpoints have not been established for *Corynebacterium*; therefore, we used the breakpoints for *Streptococcus* (3).

**Discussion.** *C. striatum* survives as a saprophyte upon the skin and mucus membranes of asymptomatic individuals (6). Proven infections have been found most commonly in the setting of immunocompromised patients with respiratory infections, recurrent or continuous instrumentation, chronic ulcers, or surgery (6, 9, 11, 12, 14). Nosocomial person-to-person spread has been documented twice (1, 10). Septic arthritis has been reported in the setting of joint replacement surgery and an accidental scalpel laceration (4, 15). In the case reported here, several factors promoted the patient's risk of infection with *C. striatum*, including an immune system compromised by age and failing health, prolonged institutionalization, the presence of chronic ulcers, the occurrence of pneumonia, a reported blunt trauma to the knee when he fell, and osteoarthritis in the involved knee (5, 6, 12, 14). In this case, the infecting organism is most likely to have gained access to the patient's circulation either through the respiratory tract, perhaps during his pneumonia, or through his persistent and open venostasis ulcers.

Gram-stained *Corynebacterium* species may be observed by light microscopy to be arranged in palisades. *C. striatum* is usually visually indistinguishable from other species, although some strains have demonstrated striations crossing the cytoplasm. Metabolic profiling is the most common method used to distinguish *Corynebacterium* species; however, phenotypic overlap among congeners limits its discriminative power, particularly with *C. striatum*. In most cases, API Coryne requires additional reagents to reliably differentiate *C. striatum* from *C. amycolatum*. These tests include lipophilia, phenyl acetate assimilation, and *N*-acetylglucosamine assimilation, most of which are not readily available except at research laboratories. Distinction may sometimes be made by measuring tyrosinase and cyclic AMP activity. If either is positive, the strain is likely to be *C. striatum*, as *C. amycolatum* lacks these enzymes. When conventional methods are used, *C. striatum* has been shown to

reduce nitrate in 100% of the cases tested (7, 13), but on API Coryne test strips the *C. striatum*-*C. amycolatum* pair reduces nitrate at a rate of only 57% (API Coryne package insert; bioMérieux, Lyon, France, 2003), perhaps indicating a lower sensitivity for this reaction. It is notable that the API test strip used on this strain was read as negative for pyrazinamidase activity, which is uncommon for *C. striatum* (API Coryne package insert). As with metabolic profiling, phenotypic overlap limits the power of compositional analysis of fatty acids to discriminate *C. striatum* from similar congeners (6). In fact, it is likely that phenotypic methods on the whole have inaccurately identified many *Corynebacterium* isolates.

Among clinical isolates of *Corynebacterium* identified with both best phenotypic methods and complete 16S rRNA gene sequencing, there was agreement for just 25% to 60% of the isolates (15, 18). For isolates where phenotypic and genetic identifications differ, close genetic homology between the test strain and its top match favors the genetic information, as does a wide discrimination between the best and second-best matches. In the case reported here, a perfect genetic match by partial 16S rRNA gene sequence analysis and a wide discrimination between the top two matches verify that *C. striatum* was the bacterium responsible for this patient's septic arthritis.

Among strains of *C. striatum*, multidrug resistance may be spreading. A decade ago, isolates showed sensitivity to beta-lactams (particularly penicillin G), fluoroquinolones, carbapenems, linezolid, and vancomycin (4, 6). In the last 5 years, pathogenic isolates exhibiting resistance to levofloxacin, sparfloxacin, penicillin, cephalosporins, clindamycin, erythromycin, minocycline, imipenem, and linezolid have been reported (8, 14, 16, 17, 19). Thus far, in vitro resistance to vancomycin has not been reported for this or any other *Corynebacterium* species. Most initial therapies for suspected infection with *Corynebacterium* should include vancomycin.

This case highlights both the growing importance of *C. striatum* as a nosocomial pathogen and the difficulty microbiology laboratories may encounter when trying to identify this species. It is likely that the number and range of clinically important infections with this organism have been underestimated. The first recognized spontaneous infection of a natural joint with *C. striatum* is reported here.

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