Corynebacterium urealyticum: rare urinary tract infection with serious complications

*Jessica Costales, DO,[1] Muhannad Alsyouf, MD,[2] Phillip Napolitan, DO,[3] Sharon Wang, DO,[3] Brian Hu, MD[2]

[1]Kaiser Permanente Los Angeles Medical Center, Los Angeles, California, USA
[2]Loma Linda University, Loma Linda, California, USA
[3]Arrowhead Regional Medical Center, San Bernardino, California, USA

COSTALES J, ALSYOUF M, NAPOLITAN P, WANG S, HU B. Corynebacterium urealyticum: rare urinary tract infection with serious complications. *Can J Urol* 2019;26(1):9680-9682.

Corynebacterium urealyticum is an organism associated with a rare chronic urinary tract infection, which can lead to calcification of the urinary tract and promote rapid lithogenesis. This case illustrates the serious complications that can arise from chronic infection with C. urealyticum, which include rapid progression of luminal and parenchymal urinary tract calcification and concomitant renal failure. This case and a review of the literature demonstrate the need for an increased awareness of this organism with early identification, aggressive management, and test of cure that may help avoid the sequela of these infections.

Key Words: *Corynebacterium urealyticum*, urinary tract infection, staghorn calculus, nephrolithiasis, struvite stones

Introduction

Urinary tract infections (UTI) are the most common type of reported healthcare-associated infections. The most frequent culprits are gram-negative bacteria, though gram-positive bacteria can also cause UTI's, often when host factors are altered.

In this case report, we describe a rare case of a multidrug resistant gram-positive chronic UTI with *Corynebacterium urealyticum*. This infection resulted in rapid progression of luminal and parenchymal calcifications with encrusted pyelitis, staghorn stone formation, prostatic calcifications, and renal failure. This case and a review of the literature illustrate the importance of clinical suspicion, the role of multimodal aggressive treatment, and test of cure to prevent significant morbidity.

Accepted for publication January 2019

*contributed equally to this article

Address correspondence to Dr. Jessica Costales, Kaiser Permanente Los Angeles Medical Center, 4950 Sunset Avenue 6th floor, Los Angeles, CA 90027 USA

Case report

This case involves a 50-year-old man with a history of stage 3 chronic kidney disease and urinary-catheter dependence due to urinary retention from benign prostatic hypertrophy. At his first visit to the emergency department 1 year prior, the patient presented with a poorly draining urinary-catheter and pelvic pain requiring a catheter exchange. Urinalysis demonstrated alkaline urine (pH of 8.4), pyuria, and triple phosphates. He was treated empirically with ceftriaxone. Urine culture later grew *Corynebacterium* species, though susceptibilities were not performed.

Subsequently, the patient had multiple emergency department visits for urinary-catheter malfunction, requiring multiple catheter exchanges. Repeat urine cultures demonstrated persistence of *Corynebacterium* species despite multiple courses of empiric treatment for UTI. Notably, one visit necessitated hospital admission, as the patient was found to have acute kidney injury. During that admission, urinalysis again showed a high pH, pyuria, and triple phosphates; and urine culture grew *Corynebacterium* species. A computed tomography (CT) scan of the abdomen and pelvis showed left hydronephrosis secondary to an obstructing 7 mm left renal pelvic stone with evidence of a calcified prostate. The patient was treated for UTI with cefepime and a left nephrostomy tube was placed for decompression.

One month later, the patient was readmitted for persistent hematuria and pelvic pain. He was found to have sepsis and worsening kidney injury. Urine culture again grew *Corynebacterium* species, though this time, susceptibilities were performed. The organism was susceptible to vancomycin, but resistant to erythromycin, clindamycin, penicillin, ampicillin, and trimethoprim-sulfamethoxazole. A repeat CT scan demonstrated significant enlargement of the previously small left renal calculi into a large partial staghorn calculi occupying the upper calyx with associated hydronephrosis. A noticeable increase in prostatic calcifications and diffuse thickening of the urinary bladder were also appreciated, Figure 1.

