Successful treatment of Corynebacterium urealyticum encrusted cystitis: a case report and literature review

Terapia medica risolutiva della cistite crostosa da Corynebacterium urealyticum: descrizione di un caso e revisione della letteratura

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INTRODUCTION

Encrusted cystitis is a very rare disease characterized by a chronic inflammatory disease of the bladder in patients with predisposing factors, caused by an urea-splitting bacterium [1-3]. Recently Corynebacterium spp. have been increasingly reported as the cause of this disease. Until now, as very few cases have been reported, clinical and microbiological indications for early diagnosis and optimal treatment are not well established.

In the present article we report the case of a Corynebacterium urealyticum encrusted cystitis in an immunosuppressed patient successfully treated with teicoplanin and offer a review of the medical literature on this topic.

CASE REPORT

A 57-year-old man, with a 10-year history of systemic erythematous lupus treated with corticosteroids, presented a long period of dysuria and urethral discomfort. Three years earlier he had a lupoid obstructive uropathy with left hydroureteronephrosis, and following a percutaneous nephrostomy drainage with ureteral stenting, he began to complain of dysuria and strangury. Ultrasonography revealed hyperechogenic materials in the bladder and left hydronephrosis. Due to persistent and increasing urinary symptoms, the patient underwent two additional percutaneous nephrostomy drainages with ureteral stenting and five cystoscopies in order to remove the plaques. Analysis of these lesions showed struvite and carbonate apatite. Although urine analyses always showed pyuria and alkaline pH (pH 7.5), several urine cultures were negative for common microorganisms and acid-alcohol resistant bacilli. One month before admission, a Computerized Tomography (CT) scan showed no renal calcifications. From the initial presentation of urinary symptoms he received multiple unsuccessful courses of antibiotic therapy. These included a three-week course with ceftriaxone and a two-week course with ciprofloxacin during the two months before admission to our hospital. When we observed the patient, he still presented remarkable dysuria and urethral discomfort and the urine analysis showed pyuria and alkaline pH (pH 9). Two urine cultures on enriched media with sheep blood agar yielded C. urealyticum after three days of incubation at 35°C. The isolate proved resistant in vitro to ampicillin, second and third generation cephalosporins and fluoroquinolones. The patient was treated with teicoplanin 400 mg/die i.m. at domicile for 2 weeks. Five days after the beginning of this antibiotic therapy, the urine analysis showed a pH 6 and disappearance of pyuria. Urine culture did not show microbial growth. After one year no recurrence of symptoms was observed.
DISCUSSION

Alkaline encrusted cystitis is a chronic inflammatory disease of the bladder, first described in 1914 by Francois [1]. Presently, *Corynebacterium urealyticum*, a urea-splitting bacterium, is reported as the principal aetiological agent of encrusted cystitis and pyelitis. This microorganism is a commensal bacterium of the skin and causes urinary infection only when it is transported into the urinary tract [2].

In the last twenty years, an increasing number of cases of alkaline encrusted cystitis and pyelitis caused by *C. urealyticum* have been described. We think that this increase in reports may be related to the increase in the use of urological endoscopic procedures and immunosuppressive therapy, that are predisposing factors for these infections. Moreover, these infections may well have been previously undiagnosed due to the difficulties in identifying *C. urealyticum*.

In all cases of encrusted cystitis reported in the literature, the patients underwent a previous urological procedure [2-6]. These procedures can favour transport of *C. urealyticum*, which is a commensal skin microorganism, into the urinary tract. The interval between urological procedure and diagnosis of encrusted cystitis or pyelitis ranges from a few days to 3 years [3]. Other reported predisposing factors are neurological bladder dysfunction and malakoplakia [1, 2].

The encrustations are due to urease produced by microorganisms. The bacterial urease hydrolyzes urea and releases ammonia, inducing alkaloinization of urine, which causes hypersaturation with ammonium, magnesium and phosphate (struvite). Precipitation of these crystals results in bladder wall encrustations. Encrusted cystitis and pyelitis are chronic diseases with long-lasting symptoms. Symptoms such as dysuria, urethral discomfort, spermatic or lumbar pain with gross haematuria are considerable and much more frequent than fever, that is reported in 25-50% of the patients [3]. Eventually, renal failure may complicate encrusted cystitis and pyelitis, making the prognosis worse [3].

Medical history, clinical context and urine analysis associated with radiological findings are the basic elements for the diagnosis of encrusted cystitis or pyelitis. Urine analysis always shows leukocyturia, haematuria, alkaline pH and triple phosphate crystals (2).

The successful isolation and culture of *C. urealyticum* can be difficult because this microorganism requires culturing for 48-72 hours at 37°C on enriched media with sheep blood agar or 5% carbon dioxide [1]. This may explain delays in the diagnosis of encrusted cystitis or pyelitis, as it was in the present case. In other circumstances the organism may be considered as a contaminant.

Ultrasonography is a useful diagnostic tool for encrusted cystitis, because it shows thickening and calcified lesions on the bladder’s mucosa [2]. CT appears to be an optimal technique to diagnose encrustation, particularly in the upper urinary tract [6]. Cystoscopy plays an important diagnostic and therapeutic role in encrusted cystitis, because it permits the direct visualization and removal of the encrusted plaques [6].

Another matter of interest is the peculiar multiple antibiotic resistance of *C. urealyticum*. Since its first description as *Corynebacterium* group D2, it proved resistant to ampicillin, cephalosporins and aminoglycosides [7]. Susceptibility to fluoroquinolones is variable and resistance was reported higher than 50% [3]. In particular norfloxacin, moxifloxacin and ciprofloxacin were not in vitro active in 76%, 53% and 60% of cases, respectively [8].

Glycopeptides are the current antibiotics of choice for treatment of encrusted diseases. All strains of *C. urealyticum* are susceptible in vitro to vancomycin and teicoplanin and these drugs showed efficacy in an experimental rat model of encrusted cystitis regardless of the urine pH [8].

Overall only 4 cases of encrusted cystitis and 2 cases with encrusted pyelitis treated with teicoplanin have been reported in the medical literature, and all were cured, as was our patient. In conclusion, encrusted cystitis is a rare disease that can cause considerable discomfort and substantial morbidity with ascending pyelitis and renal failure: alkaline urine and initial negative cultures should prompt suspicion for early diagnosis and effective therapy [9, 10]. Optimal treatment requires removal of encrusted lesions and medical therapy with glycopeptides. We propose teicoplanin as the antibiotic of choice in patients with encrusted cystitis, due to the chance of outpatient therapy.

Key words: Encrusted cystitis, *Corynebacterium urealyticum*, Teicoplanin
Encrusted cystitis is a very rare chronic inflammatory disease of the bladder characterized by precipitation and incrustation of phosphate and ammonium-magnesium salts on the vesical mucosa, caused by urinary infection due to urolithic microorganisms. *Corynebacterium urealyticum* or *Corynebacterium* group D2, a multiple antibiotic-resistant urea-splitting bacterium, is the most frequently incriminated aetiology. We report a case of a 57-year-old man affected by systemic erythematous lupus with a long history of dysuria and suprapubic pain who underwent percutaneous nephrostomy drainage with urethral stenting for lupoid obstructive uropathy. Before the diagnosis of encrusted cystitis by *Corynebacterium urealyticum* was established, the patient underwent five cystoscopies to remove the plaques and multiple unsuccessful antibiotic treatment courses. Eventually the infection was definitively cured after a two-week course with intramuscular teicoplanin.

**REFERENCES**