

Corynebacterium Urealyticum Bacteremia in A Hemodialysis Patient with Perm Catheter Infection



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Abstract

Aim: The aim of this study was to present a case with unusual *Corynebacterium* infection with recurrent perm catheter infection

Back Ground: *Corynebacterium urealyticum* (*Corynebacterium* CDC group D2 bacterium) is an aerobic, catalase-positive, gram positive bacillus with the typical appearance of diphtheroids that is unable to acidify carbohydrate, has strong urease activity, and is resistant to multiple antibiotics. It has been associated mainly with infections of the urinary tract. The isolation of this organism in cases of other infection is highly unusual.

Case Description: A 72-year-old female perm catheter infection due to a case of *C. urealyticum* that had developed recurrent spiking fever while undergoing hemodialysis through the subclavian catheter site. The final wound and blood cultures yielded *C. urealyticum*, which was confirmed to be a catheter-related bloodstream infection.

Conclusion: Appropriate antibiotic therapy and immediately removal of perm catheter is of paramount importance in *C. urealyticum* catheter infection. Clinical significance: persistent perm site redness and unknown origin infection should always put in perm catheter infection in mind.

Keywords: *Corynebacterium urealyticum*; Perm catheter infection

Background

Corynebacteria are gram positive, catalase positive, non-spore forming, non-motile bacilli that are frequently considered as contamination when they grow in blood culture, as they are found in the mucosa and on the skin of humans. The genus contains the species *Corynebacterium diphtheria* and the nondiphtherial corynebacteria, collectively referred to as diphtheroids. Non-diphtherial corynebacteria, originally thought to be mainly contaminants, but with growing numbers of immunocompromised hosts, are now recognized as a new pathogen as formerly presumed [1]. The infamous non-diphtherial corynebacteria can cause diseases including *Corynebacterium ulcerans*, *Corynebacterium jeikeium* (group JK), *Corynebacterium urealyticum* (D2), *Corynebacterium pseudotuberculosis*, *Corynebacterium hemolyticum*, *Corynebacterium striatum* and *Corynebacterium pseudodiphtheriticum*. Both *C. urealyticum* and *C. jeikeium* are strict aerobes that exhibit lipid-requiring and multidrug-resistance phenotypes. However, *C. jeikeium* can be differentiated from *C. urealyticum* because it is non-ureolytic and produces acid from glucose [2]. *Corynebacterium jeikeium* and *Corynebacterium urealyticum* are well-established human pathogens exhibiting resistance to several antibiotics.

Although formerly considered as a contaminant, *C. urealyticum* is being increasingly reported as the causative organism of many infections, especially in those at risk [3]. *Corynebacterium urealyticum* (CU) (formally the *Corynebacterium* group D2) is a strong urease activity that can infect the lower (acute or chronic cystitis) and upper (pyelonephritis and encrusted pyelitis) urinary tract [4]. CU is a commensal skin organism that an estimated 12% of healthy individuals carry, and it has been isolated in 30% of hospitalized patients [5]. CU converts urea into ammonia, creating alkaline urine, which precipitates struvite and calcium phosphate crystals, forming stones and encrustations on the infected mucosa [5]. They have been reported as causative agents of infective endocarditis with very high mortality rates [6]. Cases have also been described in hemodialysis patients with catheters and graft, with high morbidity and mortality [7,8]. Herein, we report one case of CU-related perm catheter infection with successful removal and discharge after empiric antibiotic treatment.

Case Description

A 72-year-old female with history of hypertension, type 2 diabetes mellitus, coronary artery disease, end-stage renal disease

status post hemodialysis via right subclavian perm catheter for 2 years, hyperthyroidism status post operation and adenocarcinoma of hepatic flexure colon status post right hemicolectomy presented to the emergency department with a one-day history of fever during hemodialysis. She also experienced poor appetite, fatigue and tenderness on the perm catheter insertion site. Vital signs revealed high body temperature (38.2 °C), rapid heart rate and normal blood pressure. Physical examination showed an erythematous skin change on right subclavian perm catheter insertion site. Laboratory investigation revealed leukocytosis of $12.6 \times 10^3 /\mu\text{L}$ (normal 4.0 to 11.0) with marked elevation of neutrophils (90.6%), total bilirubin 0.65 mg/dL (normal 0.3 to 1.0), alanine aminotransferase (ALT) 18 U/L (normal 7 to 52), aspartate aminotransferase (AST) 14U/L (normal 13 to 39), creatinine 1.6 mg/dL (normal 0.7 to 1.3), C-reactive protein

6.81 mg/dL (normal <1.0), and albumin 2.7 g/dL (normal 3.5 to 5.7).

Urine examination showed proteinuria (3+), leukocyturia (urine WBC of 50-99/HPF) and mild erythrocyturia (RBC of 2-5/HPF). An initial chest radiograph showed pattern of pulmonary congestion. The patient was presumptively diagnosed with urinary tract infection and was administered with ceftazidime 1.0 g intravenous route once every day and vancomycin 1.0 g intravenous route once every 5 days. The patient had experienced recurrent spiking fever especially when undergoing hemodialysis via perm catheter. Due to progressive erythematous change of skin around the area of perm catheter implantation and painful sensation told by the patient, perm catheter removed 5 days after admission due to highly suspected catheter-related bloodstream infection. She had *Enterobacter aerogenes* related urinary tract infection in the past but routine urine cultures were sterile at this admission.

