

3rd Edition of the Clinical Cases Contest related to the non-surgical clinical management of renal lithiasis.

Official template

Title: COMPLETE RESOLUTION OF MULTIPLE NEPHROLITHIATIC PATHOLOGY USING CONSERVATIVE MANAGEMENT WITH ALKALIZING ORAL CHEMOLYSIS

Keywords (between 3 and 6): nephrolithiasis; hyperuricemia; uric acid; potassium citrate; chemolysis; alkalinization.

1. Summary (not over 150 words):

- Objective: Clinical case presentation of how uric acid lithiasis can be completely dissolved using alkalizing oral chemolysis.

- Method: we describe the evaluation, diagnosis, treatment, and follow-up of a 67-year-old female patient with multiple renal lithiasis who was assessed in the emergency department and later through the urology outpatient consultation.

- Result: after urinary pH alkalization with Lit Control Up for 4 months, all the lithiasis located in the right kidney disappeared completely according to the abdominal-pelvic CT scan and the patient remains without urinary symptoms.

- Conclusions: oral chemolysis based on urine alkalization by administering potassium citrate or sodium bicarbonate allows to dissolve uric acid stones if the urinary pH is kept above 7. Urinary alkalization can be combined with allopurinol if there is hyperuricemia and/or hyperuricosuria, with urinary drainage in case of complicated renal colic or with tamsulosin to favor spontaneous expulsion.

2. Introduction

Renal-ureteral lithiasis is one of the most frequent urinary conditions. It generates a significant number of medical consultations, urological emergencies, and hospital admissions, affecting a relevant section of the working-age population.

The urinary stones prevalence varies from 1% to 20%, being influenced by genetic, geographical, and dietary factors, among others. It is a urinary condition characterized by its high recurrence rates associated to the risk of developing chronic kidney disease (CKD) (1).

Lithiasis are often composed of a mixture of substances, predominantly oxalate and calcium phosphate along with uric acid, which is the main component of 10 to 20% of all kidney stones. In addition, seventy-nine percent of uric acid stones occur in men, with a peak frequency between the ages of 60 and 65 for both genders (2).

It is important to know the composition of urinary stones, using urinary pH, radiogram, and abdominal-pelvic CT scans without contrast as support, since this is what the diagnosis and management will be based on (1).

Uric acid stones can be dissolved using oral chemolysis, which consists of alkalinizing urine (achieving a urinary pH between 7-7.2) and by administering potassium citrate or sodium bicarbonate.

3. Description of the clinical case:

a. Relevant medical history: 67-year-old female patient with a personal history of being a smoker for more than 30 years, essential hypertension, left adrenal nodule under follow-up and right renal-ureteral expulsive colics for which she has never consulted.

b. Diagnostic support studies and results: the patient was referred to urology for a new episode of expulsive renal colic for which she went to the emergency room. The following tests are requested by the urology department:

- Blood tests (to be highlighted): normal renal function, sodium and potassium, uric acid 6.5 mg/dL (upper limit 5.7 mg/dL), total cholesterol 251 mg/dL (upper limit 200 mg/dL), no leukocytosis or elevation of acute phase reactants.

- Sediment and urine tests (to be highlighted): pH 5, 5-10 leukocytes per μ l, 15-20 RBCs per μ l, negative nitrites.

- Urine culture: contaminated.

- Lithiasis analysis: 60% calcium oxalate + 40% uric acid.

- Abdominal X-ray (emergency and outpatient): difficult evaluation due to abundant gas in colic frame.

- Ultrasound scan of the urinary system: kidneys normal inn size and morphology, good cortex/medulla differentiation. Numerous microlithiasis are identified in upper and middle calyceal groups of the right kidney. Grade I-II/IV dilatation of the right urinary tract with renal pelvic ectasia and the presence of several pelvic microlithiasis are observed. Left urinary tract is not dilated.

Abdominal-pelvic CT scan with and without intravenous contrast: normal kidneys. Numerous uniform lithiasis of about 4 mm each are identified, occupying a large part of the right renal (extrarenal) pelvis and in upper and lower calyceal groups which are non-obstructive, of about 365 UH. Left renal sinus cysts.



c. **Diagnosis:** multiple right nephrolithiatic pathology with no current signs of obstructive uropathy or complication.

d. **Treatment:**

- Initially, the team decided to perform a right RIRS informing the patient that the amount lithiasis would probably require several surgical interventions. Finally, it was not possible to remove any lithiasis under this approach because there were countless numbers of them, which had an median hardness. Double J stent was left open 6Fr/28cm.

