4th Edition of the Clinical Case Contests related to the non-surgical clinical management of renal lithiasis.

Official template

Title: Chemolysis of large coralliform lithiasis with Lit-Control pH Up®.

Key words: coraliform lithiasis, Lit-Control® pH Up, uric acid, chemolysis, alkalinization.

1. Abstract

- Objective: To evaluate the usefulness of medical treatment in coralliform lithiasis of uric acid despite its large size despite its large size, in a case report.

- **Methods**: We present the case of a 52-year-old woman referred to our office for hematuria. During her follow-up, an abdomino-pelvic CT scan was performed showing a 6 cm right renal lithiasis, of coralliform morphology, extending from the renal pelvis towards the middle and lower calcific groups, producing mild ectasia of the excretory system.

- **Outcome**: After 11 months of urinary alkalinization using Lit-Control® pH Up (potassium citrate, magnesium citrate and theobromine), the patient achieved almost complete chemolysis with a pH around 6.

- **Conclusions**: We should consider alkalinizing pharmacotherapy as the first treatment option in patients with uric acid lithiasis.

2. Introducción

Uric acid stones account for 5% to 10% of urinary tract stones in the United States and Europe. The prevalence of uric acid stones in the United States is increasing, which is related to the increasing prevalence of obesity, type II diabetes mellitus, and metabolic syndrome. The tendency for low urine volume and acidic urinary pH promote uric acid precipitation. The most important biochemical risk factor is a persistently low urinary pH. Insulin resistance, through endogenous acid production (lactic acid or ketoacid) and impaired ammonium excretion, contributes to urinary acidification. Insulin resistance has been attributed as the common link between obesity, diabetes mellitus and metabolic syndrome; factors that are very prevalent in patients with uric acid lithiasis. In addition, there are certain predisposing conditions that increase the risk of uric acid stone formation: gout, chronic diarrhea, increased fractional excretion of uric acid and overproduction of uric acid.

For its diagnosis, plain radiography is not useful, since pure uric acid stones are radiolucent; however, CT without contrast is very sensitive. Uric acid stones have lower Hounsfield units. Consequently, distinguishing the chemical composition of the stone is important in guiding treatment. Another standard test in the evaluation is 24-hour urine collection, which usually does not reveal hyperuricosuria.

We can usually characterize purely uraemic lithiasic patients as follows:

- A low pH, an insficient ammonium excretion (in response to an acute, and especially chronic, acid load) and an excessive protein intake (especially meat).

- Insufficient adaptation of buffering systems: insufficient phosphate influx and poor urinary phosphate excretion and hypocitraturia in circumstances where the proximal pH decreases (dysfunction of the proximal Na+/H+ exchanger).

- Insulin resistance.

3. Description of the clinical case:

a. Relevant background

The patient is a 52-year-old Caucasian woman. As an important personal history, she presents type II diabetes mellitus in treatment with oral antidiabetic drugs (OADs) with poor glycemic control. Glycosylated hemoglobin controls between 7.9% and 8.5%.

b. Estudios de apoyo diagnóstico y resultados

- Abdominal-pelvic CT: image compatible with right renal lithiasis of 6 cm (500 HU), of coralliform morphology, extending from the renal pelvis towards the middle and lower calcific groups, producing slight ectasia of the excretory system.

- Abdominal X-ray: no images compatible with lithiasis.

- Blood analysis:
  - Hemogram: 9.74 x 10e9/L leukocytes (69.5% neutrophils), Hb 14.5 g/dL, platelets 264 x 10e9/L, other parameters anodyne.
  - Biochemistry: **glucose 206 mg/dL**, creatinine 0.57 mg/dL, glomerular filtration 118 ml/min, sodium 138 mmol/L, potassium 4.79 mmol/L, uric acid 3.1 mg/dL, LDL 138 mg/dL, HDL 49.6 mg/dL, TGs 81 mg/dL, atherogenic index 2.8, **glycosylated Hb (A1c) 8.1%.**

- Urine culture: negative

- Urine sediment:
  - Proteins: negative
  - Glucose: 100 mg/dl
  - Leukocytes: 25/microL
  - Nitrites: negative
  - Density: 1.02 g/L
  - Red cells: 60/microL
  - pH: 5

- Urinalysis:

- Leukocytes: 2-5/field
- Erythrocytes: 15-30/field
- **Uric acid crystals: abundant**

c. Diagnosis

The following images show the axial and coronal sections where the coralliform lithiasis in the right kidney can be appreciated.