The final blood and wound cultures from the removed perm catheter yielded CU. Antimicrobial susceptibility tests were performed by the Kirby-Bauer disk dilution method on Mueller-Hinton agar with 5% sheep blood. The organism was susceptible to ciprofloxacin, clindamycin, erythromycin, oxacillin, penicillin G, rifampicin, tetracycline, tigecycline and vancomycin. Investigation for mycobacteria, fungi and viruses was unremarkable. Echocardiography revealed no evidence of valve vegetation but severe mitral regurgitation and moderate tricuspid regurgitation. Due to the confirmed pathogen, we maintained intravenous vancomycin treatment for 4 weeks and another new perm catheter was implanted on the left subclavian vein after 16 days of admission. The patient was successfully discharged without any sequelae.

Discussion

CU is known to be a natural colonizer of the human skin and urinary tract, especially in patients receiving broad-spectrum antibiotics [3]. It is usually missed in routine culture because of its diphtheroid morphology (so considered a contaminant) and it requires 48 hours of incubation to grow [2]. CU is currently a common pathogen usually associated with infections of the urinary tract to cause acute cystitis, pyelonephritis, alkaline encrusted cystitis, and encrusted pyelitis [9,10]. Reports of non-urinary

infections caused by this organism are highly unusual [2] such as bacteremia [11], endocarditis, pericarditis [12], postsurgical osteomyelitis, peritonitis in outpatients with chronic peritoneal dialysis, wound infections [11,12] and it is even observed in kidney transplant groups [13]. *Corynebacterium* species has recently been shown to be associated with peritoneal catheter infection [14], and perm catheter infection during hemodialysis [7,8] After conducting a review of the English literature from Pubmed, we found that the connection between CU and hemodialysis has never been mentioned before. Bacteremia due to CU has been reported with a mortality rate up to 20% [14].

According to Pagnoux et al., risk factors of CU infection are summarized as prolonged use of a urinary catheter, hospitalization for long periods, immunocompromised patients, kidney transplantation, recent urologic procedure, chronic debilitating disease, broad spectrum antibiotic treatment, cytotoxic drug usage and history of previous urinary tract infection [3]. Our patient was a chronic hemodialysis case with frequent hospitalization and one episode of urinary tract infection caused by *Enterobacter aerogenes* but without recent Foley catheter use. Tracing back the patient's past history, she indeed received wide spectrum antibiotic treatment due to episode of infection including urinary tract infection, pneumonia and perm catheter infection.

Type 2 diabetes mellitus and colon adenocarcinoma in our patient contributed to her immunocompromised states. Positive blood culture with *Corynebacterium* species should prompt an evaluation for endocarditis, starting with a transthoracic echocardiogram, and if the suspicion is still high, a transesophageal echocardiogram should be done. This is because of high mortality associated with endocarditis caused by this organism. According to a study by Belmares et al., up to 28% of patients required valve replacement and 43.5% died [15]. Thus, if CU endocarditis is confirmed, valve replacement in conjunction with a 4-week duration of empirical antibiotic use is mandatory. The majority of CU strains are highly resistant to a large number of antibiotics, including aminoglycosides, B-lactams, and macrolides and variably susceptible to fluoroquinolones, macrolides, ketolides, rifampin, and tetracyclines [16]. CU strains are, however, uniformly susceptible to the glycopeptides like vancomycin and teicoplanin. Glycopeptide alternatives, linezolid and quinupristin-dalfopristin are also proven to be effective in vitro against multi-drug resistant CU strains [16].

According to the study by Garcia-Bravo et al, the percentage of resistance to most of the tested antibiotics was significantly higher in the strains of CU isolated from hospitalized patients than in those from non-hospitalized patients. These factors are unknown, but hospitalization and previous use of antibiotics could play a role in the appearance of resistance in this microorganism [4,16]. The perm catheter culture and blood culture in our patient showed CU, which confirmed the diagnosis of perm catheter-related bloodstream infection caused by CU. In patients with catheter-related bacteremia contributed by CU, removal of the catheter in conjunction with empiric antibiotic administration such as vancomycin are considered as major treatment regimes [11]. Our

patient also successfully recovered after courses of vancomycin in conjunction with catheter removal and implantation of another perm catheter for temporary hemodialysis.

Conclusion

In conclusion, isolated presence of *Corynebacterium* species in hemodialysis patients should not be written off as contaminants. Subtle symptoms like loss of appetite, weight loss and fever especially occurring during hemodialysis should prompt a thorough evaluation, including an echocardiogram before uncommon organisms are isolated. When catheter infection caused by CU is confirmed, the infective perm catheter should be removed as well as empiric antibiotics active against CU, mainly vancomycin, should be administered.

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