4th Edition of the Clinical Cases Contest related to the non-surgical clinical management of non-surgical clinical management of renal litiasis

Official template

Title: Prevention of recurrence of infective lithiasis in patients with bilateral pyeloureteral junction stenosis.

Key words (between 3 and 6): struvite, urinary tract infection, pyeloureteral junction stenosis.

1. Abstract

Infective lithiasis accounts for 10-15% of all lithiasis. Although they are not uncommon, the case of our patient is particularly exceptional as she developed chorionic lithiasis in the context of bilateral pyeloureteral junction (UPU) stenosis, an anatomical alteration that predisposes to repeated infections that favour the development of this type of lithiasis. The case we present is that of a 26-year-old woman who presented with urinary septic shock secondary to complete right and incomplete left choriorrhoeal struvite lithiasis and concomitant diagnosis of bilateral UPU stenosis. After acute treatment, the patient underwent percutaneous right nephrolitectomy (PCNL) and subsequently a renogram with bilateral flow obstruction was performed. She underwent bilateral pyeloplasty in two surgical stages and is currently being followed up in consultation under treatment with Lit-Control® pH Down to prevent recurrence of lithiasis.

2. Introduction

Struvite (magnesium ammonium phosphate) lithiasis is commonly referred to as "infective lithiasis" and is closely related to urinary tract infections (UTI) caused by urease-producing germs. The latter favour crystallisation, easily forming fast-growing coralliform lithiasis. They account for 10-15% of all lithiasis and occur more frequently in women, and patients with neurogenic bladder or urinary diversion[1] . 1 Moreover, patients with UPU stenosis are more predisposed to the development of urolithiasis, as urinary stasis favours the process of aggregation and lithiasis growth. [2] This is why anatomical correction of these patients is imperative to avoid recurrences. In the case of our patient, stenosis of the bilateral UPU together with UTIs caused by urease-producing germs precipitated the development of bilateral chorionic lithiasis.

3. Clinical case description:

We present the case of a 26-year-old woman from Ecuador with a history of repeated lower urinary tract infections with consecutive isolations of Proteus mirabilis and Klebsiella pneumoniae in urine culture. She was evaluated in 2017 in the emergency department for septic shock with AKIN I renal failure (Creatinine 1.38 mg/dL) with multiple bilateral pyelocaliceal lithiasis on abdominal X-ray and bilateral grade III renal ectasia on ultrasound. Bilateral urinary diversion was performed by placement of double J catheters and, subsequently, she required admission to the intensive care unit. Following this admission, an outpatient Computed Tomography Urography (UROTC) was requested, which showed complete right chorioriform lithiasis and lithiasic occupation of the left lower calyx, without hydronephrosis and with both double J catheters correctly placed (Figures 1 and 2). Urinalysis was performed and showed a pH of 8.2, positive nitrite, bacteriuria and leucocyturia.

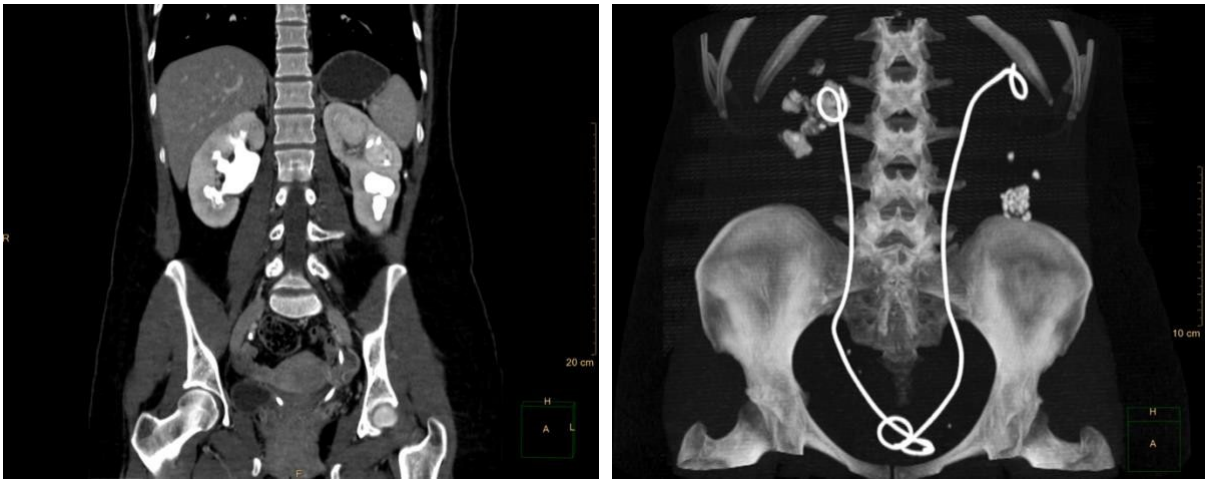

Figure 1 and 2: UROTC with leopromide contrast (ULTRAVIST 370) after bilateral urinary diversion showing complete right and incomplete left chorionic lithiasis.