Figure 1: Axial slice in abdominopelvic CT scan

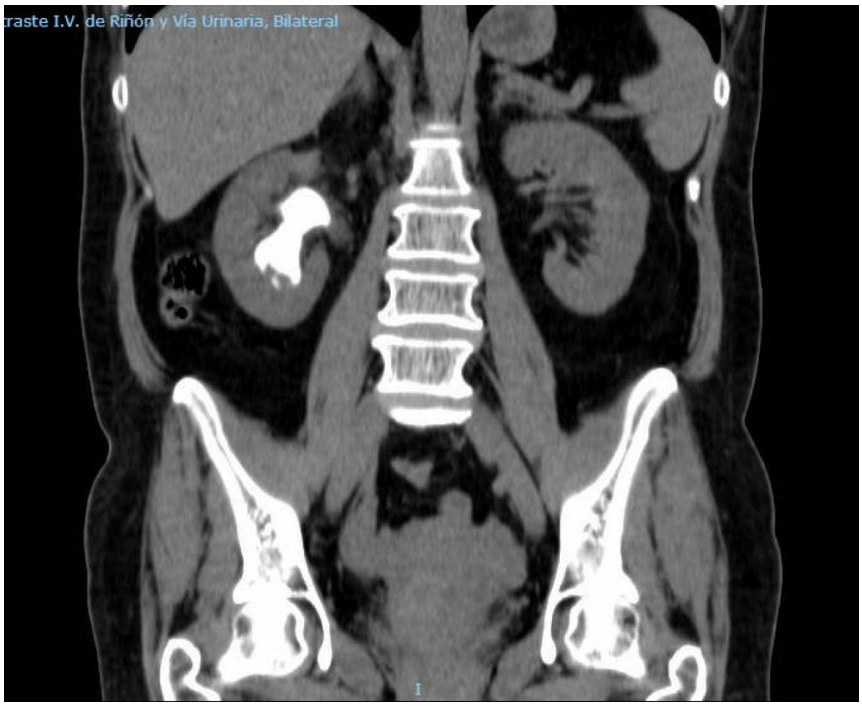

Figure 2: Coronal section in abdomino-pelvic CT scan

d. Treatment

In October 2022 she started with alkalinizing medical treatment with Lit-Control® pH Up (potassium citrate, magnesium citrate and theobromine) with a dosage of 1 capsule every 8 hours in order to try to achieve a pH> 5.5 and consequently a reduction of uric acid crystallization and dissolution of the calculus.

e. Evolution and follow-up

In March 2023, after 6 months of alkalinizing treatment, the patient was asymptomatic from the urological point of view. A metabolic study was performed, showing normalization of urinary pH to a value of 6, low diuresis (2300cc) and urinary hypercitraturia. The rest of the values were in range. A control abdominopelvic CT scan was performed showing a decrease in the size of the lithiasis: lithiasic image of linear morphology, 8 mm in extension in the pelvis, ureter of preserved caliber in all its trajectory and without evidence of other lithiasic images.