The infectious diseases service was consulted. Given the presence of encrusted urothelial disease and the multiple positive cultures for *Corynebacterum* species, the implicated organism was suspected to be *C. urealyticum*. Treatment was initiated with 6 weeks of daptomycin due to concomitant acute renal failure. After completion of a therapeutic course of antibiotics with evidence of bacterial eradication on repeat cultures, the patient underwent percutaneous nephrostolithotomy and ureteroscopy with laser lithotripsy. The patient was given an additional 4 weeks of vancomycin post-surgically. Six months after the surgery and eradication of the presumed *C. urealyticum* pathogen, the patient's renal function returned to baseline, and the patient no longer suffered from recurrent UTI or urinary-catheter malfunction.

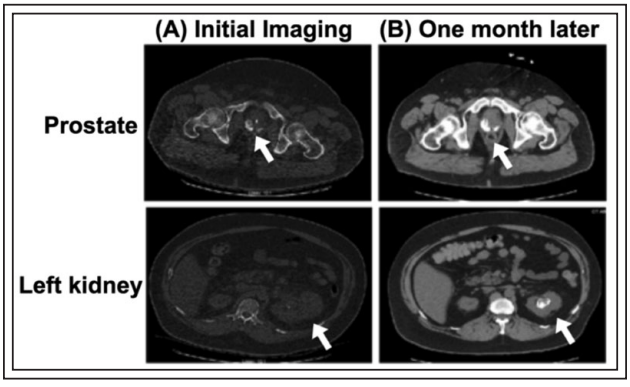

Figure 1. Rapidly progressive urinary tract calcification. Column (**A**) shows a CT scan of the abdomen and pelvis with arrows indicating prostatic calcifications and left hydronephrosis. Column (**B**) shows a repeat CT scan one month later. Arrows indicate worsening prostatic calcification, left hydronephrosis, and large staghorn calculus.

Discussion

The incidence of UTI from *C. urealyticum* is rare and has been reported to be < 1% in the general population.[1-3] It is exceedingly rare in immunocompetent, antibiotic-naïve individuals who have normal urinary tracts. Those at greatest risk for gram positive UTI have immunosuppression and existing lesions/trauma to the urothelium.[4] Most described cases of *C. urealyticum* infections occur in patients with a history of previous UTIs treated with broad-spectrum antibiotics, patients who have required prolonged hospitalizations, and patients with chronic vesical catheters.[5] This is similar to the patient presented in this case with both underlying chronic kidney disease and a chronic indwelling urinary-catheter. Previous reports have described *C. urealyticum* infections in renal transplant patients, as they are at high risk for infectious complications depending on the extent of immunosuppression.[6] In its severe forms, encrusted cystitis and pyelitis due to *C. urealyticum* infections have resulted in loss of renal graft and nephrectomy in transplant patients.[4,6,9] To our knowledge, this is the first report to describe this infection in a non-transplant patient with rapid formation of significant stone burden over a 1 month period.

C. urealyticum is a gram positive, slow-growing, lipophilic, multi-drug resistant, bacillus with diphtheroid morphology and notable urease activity.[1] When pathologic invasion of the urothelium has been achieved, its urease activity causes marked urine alkalization by hydrolyzing urea into carbon dioxide and ammonia. The alkaline environment promotes supersaturation of urine with struvite and calcium phosphate crystals, promoting lithogenesis and resulting in encrusted cystitis and pyelitis. Experimental models have demonstrated that intravesical instillation of *C. urealyticum* can produce both encrusted cystitis and pyelitis.[7] In addition to promoting nephrolithiasis

that may result in renal obstruction and subsequent post-obstructive renal injury, the byproducts of urease activity are considered to be responsible for an ammonia-induced cytotoxicity to renal epithelium and contributes to renal dysfunction.[7]

The diagnosis of *C. urealyticum* infections is difficult as this organism is slow growing. Most *C. urealyticum* isolates are missed in routine urine cultures because the organism does not grow in overnight incubation. Prolonged incubation (> 48 hours) of urine cultures in patients with alkaline urine or struvite crystals must be used to detect this organism.[7] Thus, clinicians must have a high index of suspicion to guide microbiology laboratories and extend incubation periods.[5] Additionally, susceptibilities may not be routinely performed depending upon laboratory policies.

