

## CASE REPORT

**ENCRUSTED CYSTITIS IN AN IMMUNOCOMPROMISED PATIENT: POSSIBLE COINFECTION BY *CORYNEBACTERIUM UREALYTICUM* AND *E. COLI***

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**Encrusted cystitis is a severe chronic inflammatory disease of the bladder characterized by excessively alkaline urine and calcifications within the bladder wall. A case of a 60 year-old man affected by systemic lupus erythematosus (SLE), which developed encrusted cystitis due to *Corynebacterium urealyticum* with *E. coli* coinfection, shows that the treatment of encrusted cystitis with a endoscopic debulking of the encrusted stones and an antimicrobial therapy specific for *C. urealyticum* often is not sufficient for the complete resolution of symptoms.**

*C. urealyticum* is a Gram-positive, slow-growing, multiresistant, urease-positive microorganism with diphtheroid morphology. Since 1985 it has been known as a cause of alkaline encrusted cystitis and other urinary tract infections (1), occurring mainly in patients subjected to urological manipulation. Alkaline encrusted cystitis is a condition characterized by the deposition of inorganic salts on a damaged urothelium. The patient presents symptoms of cystitis (2). Moreover *C. urealyticum* has been involved in endocarditis, pneumonia, peritonitis, osteomyelitis and soft-tissue infections (3). We report a case of encrusted cystitis due to *Corynebacterium urealyticum* in a patient with SLE.

## MATERIALS AND METHODS

A 60 year-old man, affected by SLE and in treatment with steroid therapy, presents with persistent symptoms of urinary tract infection including dysuria, pollakiuria, and

intermittent hematuria with urinary gravel. He had undergone cystoscopy, which showed stone deposits in the bladder wall. Analysis of the urinary stone deposits on the bladder mucosa revealed the presence of ammonium magnesium phosphate (struvite) and calcium hydroxy phosphate (apatite).

The urine sample was plated onto modified MacConkey agar (Oxoid) and CLED (cystine-lactose-electrolyte-deficient) agar and incubated at 37°C for 48 h. The identification and the antibiotic sensitivity testing for common pathogen germs were performed with the Phoenix identification system (Becton Dickinson, USA). The urine and pus culture for *Corynebacterium spp.* on 7% sheep blood agar (Oxoid, England) was performed with incubation at 37°C in air for 24 h. The microbiological criteria for identification of *C. urealyticum* were the presence of gram-positive bacteria with diphtheroid morphology catalase-positive and strongly urease-positive. For identification the API-Coryne identification strip (API Laboratory Products; bio-Mérieux, France) and the Phoenix identification system (Becton Dickinson, USA) were utilised. The

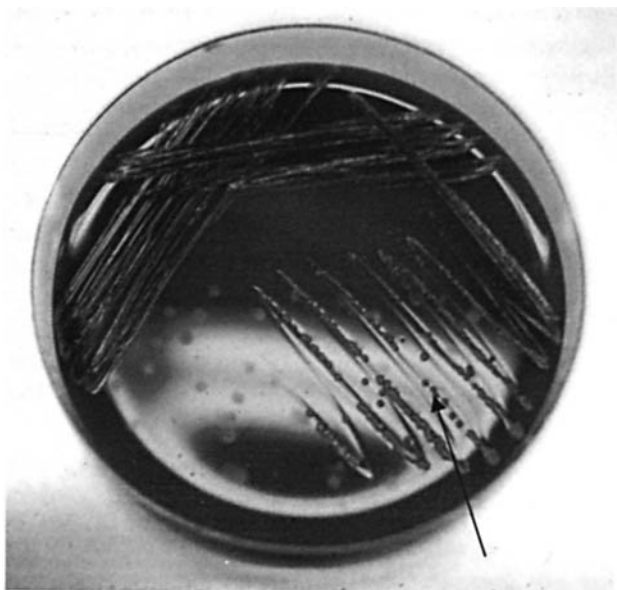
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antibiotic sensitivity testing for *C. urealyticum* was performed with Disk Diffusion Susceptibility Testing (Kirby-Bauer Method) and with the following antibiotics: cefuroxime, norfloxacin, amoxicillin/clavulanic acid, gentamicin, piperacillin/tazobactam, vancomycin and ceftazidime.