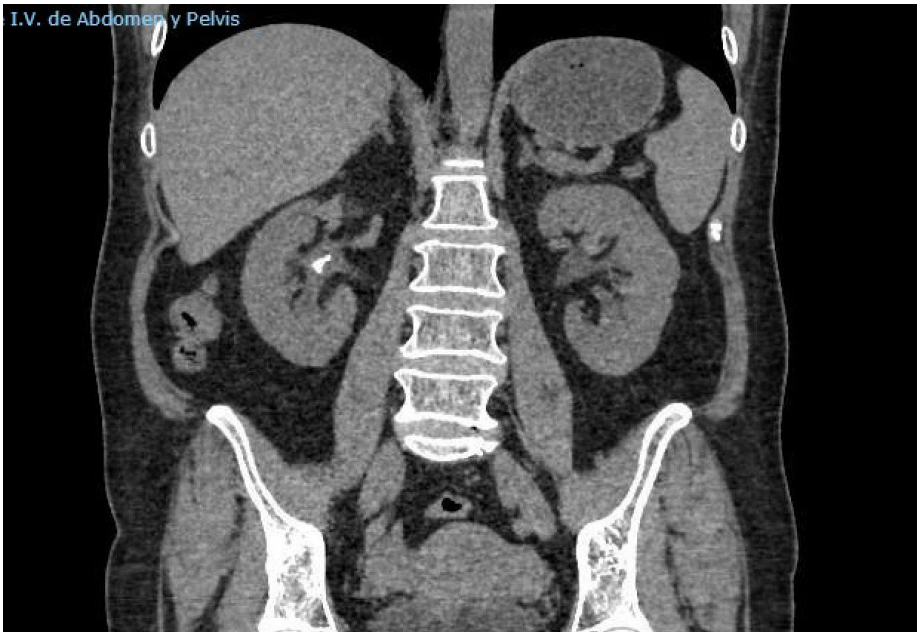

Figure 3: Coronal section in abdominopelvic CT after partial alkalinization.

f. Clinical results

In October 2023, the patient continues with alkalinizing treatment and irregular glycemic control, with glycosylated Hb around 8%. Urinary pH continues to be in range. A new control abdominopelvic CT scan was performed, showing a 2.5 mm right renal lithiasis in the lower calcific group, which means an almost complete dissolution of the calculus. We reduce the dosage to 2 capsules every 24h as preventive treatment.

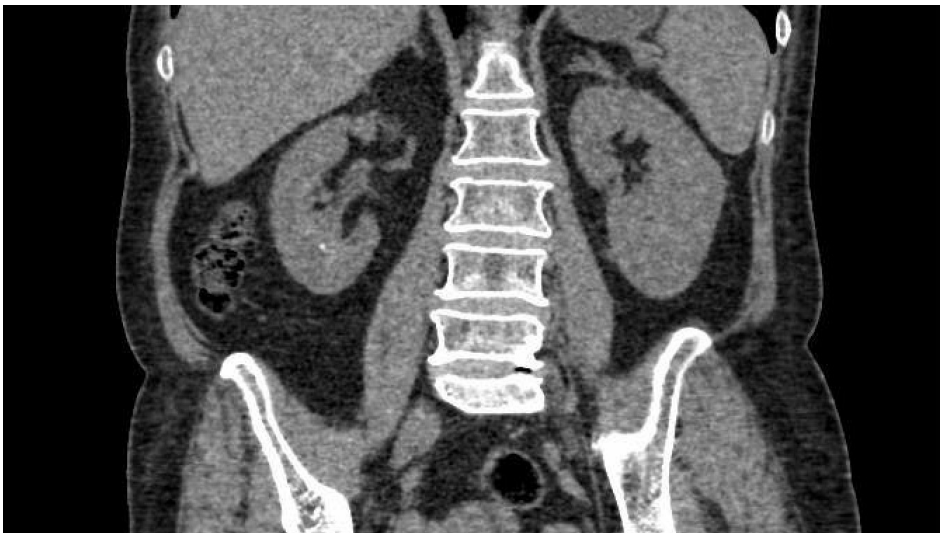

Figure 4: Coronal section in abdominopelvic CT after complete alkalinization.

4. Discussion

The prevalence of uric acid urolithiasis contributes significantly to the global burden of disease, due to high recurrence rates and diagnostic challenges. Dissolution therapy plays a valuable role in the conservative management of uric acid stones, reducing the number of surgical interventions.

On the other hand, we cannot forget that the prevalence of uric acid stones is significantly higher in one subtype of lithiasic patient, that is those afflicted with diabetes mellitus II.