Successful treatment usually requires close collaboration between infectious diseases specialists, urologists, and microbiologists. A multimodal approach of culture-directed antibiotic therapy for microbial eradication and surgical management of infectious stones is required to eradicate the infection and minimize morbidity. *C. urealyticum* strains have demonstrated multi-drug resistance patterns to commonly-chosen empiric antibiotics for UTIs, such as β-lactams, fluoroquinolones and macrolides.[7] Glycopeptide antibiotics, such as vancomycin and teicoplanin are the drugs of choice, as *C. urealyticum* strains have shown uniform susceptibility to these antimicrobials.[4,5,7] These resistance patterns highlight the importance of culture-directed therapy and advocate for repeating the culture to confirm microbial eradication after completion of antibiotic therapy.[8,9] Additionally, some authors have advocated for concomitant therapy with oral agents that result in urine acidification as an adjuvant to antimicrobial therapy to neutralize the effect of urease-induce urinary alkalization.[8] In the setting of renal dysfunction, renal dosing of antibiotics is required and likely requires in-hospital management.

This case illustrates the serious complications that can arise from chronic infection with *C. urealyticum*. Here, there was persistence of the pathogen on multiple cultures, causing rapid progression of urinary tract calcification and concomitant renal failure. It is of paramount importance for clinicians to be aware of this rare cause of UTI in order to avoid delay in diagnosis, administer the appropriate treatment, and prevent significant long term morbidity.

Conclusion

C. urealyticum is a rare cause of UTI, and a high-index of suspicion is necessary as the slow-growing bacteria may lead to the isolates being missed on routine urine cultures. The infection can lead to rapid stone formation, as demonstrated in our case, with stones and encrustation of parenchyma leading to increased morbidity. To aid in the diagnosis, early imaging to detect urinary tract calcification may be beneficial. We advocate a multimodal approach to management of this infection, culture-directed therapy, and a confirmatory culture of bacterial eradication after completion of antibiotic treatment. □

References

1. Salem N, Salem L, Saber S, Ismail G, Bluth MH. Corynebacterium urealyticum: a comprehensive review of an understated organism. *Infect Drug Resist* 2015;8:129-145.
2. De Briel D, Langs JC, Rougeron G, Chabot P, Le Faou A. Multiresistant corynebacteria in bacteriuria: a comparative study of the role of Corynebacterium group D2 and Corynebacterium jeikeium. *J Hosp Infect* 1991;17(1):35-43.
3. Ryan M, Murray PR. Prevalence of Corynebacterium urealyticum in urine specimens collected at a university-affiliated medical center. *J Clin Microbiol* 1994;32(5):1395-1396.
4. Lopez-Medrano F, Garcia-Bravo M, Morales JM et al. Urinary tract infection due to Corynebacterium urealyticum in kidney transplant recipients: an underdiagnosed etiology for obstructive uropathy and graft dysfunction-results of a prospective cohort study. *Clin Infect Dis* 2008;46(6):825-830.
5. Aguado JM, Ponte C, Soriano F. Bacteriuria with a multiply resistant species of Corynebacterium (Corynebacterium group D2): an unnoticed cause of urinary tract infection. *J Infect Dis* 1987;156(1):144-150.
6. Alangaden GJ, Thyagarajan R, Gruber SA et al. Infectious complications after kidney transplantation: current epidemiology and associated risk factors. *Clin Transplant* 2006;20(4):401-409.
7. Soriano F, Tauch A. Microbiological and clinical features of Corynebacterium urealyticum: urinary tract stones and genomics as the Rosetta Stone. *Clin Microbiol Infect* 2008;14(7):632-643.
8. Soriano F, Ponte C, Santamaria M et al. Corynebacterium group D2 as a cause of alkaline-encrusted cystitis: report of four cases and characterization of the organisms. *J Clin Microbiol* 1985;21(5): 788-792.
9. Meria P, Margaryan M, Haddad E, Dore B, Lottmann HB. Encrusted cystitis and pyelitis in children: an unusual condition with potentially severe consequences. *Urology* 2004;64(3):569-573.