Encrusted pyelitis: an underdiagnosed condition?

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Introduction

The first description of encrusted pyelitis (EP) was reported by Morales et al. in 1992 [1]. EP is an infectious disease defined as the presence of encrustations in the wall of the pelvicaliceal system, sometimes extending to the ureter, associated with inflammation of the surrounding tissues [2,3]. EP may be associated with encrusted cystitis, in which the pathophysiology is identical. The development of EP requires predisposing factors including the presence of urea splitting bacteria responsible for alkaline urine, a preceding urological procedure or a pre-existing mucosal lesion. The presence of a stent in the collecting system increases the risk of EP. Associated immunosuppression is an important cofactor, present in most of the patients [2–5]. Early urological complications after renal transplantation that require a secondary procedure were shown to be a predisposing factor to the development of EP within the graft [2]. Kidney transplant recipients are at particular risk due to the combination of urological procedures and immunosuppression, which explains the increasing number of cases of EP reported in these patients [1,2,5–7]. The incidence of EP in this group of patients varies from 0.2 to 1% [2,7], but EP can involve the native kidney, particularly in patients with chronic debilitating diseases [4]. In nearly all cases, EP is a nosocomially-acquired disease.

Pathophysiology: the role of Corynebacterium group D2

Many urea splitting bacteria can be responsible for EP but presently Corynebacterium group D2 (CGD2), now called Corynebacterium urealyticum, is implicated in most of the cases. CGD2 is a commensal microorganism of the skin whose pathogenic role in urine was demonstrated in vitro and in vivo [8,9]. CGD2 is a non-haemolytic Gram-positive, aerobic non-spore-bearing bacillus, with high urease activity. It infects the urinary tract and causes acute and chronic diseases involving the bladder and/or the upper urinary tract. Aguado et al. emphasized the selective role of prolonged antibiotic therapy that increases the pathogenic role of CGD2 and leads to the development of chronic encrusted disease [2]. CGD2 has a marked tropism for uroepithelial cells, as demonstrated by Marty et al. [8], which explains its ability to reach the upper urinary tract and to produce mucosal encrustations of the collecting system. Like other urealytic microorganisms, CGD2 is responsible for ammonia formation, which increases urinary pH to alkaline values. The infected urine becomes saturated with struvite and calcium phosphate which precipitates in a suitable ground resulting in mucosal encrustations, sometimes associated with free stones. Crystallographic analysis of encrustations and stones reveals predominantly struvite, in association with apatite crystals and minor compounds such as proteins [3].

Diagnosis: value of imaging and laboratory techniques

Clinical symptoms of EP are not specific. Patients present with flank pain and gross haematuria in most cases and fever is present in two-thirds [3]. The urine may contain pus or blood but the smell of ammonia is rarely described in EP, although the pH is alkaline. Renal failure is present in kidney transplant recipients and in patients with bilateral EP involving native kidneys [2,4,7]. Patients with associated encrusted cystitis present with lower urinary tract symptoms that may be severe. Encrustations may be seen in the urine [4]. All these symptoms, although non-specific, must be taken into account and EP must be suspected. The diagnosis of EP is based essentially on non-contrast CT scan and the search for CGD2 in urine, blood, and expelled encrustations. Non-contrast CT scan shows high-density edging lesions of the upper urinary tract (Figure 1). These linear calcifications of various thicknesses are specific to EP and may be associated with non-calcified stones consisting of protein matrix. Micro-abcesses of the renal parenchyma may be present in contact with encrustations. The high sensitivity and specificity of CT scan makes it the best imaging technique for follow-up after treatment [4,5]. If performed, ultrasonography shows hyperechogenic images in contact with the collecting system of the involved kidney, but this technique is not as specific as CT scan.

Urine analysis shows alkaline pH in all cases in association with red blood cells, leukocytes and struvite crystals. CGD2 culture requires special care and must
be performed at 37°C for 48 or 72 h on selective media associated with carbon dioxide atmosphere [8,9]. A selective medium containing Tween 80 and antibiotics may be helpful to identify CGD2 [10]. CGD2 may be associated with other more easily identifiable micro-organisms and thus the risk is to treat only those micro-organisms and forget the specific search for CGD2 [10]. The absence of micro-organisms on direct examination or after culture of the usual media often explains the delayed diagnosis in patients with long-lasting symptoms. The presence of alkaline urine containing struvite crystals must be taken into account and CGD2 must be considered. Specific cultures must be ordered irrespective of the presence of other microorganisms. The presence of CGD2 in urine should always be considered abnormal, despite counts below 100 000 per colony-forming units. CGD2 may also be detected in expelled calculcations, which can be helpful if urine culture remains negative [4]. CGD2 has been rarely identified in blood cultures drawn during bacteraemia [2].