The formation of uric acid crystals depends on three main factors: uric acid concentration, low urine output and urine pH, which is the most important. Insulin resistance, associated with obesity, diabetes mellitus and metabolic syndrome, has been associated with low urinary pH levels. Alkalinization therapy should aim for a urine pH between 6.5 and 7.

There are three treatment options for uric acid nephrolithiasis including:
- Urine alkalinization.
- Increased fluid intake
- Reduction of uric acid production with reduced intake of purines and xanthine oxidase inhibitors. In this case, xanthine oxidase inhibitors are generally reserved for patients who continue to have stones despite urinary alkalinization and increased fluid intake prescribed.

No randomized trials have evaluated the efficacy of urinary alkalinization in the recurrence or dissolution of uric acid stones. However, alkalinization is associated with a marked reduction in recurrent stone episodes in observational studies. For example, the mean rate of recurrent uric acid stones among 18 patients was reduced from 1.2 to 0.01 stones per patient per year with long-term treatment with potassium citrate (1).

In our case, we are dealing with a patient with poor compliance with the hygienic dietary measures recommended for the control of uric acid lithiasis, in addition to persistent poor glycemic control despite treatment with oral antidiabetic drugs. Likewise, she presents irregular control in the measurement of pH values. After insisting on regular measurements to try to adjust the alkalinizing dose individually, it was finally not feasible. However, after months of urine alkalinizing treatment with Lit-Control pH Up®, she achieved an increase in urinary pH and almost complete dissolution of the 6 cm coraliform calculus. Likewise, maintaining urinary pH control between 5.5 and 6.2 is essential to avoid recurrence of calculi. Currently, the patient is referred to the endocrinology outpatient clinic for

evaluation and follow-up of her diabetes in order to obtain good glycemic control.

5. Conclusions and recommendations

Dissolution therapy is a safe and effective method for the short-term conservative management of uric acid stones. However, further research should be conducted to develop evidence-based clinical guidelines for the diagnosis, treatment, and prevention of urolithiasis. Of note is the fact that epidemiological studies have amply demonstrated an association between uric acid urolithiasis and insulin resistance, so all actions for treatment and prevention are also measures to be used in patients with this type of stone.

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

1. ** Ong A, Brown G, Tokas T, et al. SelecQon and Outcomes for DissoluQon Therapy in Uric Acid Stones: A SystemaQc Review of Literature. Curr Urol Rep 2023; 24:355.
2. Pak CY, Sakhaee K, Fuller C. Successful management of uric acid nephrolithiasis with potassium citrate. Kidney Int 1986; 30:422.
3. **Rodman JS. Prophylaxis of uric acid stones with alternate day doses of alkaline potassium salts. J Urol 1991; 145:97.
4. Riese RJ, Sakhaee K. Uric acid nephrolithiasis: pathogenesis and treatment. J Urol 1992; 148:765.
5. Abate N, Chandalia M, Cabo-Chan AV Jr, et al. The metabolic syndrome and uric acid nephrolithiasis: novel features of renal manifestaQon of insulin resistance. Kidney Int 2004; 65:386.
6. Cameron MA, Maalouf NM, Adams-Huet B, et al. Urine composiQon in type 2 diabetes: predisposiQon to uric acid nephrolithiasis. J Am Soc Nephrol 2006; 17:1422.
7. **Daudon M, Traxer O, Conort P, et al. Type 2 diabetes increases the risk for uric acid stones. J Am Soc Nephrol 2006; 17:2026.
8. Cameron MA, Sakhaee K. NefroliQasis de ácido úrico. Urol Clin N Am. 2007; 34: 335-346
9. *Urinary lithiasis: EQology, epidemiology, and pathogenesis. In: kavoussi LR, Novick AC, ParQn AW, Peters CA eds. Campbell-Walsh Urology. 10th ed. Philadelphia, PA: Saunders Elsevier. 2010; 1277-1279.
10. Wiederkehr MR. Uric Acid Nephrolithiasis: A systemic metabolic Disorder. Clin Rev Bone Miner Metab. 2011; 9: 207-2017.