## RESULTS

The first urine culture for common pathogen germs performed in MacConkey and CLED agar and incubated at 37°C for 48 h. was negative. Microscopic analysis of the urine showed 10-20 leucocytes with +++ bacteria/field (m.f.). The urine pH was >9.0. Two months later the patient presented again with persistent symptoms of urinary tract infection. A second cystoscopy was performed and revealed the reappearance of stone deposits in the bladder mucosa. In addition, a biopsy was performed on both pathologic and healthy tissues. Histological examination of a biopsy taken from the bladder wall showed a chronic ulcerative and necrotic inflammation (infiltrates of lymphocytes, plasma cells and neutrophilic granulocytes) with no signs of malignancy. Moreover, the urine culture for *Corynebacterium spp.* was also performed. The



**Fig. 1.** Growth of *C. urealyticum* on blood agar. The culture on 7% sheep blood agar (Oxoid, England) after 24 h of aerobic incubation at 37°C in air revealed non hemolytic pinpoint colonies (arrow).

culture revealed non-hemolytic pinpoint colonies. The microbiological criteria for identification of *C. urealyticum* were the presence of gram-positive bacteria with diphtheroid morphology catalase-positive and strongly urease-positive. The API-Coryne identification strip, profile obtained (2101004), identified as *C. urealyticum* in the isolate with 99.9% probability. The antibiotic sensitivity testing was performed using the Kirby-Bauer Method and showed susceptibility to cefuroxime, norfloxacin, amoxicillin/clavulanic acid, gentamicin, piperacillin/tazobactam and vancomycin. The patient was treated successfully with amoxicillin/clavulanic acid for ten days. On follow-up the patient was clinically well, with resolution of his complaints. Urine culture for *C. urealyticum* one month after the start of antibiotic therapy was negative, whereas the urinary sediment culture was positive again for *C. urealyticum*; identification was confirmed by the API-Coryne system, profile code 2101004. The results of antibiotic sensitivity testing were identical to the previous test, therefore the patient was treated with vancomycin for 10 days. One month after the following antibiotic therapy, the urine contained mucus, pus and blood, with a strong odor of ammonia and the patient presented with dysuria, urethral discomfort and urinary urgency. The pus culture for *C. urealyticum* search was negative, but was positive for gram-negative bacteria. In fact, the Phoenix identification system revealed *E. coli* (10.000 UFC/ml). The patient was treated successfully with ciprofloxacin for 10 days. The last urine culture for *C. urealyticum* and for common pathogens search was negative.

## DISCUSSION

*C. urealyticum* is a Gram-positive, slow-growing on blood agar (Fig. 1), nonmotile, catalase-positive, multiresistant, urease-positive microorganism with filamentous morphology (*Corynebacteria* are often pleomorphic). This bacterium has been involved in endocarditis, (4) pericarditis (5), bacteriemia (6), peritonitis (7), osteomyelitis (8), necrotic infections of soft-tissue(3), and wound infections (9). Since 1985 it has been known as a cause of alkaline encrusted cystitis and other urinary tract infections (UTI) (1), occurring mainly in debilitated or transplanted patients

subjected to urological manipulation (10). Alkaline encrusted cystitis is a condition characterized by mucosal inflammation with deposits of ammonium magnesium phosphate on the urothelium. This occurs when urease-producing microorganisms cause a rise in the pH of the urine which, in turn, precipitates the deposition of the inorganic salts. The patient presented with symptoms of cystitis (11). Symptoms of UTI in the presence of urine with alkaline pH and struvite crystals are strongly suggestive of infection with *C. urealyticum* (12). The incidence of UTIs due to *C. urealyticum* is less than 2% worldwide (13). Treatment of *C. urealyticum* urinary infection may be difficult. This microorganism has been found to be highly resistant to antimicrobial agents, including nitrofurantoin, trimethoprim-sulfamethoxazole, ampicillin and cephalothin, those agents commonly used to UTIs (14). In our case, however, the strain was susceptible to many antibiotics; therefore the patient was treated with amoxicillin/clavulanic acid and subsequently with vancomycin. After treatment, even though the last urine culture for *C. urealyticum* was negative, the patient presented with a UTI positive for *E. coli*. Therefore, the patient was treated with ciprofloxacin for ten days and finally he was clinically well with complete resolution of his complaints.

