Rare disease

Alkaline-encrusted pyelitis and cystitis: an easily missed and life-threatening urinary infection

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Summary

Alkaline-encrusted pyelitis is a urinary infection characterised by encrustations in the wall of the urinary tract. It is caused by fastidious growing urea splitting microorganisms mainly *Corynebacterium* group D2. The diagnosis is easily missed and should be evoked on basis of sterile pyuria, alkaline urine pH and calcifications of the urinary excretion ways on the CT scan and then confirmed by prolonged culture on appropriate media. The authors report here the case of a patient who died after a delayed diagnosis from recurrent septic urinary infections.

BACKGROUND

Alkaline-encrusted pyelitis/cystitis (EP/C) is a urinary tract infection caused by an urea-splitting bacteria, most often *Corynebacterium urealyticum* or D2 (CD2) and characterised by encrustations in the wall of the upper urinary tract and/or the bladder.^{1 2} CD2 is a gram-positive, slow-growing microorganism that is multi-resistant against antibiotics.

CD2 infection causes a continuous increase in the urinary pH, above 7.5, which plays a key role in the pathogenesis of encrustations. Breakdown of urea by bacterial urease leads to the formation of ammonium (NH₃) which increases pH by binding urinary H⁺ ions thereby favouring the oxidation of dissolved CO₂ into carbonate. The high pH favours precipitation of NH₄⁺ with magnesium and phosphate leading to the formation of struvite, and precipitation of carbonate with phosphate leading to formation of carbapatite. These mineral compounds are responsible for encrustations along the infected mucosa and debris/stone formation.³

Clinical manifestations of EP/C are non-specific and can be minimal for a prolonged period. They include gross haematuria and pyuria, eventually with elimination of pus, urinary debris and stones. Ultimately, EP/C can lead to urinary tract obstruction and loss of renal function. Fever is present in two-thirds of patients.³

Unfortunately, the diagnosis can be easily overlooked because *C urealyticum* grows fastidiously in common culture conditions.

Treatment is based on appropriate antibiotic therapy, acidification of urine and if required, surgical removal of the encrustations.

The prognosis for patients with infections caused by *C urealyticum* appears to be reasonably good, provided the

microbiological diagnosis is made and medical intervention started timely.^{1 2}

We report here a case with fatal course and recall how the diagnosis can be easily overlooked and how it must be evoked on clinical ground.

CASE PRESENTATION

A man in his 60s was hospitalised at the intensive care unit for acute renal failure (urea: 419 mg/dl, creatinine: 5.2 mg/dl, K: 7.1 mEq/l, bicarbonate 19 mEq/l) with gross haematuria and debris in the urine.

Medical history included tabagism, carcinoma of the tongue, cerebral infarction with residual right hemiparesis and epilepsy caused by a left carotid artery stenosis that was treated by thromboendarterectomy. The patient was institutionalised and had a permanent bladder catheterisation.

A few months before the hospitalisation, he had consulted at the Urology outpatient clinic for gross haematuria. The patient had normal renal function. Microscopic urine examination also showed 73 white blood cells (WBC)/μl and bacteria 2+, but culture remained negative. Urine pH was not measured.

INVESTIGATIONS

A cystoscopy showed two necrotic lesions, with local bleeding which persisted at a control cystoscopy performed 2 weeks later. Histologically, the bladder mucosa was covered with a thin layer of fibrin mixed with calcified necrotic debris. The underlying lamina propria was infiltrated by numerous lymphocytes and plasma cells. The urothelium displayed slight reactive atypia (figure 1). A new microscopic urine examination confirmed the leucocyturia

Figure 1 H&E staining of bladder biopsies, showing congestion and inflammatory infiltrations of the bladder mucosa (A). Some samples were composed of necrotic tissue with calcified encrustations on the wall (arrows) (B).

Figure 2 Bilateral hydronephrosis (arrows) (A) with calcifications of the calyces of the left kidney and the bladder wall (arrows) (B).

and bacteriuria, but culture still remained negative. At that time, renal ultrasound was still normal.

