

# Corynebacterium Striatum Bacteremia in End-Stage Renal Disease: A Case Series and Review of Literature

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## ABSTRACT

*Corynebacterium striatum* is emerging as an opportunistic pathogen in immunocompromised hosts. End-stage renal disease remains an underappreciated state of immunocompromise. We present a series of individuals with end-stage kidney disease on hemodialysis who developed *Corynebacterium striatum* bacteremia, which was initially thought to be a contaminant, but eventually recognized as the culprit pathogen. We review the bacteriology of *C. striatum*, increasing resistance, as well as known cases of *C. striatum* bacteremia in the setting of end-stage renal disease. These cases highlight the importance of a high index of suspicion when interpreting bacterial cultures in patients with end-stage renal disease.

**KEYWORDS:** end-stage renal disease, hemodialysis, immunocompromised, *Corynebacterium*

## INTRODUCTION

*Corynebacterium striatum* (*C. striatum*), first described by von Besser in 1889, is a common nondiphtherial Corynebacterium.<sup>1</sup> It is a non-sporulating, non-acid fast, gram-positive rod that is facultatively anaerobic and colonizes the skin and upper respiratory tract.<sup>2</sup> Nondiphtherial Corynebacterium are usually dismissed as common contaminants when isolated from clinical sample.<sup>3</sup> In immunocompromised individuals, *C. striatum* is emerging as a cause of life-threatening infections, such as bacteremia with unknown focus and infective endocarditis.<sup>4</sup>

Individuals with end-stage renal disease (ESRD) requiring long-term dialysis have an increased risk of infection, averaging about 5.7 events per 1000 dialysis days.<sup>5</sup> The etiology of immunologic dysfunction in patients with ESRD is multifactorial, involving alterations in both the innate and adaptive immune systems.<sup>6</sup> For example, ESRD impairs secreted pattern recognition receptors, toll-like receptors and cytokine production.<sup>6</sup> ESRD and its complications also causes the malfunction of antigen presenting cells (APCs) and T lymphocytes.<sup>6-8</sup> Therefore, ESRD should be considered a state of immunologic dysfunction and here we report two cases in which *C. striatum* presents an opportunistic infection in patients with ESRD.

## CASE 1

A 59-year-old man with ESRD secondary to autosomal dominant polycystic kidney disease on hemodialysis for approximately 10 years via femoral arteriovenous fistula (due to a history of multiple failed fistulas due to recurrent fistula thrombosis), presented to the emergency department with abdominal pain, fever, and chills for one day. The patient reported a sudden onset of sharp, burning epigastric pain associated with nausea and vomiting. Past medical history was significant for heart failure with reduced ejection fraction, atrial fibrillation (not on anticoagulation) and cirrhosis. On admission, vital signs were notable for a temperature of 97.8 F, heart rate of 92 beats per minute, and a blood pressure of 93/57 mmHg. Labs were significant for a sodium of 127 mEq/L, potassium of 5.4 mEq/L, venous lactate of 3.1 mEq/L and white blood cell count of 7.6<sup>9</sup> cells/L with 6% bands. Abdominal exam was notable for diffuse tenderness, distention, and hyperactive bowel sounds. Cardiopulmonary exam did not reveal any abnormalities. Skin exam revealed a decubitus ulcer on his left foot that had been present for over a month. Two sets of blood cultures were obtained and the patient was started empirically on IV vancomycin and piperacillin/tazobactam. Computerized tomography of the abdomen and pelvis with intravenous (IV) contrast revealed cirrhosis, splenomegaly and bilateral changes of polycystic kidney disease, without evidence of an acute inflammatory process to explain the abdominal pain. His abdominal pain spontaneously resolved while in the emergency department. The following day, *C. striatum* was isolated from both sets of blood cultures. Initially thought to be a contaminant, repeat blood cultures were obtained and *C. striatum* bacteremia was confirmed. Culture of the decubitus ulcer on his left foot grew *C. striatum*, *Methicillin-Sensitive Staphylococcus aureus*, and gram-negative rods. Magnetic resonance imaging (MRI) of the left foot confirmed a small focus of osteomyelitis on the medial aspect of the metatarsal head. He was treated with 6 weeks of IV vancomycin with dialysis with a goal trough of 15-20 mg/mL. Three months after completion of antibiotic use, a repeat MRI was negative for osteomyelitis.