Given these findings, a right LNL was indicated in January 2018. The preoperative urine culture was positive for E coli and was treated prior to surgery. The postoperative course was favourable and he was discharged 48h after surgery. After analysis of the stones, it was determined that they were lithiasis of heterogeneous composition of struvite and apatite.
At the follow-up visit, a 0.8mm fragment was visualised in the right lumbar ureter, which was treated by means of an extracorporeal lithotripsy (ESWL) session. The study was completed with a urinary metabolic study with complete blood count and 24-hour urine measurement. This showed a glomerular filtration rate >90mL/min/1.73m2, parathyretin values within normal range, an alkaline urinary pH of 8 and hypocitraturia of 112 mg/24h.

After surgery, she persisted with bilateral ectasia and a renogram was performed showing bilateral obstruction to flow (figure 3) with preserved renal function. Bilateral pyeloplasty was proposed but the patient was in the process of achieving pregnancy so treatment was postponed. Consultations were erratic as the patient was often unable to attend. She spent several months on suppressive antibiotic treatment but, three years after the first surgery, and due to significant regrowth of the right renal lithiasis, it was decided to perform a right pyeloplasty with extraction of the lithiasis. Subsequently, in 2022, and after another new pregnancy of the patient, it was found that the lithiasis had

The left renal lithiasis grew and several episodes of urinary tract infections were observed. An updated renogram was performed which confirmed a left flow obstruction and it was decided to perform a left pyeloplasty with removal of the lithiasis (90% apatite, 10% struvite).

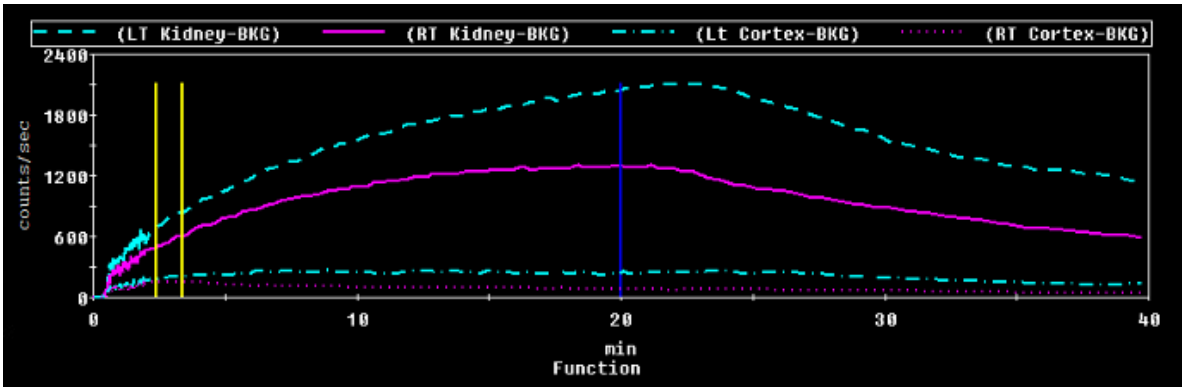

Figure 3: dynamic study of renal function with 99m Tc mertiatide in basal conditions followed by diuretic after 20 minutes. Study compatible with organic obstruction to the flow of both kidneys.

After this, treatment was started with L-methionine 500mg every 8 hours without success in acidifying the urine (pH control: 8). It was decided to switch to Lit-Control® pH Down twice a day with good tolerance and pH control was requested at 3 and 6 months. One year after the last surgery, the patient is asymptomatic and there is no evidence of recurrence of lithiasis. A control renogram was performed showing a significant improvement in the elimination curves of both kidneys with spontaneous elimination (figure 4).