On admission, at the intensive care unit, a renal CT scan showed a bilateral hydronephrosis with calcifications of the calyces of the left kidney and the bladder wall (figure 2).

Microscopic urine examination showed an important pyuria (1359 WBC/ μ l and numerous crystals). Urine pH was repeatedly ≥ 8.0 units. On the basis of sterile pyuria, alkaline pH and calcifications of urinary mucosa a diagnosis of EP/C was suspected. A prolonged urine culture was asked and intravenous vancomycin was started. The culture confirmed the diagnosis, being positive after 90 h for CD2. *Mycobacterium* cultures remained negative.

DIFFERENTIAL DIAGNOSIS

Urothelial wall encrustation, particularly in the bladder, can also be observed in Schistosomiasis, tuberculosis, necrotic urothelial carcinoma, malakoplakia or after intravesical instillations of cyclophosphamide or mitomycin.⁴

TREATMENT

The patient was treated with dialysis on the first and third day of hospitalisation, followed by bilateral nephrostomy with progressive improvement of his renal function (creatinine 1.1 mg/dl, 10 weeks after the first dialysis). The *Corynebacterium* infection was treated classically with intravenous vancomycin and long-term chemolysis by anterograde rinsing with an acidic solution (Suby's G solution). Glycopeptide antibiotics are the first line antibiotics because *C urealyticum* has always demonstrated to be sensitive in vitro and in vivo to those antibiotics.³

Urine acidification has a synergistic effect with that of antibiotics. Oral acidification is often not sufficient at the beginning of treatment, requiring additional topical acidification. In our patient, this was performed with installation of a Suby's G solution directly in the excretory system via bilateral percutaneous nephrostomy catheters. Urine acidification will dissolve the calcified encrustations and prevent oversaturation of calcium salts. Complications of urinary acidification include local pain, metabolic acidosis

and fungal urinary tract infections, which all remained absent in our patient.

Surgical removal of the renal encrustations or nephrectomy was discussed, but was never possible due to the poor general condition and repeated episodes of septic shock. Urine analysis persistently showed alkaline pH, countless RBC and WBC, although urine cultures remained negative for CD2.

OUTCOME AND FOLLOW-UP

Repeated urine cultures, urine pH measurement and follow-up CT scan should be performed at various intervals to assess treatment efficacy. Therapy must be administered for several weeks, according to the evolution. In our patient, the diagnosis was overlooked leading to a 3-month delay before the start of an appropriate treatment, which certainly played a critical role in the fatal clinical course.

Despite the therapy, the patient died from septic shock 75 days after admission. An autopsy brought no further information.

DISCUSSION

Predisposing factors for EP/C includes long-period hospitalisation with broad-spectrum antibiotic therapy, immunosuppression, underlying urologic disease, manipulations of the urinary tract and prolonged bladder catheterisation,⁵ as was the case in our patient.

Histological examination of the involved tissues showed, a first zone characterised by necrosis and microcalcifications, a second inflammatory zone and eventually a third zone of underlying normal tissue.⁶ The bladder biopsy of our patient was compatible with the diagnosis, that was unfortunately not evoked.

Clinical suspicion should prompt physicians to start vancomycin and order prolonged urine cultures on media enriched with 5% CO₂ and sheep blood agar.⁷ The diagnosis can also be established by DNA PCR.⁸

Learning points

- ▶ Clinical manifestations of EP/C are non-specific and can be minimal for a prolonged period. As urine culture often remains negative, diagnosis can be easily missed
- ▶ EP/C causes sterile pyuria, alkaline pH and calcifications of urinary mucosa. High index of suspicion is required if one of these clinical features are present
- ▶ Delay in diagnosis and appropriate treatment can be fatal
- ▶ In case of suspicion, a prolonged urine culture must be asked.

Competing interests None.

Patient consent Not obtained.

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