- Title: Metabolic alterations and lithiasis in patients with orthotopic ileal diversion. A case reports.
- Keywords: Lithiasis, Neobladder, Metabolic Alterations and Medical Management.

1. Abstract (no more than 150 words)

Objective: Bacterial colonization, anatomical alterations and metabolic abnormalities increase the risk of lithiasis in patients with neobladder, often requiring a complex medical and surgical approach. The aim of this work is to analyze these alterations and their medical treatment.

Methods: We present the case of a 66-year-old male with a history of cystectomy plus orthotopic bypass three years ago, who presented coralliform lithiasis in the right kidney. History of several lithiasis, as well as calcification of double J.

Result: The combination of medical and surgical treatments treats the patient's lithiasis, with medical management being especially important in the prevention of future lithiasis events.

Conclusions: Diagnosing and treating metabolic disorders and chronic infections in patients with neobladder may reduce the occurrence of lithiasis in patients with neobladder.

2. Introduction

Reconstruction of the urinary tract after cystectomy has evolved over the last decades. Currently the most frequently used bypasses in clinical practice are ureter ileostomy, orthotopic ileal reconstruction or neobladder and cutaneous ureterostomy.[1,2]

The ideal patient for orthotopic reconstruction is one who has no involvement of the prostatic urethra (or bladder neck in women), has preserved renal function, is continent, has no hepatic impairment and does not suffer from inflammatory bowel disease.[3]

Patients with neobladder have a high risk of forming lithiasis, a complication that can appear in the long term.[4,5] The factors involved in lithogenesis are varied and in the case of patients with neobladder involve anatomical causes, bacterial colonization and metabolic abnormalities. The prevalence of lithiasis is higher than in the general population,[6] varies according to the type of reservoir used, between 2.7% published by Hautmann et al. after a median follow-up of 55 months,[1] up to 12.9% with Indiana reservoir type and 43% with Kouch type.[4] Lithiasis can develop in both the reservoir and the upper urinary tract. The risk of recurrence at five years may be as high as 63%, especially in those with chronic urinary tract infections[7]

Regarding bacterial colonization, infective stones are produced by the chronic presence of urease-producing germs such as Proteus, Klebsiella, Pseudomonas and Staaphylococcus.[6] Urease breaks urea into ammonium and carbon dioxide thereby increasing the pH of the urine and promoting crystallization. This reaction will also create bicarbonate, which alkalinizes the urine. All this favors the formation of apatite and magnesium phosphate crystals in the presence of alkaline urine.[8] Therefore, treatment of symptomatic urinary tract infections and prophylaxis in indicated cases is important[5,6]

The anatomical alteration resulting from the neobladder may be associated with vesicoureteral reflux, urinary stasis and the presence of intestinal mucus, which favor lithogenesis.[7]

Regarding metabolic alterations, patients with neobladder have a higher risk of hyperchloremic metabolic acidosis, especially in the presence of renal failure or urinary tract infections.[2] It is produced as a consequence of the absorption of ammonium and chloride in the reservoir exchanging it with bicarbonate at the level of the neobladder. This chronic acidosis favors calcium reabsorption in the proximal tubule and decreases renal production of citrate.[9] Bicarbonate supplementation may be useful to correct ionic disturbances in these patients[2]

Another consequence of the utilization of long intestinal segments is the malabsorption of fatty acids. Fatty acids bind to calcium, which under normal conditions would bind to oxalate, so that the oxalate available for absorption and urinary elimination is increased. Enteric hyperoxaluria occurs and is associated with other disorders such as hypomagnesuria.[5,9,10]

All these events will produce hyperoxaluria, hypercalciuria, hypocitraturia, hypomagnesuria, alkaline urine (pH >6.5) and abundant phosphate and ammonium ions, which in turn favor the formation of lithiasis of magnesium ammonium phosphate, calcium phosphate, calcium oxalate or combinations of different types of lithiasis.[4]

The management of lithiasic pathology in these patients poses a medical challenge due to the coexistence of various alterations and because of the greater difficulty in performing retrograde endoscopic techniques[5]

3. Description of the clinical case:

Significant background: 66-year-old patient with a history of radical cystoprostatectomy and Hautmann[1] neobladder bypass for bladder urothelial neoplasia (T3N0M0) 3 years ago. Chronic renal insufficiency grade IIIB (basal GFR 35 ml/min).