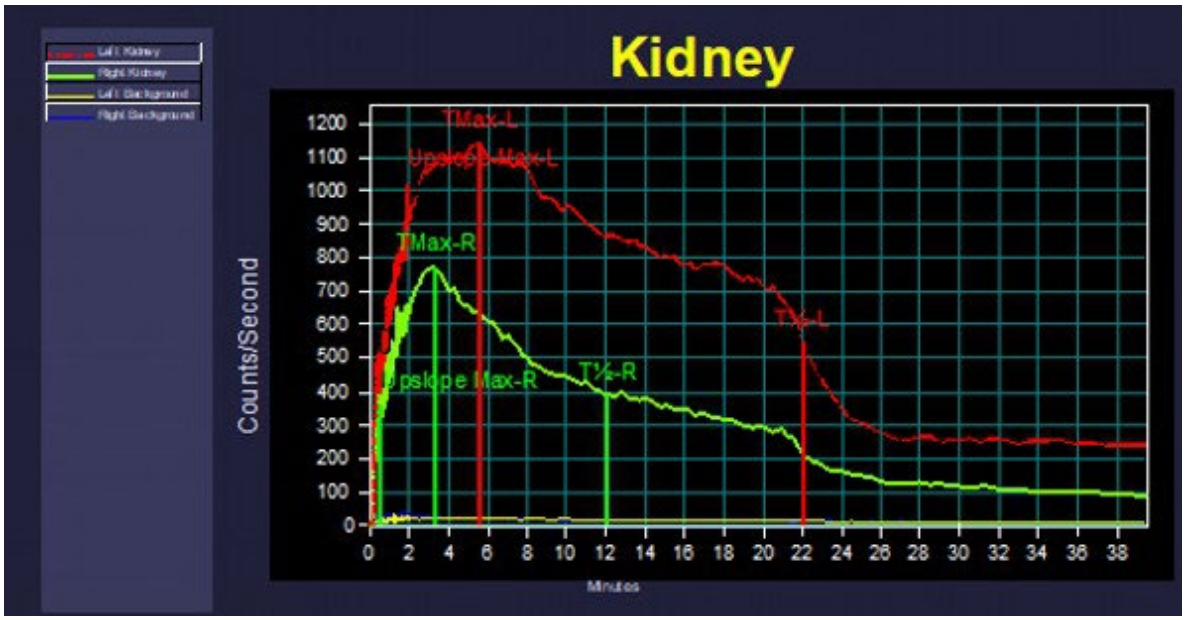

Figure 4: dynamic study with 99Tc mertiatide under baseline conditions followed by diuretic at 20 minutes. Significant improvement is observed in both kidneys compared to the study prior to surgery, with spontaneous elimination and no cumulative patterns.

4. Discussion

Infective lithiasis is caused by urease-producing germs such as those present in our patient (Proteus mirabilis, Klebsiella pneumoniae, Cornynebacterium species, or Ureaplasma urealyticum). These germs hydrolyse urea, producing ammonium and carbon dioxide, which increases urinary pH and promotes crystallisation[3]. Ammonium damages the glycoasminoglycan layer of urothelial cells, favouring bacterial penetration and the formation of biofilms. These biofilms, together with the alkaline urinary pH, result in precipitation of struvite and apatite crystals[4]. These lithiasis are usually fast growing and, as was the case when analysing our patient's lithiasis, they are usually heterogeneous in a variable percentage of monomonic urate or apatite[5].

Generally, medical treatment is insufficient and surgical treatment is required for resolution, the standard treatment being percutaneous nephrolithoctomy. Regarding conservative treatment, long-term studies show a higher mortality rate in patients who do not undergo surgery[6].

The pathogenesis is infectious, so eradicating the infection by antibiotic therapy is essential in the comprehensive treatment of these patients. If lithiasic remnants persist after surgery, it is essential to resolve them, as this increases the risk of recurrences. In the case of our patient, in the presence of small lithiasic remnants after percutaneous nephrolithoctomy, we performed a session of ESWL for complete resolution.

Once the infection and lithiasis have been resolved, the greatest challenge for urologists is to avoid recurrences. To this end, it is essential to avoid an alkaline pH that favours bacterial growth, as in the case of our patient who, after anatomical correction of the bilateral UPU stenosis, persisted with pH values of around [8]. Conservative treatments that may favour pH acidification include both dietary modifications and medical treatments. It is recommended to avoid excessive vegetarian diets, citrus or carbonated beverages, and to favour the consumption of urinary acidifiers [7].

Among the medical treatments that can be employed are urease inhibitors such as acetohydroxamic acid (AHA), which perform a complete non-competitive inhibition of urease production. They have shown modest benefit in the treatment of struvite stones but acceptable control of struvite stone growth. However, the adverse effects experienced by patients (palpitations, nausea and vomiting) mean that this drug is rarely used in clinical practice [8]. In addition to urease inhibitors, there are dissolving therapies such as renacidine R, which was disapproved by the FDA (Food and Drug Administration) in 19624 due to its side effects.

Finally, urine acidifying agents such as ascorbic acid, ammonium chloride, ammonium sulphate, ammonium nitrate and L-methionine have been used to eliminate residual fragments and prevent relapses. The use of the essential amino acid L-methionine is recommended by the European Association of Urology for the treatment of struvite urolithiasis[9]. Lit-Control® pH Down, which contains L-Methionine and rice bran extract (rich in calcium magnesium phytate) generates an acidification of urinary pH and inhibits crystallisation, with good tolerance and few side effects.

Similarly, it is necessary to monitor urinary pH to levels of 5.8-6.2. Traditionally, patients have used urine strips, however, urine strip measurements are not always reliable. In recent years, new electronic pH monitoring devices such as the Lit-Control® pH Meter have been developed with very good correlation between measurements and actual laboratory pH values.

5. Conclusions and recommendations

Patients with UPU stenosis are predisposed to the development of urolithiasis and urinary tract infections. In the case of struvite lithiasis, complete resolution and control of the urinary tract infections that promote the development of these lithiasis is essential. Once the lithiasis has been resolved, the primary objective in these patients is to avoid recurrence, for which, among other measures, it is essential to maintain a neutral urinary pH that hinders bacterial growth and crystallisation.

Lit-Control® pH Meter, based on L-methionine, is one of the most widely used acidifiers in clinical practice. Patient adherence to treatment and urinary pH monitoring with Lit-Control® pH Meter is key to avoid relapses.

6. Bibliographical references (*of special interest, **of extraordinary interest)

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