The present paper discloses an uncommon case of encrusted cystopathy with alkaline urine associated to uroinfection by *C. urealyticum* and *E. coli*. The coexistence of encrusted cystitis (15) and *E. coli* superinfection remains unknown. Our data show that the treatment of encrusted cystitis with a cystoscopic resection of the encrusted stones and an antimicrobial therapy specific for *C. urealyticum* often is not sufficient for the complete resolution of symptoms in cases of *E. coli* superinfection.

#### REFERENCES

1. Soriano F., C. Ponte, M. Santamaria, J.M. Aguado, I. Wilhelmi, R. Vela and L.C. Delatte. 1985. *Corynebacterium* group D2 as a cause of alkaline-encrusted cystitis: report of four cases and characterization of the organisms. *J. Clin. Microbiol.* 21:788.
2. Berney D.M., I. Thompson, M. Sheaff and S.I. Baithun. 1996. Alkaline encrusted cystitis associated with malakoplakia. *Histopathol.* 28:253.
3. Saavedra J., J.N. Rodriguez, A. Fernandez-Jurado, M.D. Vega, L. Pascual and D. Prados. 1996. A necrotic soft-tissue lesion due to *Corynebacterium urealyticum* in a neutropenic child. *Clin. Infect. Dis.* 22:851.
4. Ena J., J. Berenguer, T. Pelaez and E. Bouza. 1991. Endocarditis caused by *Corynebacterium* group D2. *J. Infect.* 22:95.
5. Ojeda-Vargas M., M.A. Gonzalez-Fernandez, D. Romero, A. Cedres and C. Monzon-Moreno. 2000. Pericarditis caused by *Corynebacterium urealyticum*. *Clin. Microbiol. Infect.* 6:560.
6. Wood C.A. and R. Pepe. 1994. Bacteremia in a patient with non-urinary tract infection due to *Corynebacterium urealyticum*. *Clin. Infect. Dis.* 19:367.
7. Van Bosterhaut B., G. Claeys, J. Gigi and G. Wauters. 1987. Isolation of *Corynebacterium* group D2 from clinical specimens. *Eur. J. Clin. Microbiol. Infect. Dis.* 6:418.
8. Chomarar M., P. Breton and J. Dubost. 1991. Osteomyelitis due to *Corynebacterium* group D2. *Eur. J. Clin. Microbiol. Infect. Dis.* 10:43.
9. Soriano F., C. Ponte, P. Ruiz and J. Zapardiel. 1993. Non-urinary tract infections caused by multiply antibiotic-resistant *Corynebacterium urealyticum*. *Clin. Infect. Dis.* 17:890.
10. Vazquez V., M.D. Morales, C. Serrano, M. Reus, S. Llorente and J. Garcia. 2004. *Corynebacterium urealyticum* in renal trasplantation. CT and sonography imaging characteristics of encrusted cistitis and pielitis. *Nefrologia* 24:288.
11. Giannakopoulos S., G. Alivizatos, C. Deliveliotis, A. Skolarikos, J. Kastriotis and F. Sofras. 2001. Encrusted cystitis and pyelitis. *Eur. Urol.* 39:446.
12. Karayannis A., D. Picramenos, F. Sofras, D. Karanastasis, I. Stenos and T. Becopoulos. 1993. Encrusted cystitis: aetiology, clinical aspects and management. *Br. J. Urol.* 72:571.
13. Nebreda-Mayoral T., J.L. Munoz-Bellido and J.A. Garcia-Rodriguez. 1994. Incidence and characteristics of urinary tract infections caused by *Corynebacterium urealyticum* (*Corynebacterium* group D2). *Eur. J. Clin. Microbiol. Infect. Dis.* 13:600.
14. Santamaria M., C. Ponte, I. Wilhelmi and F. Soriano. 1985. Antimicrobial susceptibility of

Corynebacterium group D2. *Antimicrob. Agents Chemother.* 28:845.

15. **Romero Perez P., M. Amat Cecilia, A.R. Omera**

**Arbash and E. Andrada Becerra.** 1992. Encrusted cystitis. Review of the literature and report of a case. *Actas. Urol. Esp.* 16:496.