Diagnostic support studies and results: The patient presented with colicky pain in the right renal fossa and a 20mm lithiasis in the right pyeloureteral junction on abdominal X-ray and abdominal CT scan (Figure 1).

Diagnosis: Diagnosis of complicated right Reno ureteral colic secondary to 20mm lithiasis in the right pyeloureteral junction.

Evolution:

In the presence of fever and deterioration of renal function (GFR 22 ml/min), it was decided to place a double right J, which was performed retrograde, without incident.

After 2 months, URS was considered, and preoperatively significant calcification of the JJ was observed, so combined access (percutaneous antegrade + endoscopic retrograde) was decided for the extraction of the calcified JJ, as well as the resolution of the pyelic lithiasis (Figure 2), without immediate complications. The patient was treated with Cefuroxime at therapeutic doses after pre-surgical culture positivity for Proteus Mirabilis.

At six months of follow-up, a control X-ray showed coralliform lithiasis occupying the lower and middle calyces of the right kidney, as well as multiple lithiasis in the left renal unit (Figure 3).

During this period the patient was not treated with any urine acidifier or alkalinize. Neither did he receive bicarbonate or potassium citrate supplements. Several antibiotics were administered at therapeutic doses adjusted to the antibiogram of urine cultures after symptomatic UTI.

In view of these findings, a proposal was made for percutaneous right nephrolithotomy and left RIRS in two surgical stages, leaving a 4mm remnant in the lower calyx of the right kidney. The predominant composition of the calculus was magnesium ammonium phosphate.

A metabolic study was performed and showed hypocitraturia, hypomagnesuria and hyperoxaluria. A daily voiding volume of 1300cc and a pH of 7. Arterial blood gasometry was requested with a pH of 7.31 and a bicarbonate in venous blood of 15.8 mEq/L.

Antibiotic prophylaxis with Trimethoprim-Sulfamethoxazole 160/800mg every 24 hours and acidifying treatment with Lit-Control pH Down® every twelve hours was proposed. Hygienic and dietary recommendations were reinforced and close follow-up was initiated.

Clinical results: Two years after the last surgery the patient remains free of disease, the lithiasic remnant has not grown, he has a good quality of life and has had no new lithiasic episodes or progression of renal failure (current GFR 35ml/min).

A control metabolic study was performed 10 weeks after starting treatment, verifying the correction of the metabolic alterations, and subsequently an annual metabolic study has been performed. Urine cultures and imaging tests have been performed periodically.

4. Discussion

Patients with neobladder are at increased risk of developing upper urinary tract lithiasis.[6] Several risk factors must be corrected for prevention.[7] Chronic bacteriuria is the most frequent risk factor, especially in patients in whom the stones are predominantly magnesium ammonium phosphate, as in the case described. Urinary stasis and metabolic disturbances at systemic and urinary level also influence lithogenesis. It is therefore especially important in these patients to keep the urine sterile and to correct metabolic abnormalities.[5]

During follow-up, anamnesis will provide information on episodes of infection or a history of Reno ureteral colic. The analysis of previous calculi can provide useful information on the potential underlying metabolic disorder; however, it is important to analyze the lithiasis in each episode since changes in its composition may occur.[6]

Close follow-up is necessary.[5] Regarding imaging techniques, in addition to CT scans for oncologic control, periodic abdominal radiography may be a good option to control radiopaque lithiasis due to its low radiation and cost.