## CASE 2

A 66-year-old man with ESRD secondary to diabetic nephropathy on hemodialysis via tunneled dialysis catheter, presented to the emergency department with discoloration of all the digits on his left foot, fever (measured at 103.2 F at home) and chills. The patient had a recent history of a large blister on his left foot that had been recently deroofed. His past medical history was significant for peripheral arterial disease, heart failure with reduced ejection fraction and a sacral decubitus ulcer with chronic osteomyelitis of the coccyx. He had recently completed a 10-day course of levofloxacin for a diabetic wound infection. Vitals were significant for blood pressure 128/72 mmHg, pulse 92 and irregular, temperature 97.7 degrees Fahrenheit, respiratory rate 19, and oxygen saturation 100 percent on room air. Physical examination was notable for purple/black discoloration of multiple toes on the left foot with large areas of lanced blisters on the lateral aspect of the left foot. Cardiopulmonary exam was unremarkable. The exit site of the tunneled catheter was without evidence of infection. X-ray of the left foot was notable for diffuse demineralization with second digit proximal interphalangeal (PIP) joint erosive changes and computerized tomography demonstrated atherosclerotic disease as well as edema around decubitus ulcer. He was empirically started on daptomycin and levofloxacin for diabetic wound infection, based on prior culture data and allergies. On hospital day 3, he was broadened to daptomycin and meropenem for anaerobic coverage. Blood cultures drawn on admission were positive for gram-positive rods which speciated *C. striatum*. This was initially felt to be a contaminant so repeat cultures were drawn and 6 of 9 blood cultures grew *C. striatum*, the remaining cultures were negative. Wound culture grew coagulase negative staphylococcus. A transmetatarsal amputation was performed and histology revealed acute osteomyelitis with no organism isolated. Given persistent bacteremia, the indwelling tunneled catheter was removed. After removal of the catheter, cultures cleared. Sensitivities for the *C. striatum* revealed Daptomycin resistance (MIC > 256) and he was transitioned to Linezolid, which he completed as a 6-week course.

## DISCUSSION

*C. striatum* is an opportunistic colonizer with low virulence but it is emerging as a nosocomial source of infection.<sup>9,10</sup> Since it was first reported as the cause of bacteremia and empyema in 1980, *C. striatum* has been recognized as the causative agent of various illnesses.<sup>11,12</sup> Patients infected with *C. striatum* often have significant underlying disease, and recovery of this organism from culture is often assumed to be a contaminant or incidental finding unless repeated cultures produce the same bacterial species.<sup>12,13</sup> *C. striatum* is generally isolated from a variety of specimens, such as tissue, wounds, devices and blood cultures. It is commonly co-isolated with *S. aureus*, coagulase-negative staphylococci

and *Pseudomonas aeruginosa*.<sup>9,10</sup> Using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), Kang et al., analyzed 300 gram-positive bacilli isolated from blood cultures of patients and of these 65 (21.7%) were identified as *C. striatum*.<sup>14</sup> They also observed that patients with multiple blood cultures had significantly higher level of biofilm production, suggesting that biofilm phenotype could contribute to the determination of clinical significance of *C. striatum* in patients.<sup>14</sup> Ishiwada et al noticed that only 60% of episodes of *C. striatum* bacteremia are associated with fever >38°C and about half of patients with bacteremia improve with inappropriate antibiotic therapy or no therapy.<sup>15</sup> *C. striatum* in these cases were regarded as contaminants and the cases where patients received appropriate antibiotic treatment were regarded as true infections.<sup>15</sup>

*C. striatum* is typically pathogenic in immunocompromised patients, including those with ESRD. A literature search identified six other cases of *C. striatum* infection in patients with ESRD (Table 1). Patient's ranged from 46 to 83 years (average age of 67 years old). Their manifestations included sepsis, endocarditis, mediastinitis and septic arthritis.<sup>16-21</sup> Hypertension, diabetes mellitus type II and heart failure with reduced ejection fraction were the most common comorbidities similar to our patients, with two patients falling under each category. *C. striatum* was originally considered a contaminant in many of these cases and was only subsequently considered to be the likely culprit. Four patients were started on antibiotic regimens that included vancomycin; two patients survived under these regimens.<sup>16,17,21</sup> Two of the eight patients were on an antibiotic regimen that included daptomycin; only one of the patients survived.<sup>18,20</sup> The second patient that was presented began treatment on daptomycin and levofloxacin but sensitivities for the strain he was infected with revealed a daptomycin resistance. He was switched to linezolid and survived.

*C. striatum* is an emerging, multidrug-resistant pathogen among immunocompromised and chronically ill patients.<sup>4,22</sup> In hospitalized settings, this organism has the potential to acquire vectors containing genes that make it resistant to multiple antimicrobials.<sup>10, 22, 23</sup> *C. striatum* has shown resistance to penicillin, cephalosporins, ciprofloxacin, meropenem, tetracycline, and clindamycin.<sup>10</sup> Aminoglycosides are usually used as second-line treatment of corynebacterium infections and some strains are now highly resistant to them.<sup>23</sup> Daptomycin is usually a last line of defense in the treatment of infections from gram-positive organisms and there is a rapid development of high level of daptomycin resistance.<sup>20</sup> Resistance to fluoroquinolones has also been noted when there is a combination of two mutations in the *gyrA* gene leading to increased MICs of ciprofloxacin and levofloxacin.<sup>24</sup> Transposable elements are associated with macrolide, lincosamide, and aminoglycoside resistances.<sup>22</sup> Vancomycin, linezolid and telavancin have shown good activity against *C. striatum* in vitro.<sup>10</sup>