Conservative rather than surgical management

Surgical removal of encrusted material was widely performed after the first description of EP [1,2,6]. The results were only partially successful, and some cases of kidney transplant loss occurred, mostly due to poor knowledge of EP and its main causative agent. Nevertheless, Aguado et al. emphasized the importance of antibiotic therapy in association with specific treatment of encrustations [2]. To avoid or delay surgical management our attitude was to propose a more conservative approach as first line treatment [3,4].

Three elements of treatment are necessary: antibiotic therapy, acidification of urine and chemolysis, and, when needed, elimination of encrustations. CGD2 is always sensitive to vancomycin and teicoplanin. The latter has the advantage of intramuscular administration. Vancomycin has proven efficacy even in alkaline media. The constant sensitivity to glycopeptides make these mediators the first-line antibiotic treatment of CGD2 infections [3]. Alternatives may be considered only after in vitro assessment of other antibiotics. CGD2 demonstrated high susceptibility to pristinamycin and rifampicin; they may be used as second-line therapy. Fluoroquinolones were widely used but the resistance rate of CGD2 to these antibiotics is presently above 50%, which makes them less useful [3]. Antibiotic therapy must always be started before any other procedures.

The calcified encrustations, which contain micro-organisms, may be dissolved by oral or topical acidification. The effect is synergistic with that of antibiotics. Oral acidification is not sufficient at the beginning of treatment and we prefer topical administration of low pH solutions such as Thomas C 24 (sodium gluconate 27 g, citric acid 27 g, malic acid 27 g, distilled water 1000 ml) or Suby’s G solution (citric acid 32.3 g, sodium carbonate 4.4 g, magnesium oxide 3.8 g, distilled water 1000 ml). Administration is by continuous intrapelvic instillation of the solution via a nephrostomy catheter. The outflow of the solution is obtained by ureteral stent or a second nephrostomy catheter. During irrigation, the intrapelvic pressure must be monitored carefully and maintained below 25 cm water [11]. The rate of irrigation is 20–50 ml/h according to the patient’s tolerance [4,11]. Direct chemolysis requires close medical follow-up because complications such as flank pain, mild metabolic acidosis and fungal urinary tract infection may occur and require specific treatment [4,11]. Urine cultures and control CT scans are performed at various intervals to assess treatment efficacy. Combined antibiotic therapy and urine acidification must be administered for several weeks, according to the outcome. Total duration of treatment is not well established as it depends on the results obtained. Two recent reports showed that antibiotics and topical acidification were administered for a mean of 1 month [4,7]. Conservative treatment requires hospitalization, which makes it expensive. Urine acidification may be continued orally, if well tolerated, to complete the treatment. Percutaneous stone removal was proposed as an alternative but the tight adhesion of encrustations to the pelvicaliceal mucosa makes this treatment very difficult and requires secondary percutaneous topical acidification [3]. Long-term follow-up must be done with repeated imaging techniques, urinanalysis and surveillance of urine crystals.

Prognosis and outcome: risks in kidney transplant recipients

At initial report, EP was considered a ‘threatening’ complication of kidney transplant [2]. Aguado et al. clearly demonstrated that with adequate medical therapy, associated with the treatment of encrustations, kidney loss was avoidable [2]. In spite of moderate complications of the treatment, conservatively treated patients had a favourable outcome and no kidney loss
was observed [4,7]. Bilateral EP in native kidneys with or without impaired renal function may also be cured by conservative management [4]. Small residual encrustations can be observed after conservative management and require surveillance, in the absence of relapse [4]. The presence of renal abscesses, which develop mainly in transplanted kidneys, is probably due to delayed diagnosis and/or inadequate treatment. This complication was responsible for graft removal in some cases but is rarely reported at the present time.

The main complication of EP in transplanted kidneys is the development of ureteral or pyelo-ureteral strictures that may occur even after conservative management [2,4,7,12]. This complication was most often described in transplanted kidneys. In the first descriptions of EP, some patients required pyelo-pyelic anastomosis or permanent nephrostomy to treat obstructive complications of EP [1,2]. In patients treated conservatively with topical acidification, mucosal toxicity induced by acidic solutions was suspected, but this toxicity proved to be transient and ureteral strictures in transplanted kidneys are mostly due to EP itself [4,7]. As demonstrated in the most recent reports, these strictures can be straight and inaccessible to endo-urologic procedures [4,7]. Reconstructive ureteral surgery is then required and uretero-ileoplasty or calico-ileoplasty may be proposed as definitive treatment [4,7].

References