Metabolic evaluation should be expanded to include 24-hour urine determinations[3,5]

Regarding treatment, in general, all patients should comply with preventive dietary and hygienic rules, including increased water intake, which has been shown to reduce lithiasis events. It is recommended to reduce the intake of salt and animal protein, especially in cases of hypercalciuria.[4,5,6]

Urine acidification aims to maintain a pH below 6.5 to prevent crystallization of magnesium ammonium phosphate. In addition, acidification improves the efficacy of antibiotics.[6] Therefore, it is important to monitor and control urinary pH to prevent and treat kidney stones[8]

In hyperoxaluria of intestinal origin, an extra oral calcium intake should be made in order to trap intestinal oxalate and eliminate it in the feces, reducing its excess in the blood. Magnesium and potassium citrate may also be necessary.[5]

To prevent reservoir stones, intermittent clean catheterization should be considered in patients with high postvoid residual,[5] and it has also been suggested that bladder irrigation could help reduce bladder stones from 12% to 5%[4]

In infective stones or urease-producing germs, surgical treatment should achieve total stone removal, whenever possible, to prevent recurrence and achieve sterilization of the urine.[6]

5. Conclusions and recommendations

In all patients with neobladder, lithogenic risk factors should be investigated, the stone should be analyzed whenever available, and a complete metabolic study should be performed.

The absence of lithiasic debris after surgery in patients with infective stones has been shown to reduce recurrences.

Chronic urinary tract infections as well as systemic and urinary metabolic disturbances should be treated.

Figure 1. 20mm lithiasis in the pyeloureteral junction of the right kidney.

Figure 2: Resolution of the lithiasis after the first treatment

Figure 3: Coralliform lithiasis in the right kidney.

6. Bibliographic references (*of special interest, **of outstanding interest)

1.-* Hautmann RE, de Petriconi R, Gottfried HW, Kleinschmidt K, Mattes R, Paiss T. The ileal neobladder: complications and functional results in 363 patients after 11 years of follow up. J Urol. 1999; 161(2): 422-7.

2.- Cho A, Min Lee S, Woo Noh J, Kyoung Choi D, Lee Y, Tae Cho S, Kyung Kim K, Goo Lee Y, Ki Lee Y. Acid-base disorders after orthothopic bladder replacement: comparison of an ileal neobladder and ileal conduit. Ren Fail. 2017;39(1):379-384.

3.-** Álvarez Ardura M, Llorente Abarca C, Studer UE. Manejo perioperatorio y resultados en pacientes con neovejiga ileal ortotópcia. Actas Urol Esp. 2008; 32(3):297-306.

4.- Terai A, Ueda T, Kakehi Y, Terchi T, Arai Y, Okada Y, Yoshida O. Urinary calculi as a late complication of the Indiana continent urinary diversion: comparison with the Koch pouch procedure. J Urol. 1996;155(1):66-68. 5.-* Türk C, Neisius A, Petrik A, Seitz C, Skolarikos A, Thomas K et al. EAU Guidelines on Urolithiasis. Edn. presented at the EAU Annual Congress Amsterdam; 2020. https://uroweb.org/guideline/urolithiasis/ (último acceso 22 septiembre 2020).

6.- Straub M, Strohmaier WL, BergW, Hoppe B, Laube N, Lahme S, et al. diagnosis and metaphylaxis of stone disease. Consensus concept of the National Working committee on Stone Disease for the upcoming German Urolithiasis Guideliine. World J Urol. 2005;23(5):309-323.

7.- Cohen TD, Streem SB, Lammert G. Long-term incidence and risks for recurrent stones following contemporary management of upper tract calculi in patients with a urinary diversion. *J Urol* 1996; 155:62-5.

8.-** Galan-Llopis GA, Torrecilla-Ortiz C, Luque-Gálvez MP, Prevent-Lit Group, Peris-Nieto X, Cuñé-Castellana J. Urinary pH as a Target in the Management of Lithiasic Patients in Real-World Practice: Monitoring and Nutraceutical Intervention for a Nonlithogenic pH Range. Clinical Medicine Insights: Urology. 2019; 12:1-8.

9.-* Roth JD, Koch MO. Metabolic and Nutritional Consequences of Urinary Diversion Using Intestinal Segments to Reconstruct the Urinary Tract. Urol Clin North AM. 2018;45(1):19-24.

10.-** Okhunov Z, Duty B, Smith AD, Okeke Z. Managemente of urolithiasis in patients after urinary diversions. BJU Int. 2011;108(3):330-6.