**Table 1.** Summary of *Corynebacterium striatum* Cases Associated with ESRD Found in Literature

Case Description	Comorbidities	Treatment	Survival	Reference
83-year-old female presented to the emergency department after cardiac arrest secondary to aspiration pneumonia. She was found to have acute kidney injury and started on hemodialysis. On hospital day 26, she developed <i>C. striatum</i> bacteremia with dialysis catheter felt to be the source.	<ul style="list-style-type: none"> <li>• CKD</li> <li>• Hypertensive cardiovascular disease</li> </ul>	Amoxicillin/Clavulanic acid + Vancomycin	Expired	11
77-year-old male presented with 1 week of worsening right shoulder pain not relieved by opioids. An arthrocentesis was performed and aspirate contained 32,700 nucleated cells/mm <sup>3</sup> with no crystals. Cultures grew <i>C. striatum</i> . A surgical washout of the glenohumeral joint was performed.	<ul style="list-style-type: none"> <li>• Bilateral lung transplant for severe COPD on immunosuppressive treatment</li> <li>• Hemodialysis dependent ESRD</li> <li>• Hypertension</li> <li>• Drug-induced Pancytopenia</li> </ul>	Empirically on vancomycin and Ceftriaxone. Then narrowed to vancomycin.	Survived	12
46-year-old female presented with fever, chills and chest pain. A month prior, she underwent removal of an infected left femoral graft used to repair a pseudoaneurysm of the left femoral artery. She was found to have <i>C. striatum</i> bacteremia with tricuspid valve endocarditis.	<ul style="list-style-type: none"> <li>• Hemodialysis dependent ESRD</li> </ul>	Daptomycin and rifampin	Survived	13
80-year-old male presented 15 days after aortic arch replacement with fevers and leukocytosis. There was erythema, tenderness and serous exudate from the wound of the mid-chest. Blood and wound exudate cultures grew out <i>C. striatum</i> . He was diagnosed with Corynebacterium-associated mediastinitis	<ul style="list-style-type: none"> <li>• ESRD</li> </ul>	Debridement. Glycopeptide antibiotic	Survived	14
56-year-old male presented with 1 week of fever, lethargy, and dyspnea. He previously received two 6-week courses of daptomycin for catheter-related MRSA bacteremia and osteomyelitis. He was found to have native mitral valve endocarditis with cultures positive for <i>C. striatum</i> .	<ul style="list-style-type: none"> <li>• DM II</li> <li>• ESRD</li> </ul>	Mitral valve replacement, daptomycin and IV telavancin	Expired	15
69-year-old female presented with acute thrombosis of dialysis fistula in her left arm. She was found to have fevers and a grade I systolic murmur over the cardiac apex. Two sets of blood cultures grew out <i>C. striatum</i> and echocardiogram revealed a large vegetation on her mitral valve.	<ul style="list-style-type: none"> <li>• ANCA-associated vasculitis</li> <li>• ESRD</li> </ul>	Vancomycin Rifampin	Expired	16
59-year-old male presented with a one day history of diffuse abdominal pain, fevers, and chills. Found to have chronic left foot ulcer. MRI depicted a small focus of osteomyelitis on the medial aspect of the metatarsal head of the left foot. Blood and wound cultures grew <i>C. striatum</i> .	<ul style="list-style-type: none"> <li>• ESRD</li> <li>• Autosomal dominant polycystic kidney disease</li> <li>• HF with reduced ejection fraction</li> <li>• Atrial fibrillation</li> <li>• Cirrhosis</li> </ul>	Vancomycin	Survived	
66-year-old male presented with fever, chills, and discoloration of left foot digits. He was found to have <i>C. striatum</i> bacteremia. Transmetatarsal amputation was performed revealing acute osteomyelitis with no organism isolated. Bacteremia cleared after removal of tunneled dialysis catheter.	<ul style="list-style-type: none"> <li>• ESRD</li> <li>• Peripheral artery disease</li> <li>• DM II</li> <li>• HF with reduced EF</li> <li>• Chronic osteomyelitis of the coccyx</li> </ul>	Started on empiric daptomycin and Levofloxacin. Sensitivities for the <i>C. striatum</i> revealed Daptomycin resistance and he was transitioned to Linezolid	Survived	

**Legend:** chronic kidney disease, CKD; chronic obstructive pulmonary disease, COPD; end-stage renal disease, ESRD; diabetes mellitus type II, DM II; heart failure, HF; ejection fraction, EF

## CONCLUSION

Although nondiphtherial *Corynebacteria* are often dismissed as contaminants due to their low virulence, *C. striatum* is emerging as a multidrug-resistant, opportunistic pathogen. As the organism can be transmitted from person-to-person, once it has been identified as the etiology, universal hygiene measures should be observed to contain the spread of this organism. Failure to follow these measures can pose a threat to vulnerable individuals.

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## Disclosures

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## Conflict of Interest

All authors declare no conflict of interest

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