- The next therapeutic option (although percutaneous nephrolithectomy was considered), due to the presence of uric acid lithiasis, acidic urinary pH and hyperuricemia, was chemolysis with Lit Control Up 1 tablet with both breakfast and dinner (potassium citrate + magnesium nitrate + theobromine) and 300 mg of allopurinol every 24 hours. The double J stent is maintained, and water intake is encouraged to keep a diuresis of 2.5 liters per day.

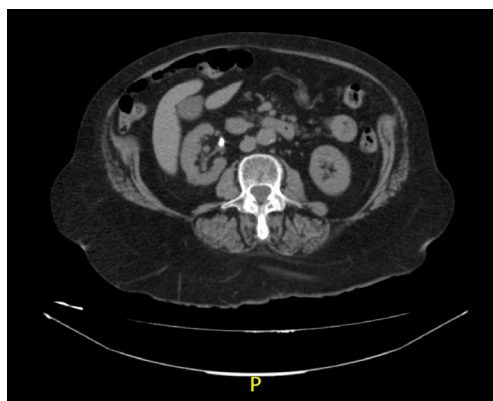
e. **Evolution and monitoring:** follow-up is scheduled in four months for urology outpatient consultation, along the following tests results:

- Blood tests (to be highlighted): renal function, normal sodium and potassium, uric acid 3.8 mg/dL (upper limit is 5.7 mg/dL), no leukocytosis or elevation of acute phase reactants.

- Sediment and urine tests (to be highlighted): pH 7, negative leukocytes, 1-5 RBCs per μ l, negative nitrites.

- Urine culture: negative.

- Abdominal-pelvic CT scan without contrast: right double J stent slightly lowered showing the proximal end within the pyeloureteral junction. Complete resolution of right renal lithiasis. No right ureteral lithiasis, no dilation of the right urinary tract.



f. **Clinical results:** the patient is currently asymptomatic and without new episodes of renal colics. The double J stent is removed after verifying the resolution of the stones, the urinary alkalizing treatment and allopurinol are maintained and follow-up is scheduled in 4 months with blood, sediment and urine tests and a new abdominal-pelvic CT scan without contrast. The results continue to show complete chemolysis of uric lithiasis, alkaline urinary pH and blood uric acid within range.

4. Discussion

In patients with urolithiasis, an adequate diagnosis is essential to guide treatment decisions. The stones can be classified according to their simple radiographic appearance, the CT scan without contrast provides information about their density, structure and composition. Urinary pH can also provide information about the type of stone. In addition, lithiasis analysis must be performed on all patients that develop stones for the first time using a valid procedure (X-ray diffraction, infrared spectroscopy or polarization microscopy) (1). The thorough and correct study of our patient allowed us to know the composition of the stones, among which was uric acid, being able to offer from conservative treatment based on oral chemolysis to antegrade or retrograde surgery.

It is important to properly select those patients who are good candidates for active lithiasis treatment, since these can affect renal function. Gambaro G et al in their systematic review focus on looking for CKD risk factors in stone formers and the impact of urological surgery. They conclude that the number and complexity of urological treatments, staghorn lithiasis, lithiatic load and previous advanced CKD seem to be the most relevant risk factors for CKD after urological treatment of lithiasis (3). In this case, we have proposed a conservative treatment considering the stone composition before attempting repeated flexible ureterorenoscopy or percutaneous nephrolithectomy.

Conservative treatment of uric acid stones has been based on urine alkalization (mainly by oral agents) along with adequate hydration, diet regularization and urinary tract infections control. Although urinary alkalization has been used for decades, there are no randomized clinical trials that support it.

Since most uric acid stone formers have persistently more acidic urine than non-lithiasis formers or calcium stone formers, the medical treatment for urate stones is mainly based on regulating urinary pH. As pH increases, the solubility of uric acid increases: at pH 5, the solubility is less than 150 mg/L, while at pH 7 it increases to almost 2000 mg/L (2).

Becker G in his article reviews different prospective studies where it is shown that with urinary pH around 6.5-7 using oral alkalinizers (doses of 30-80 mEq/d in the case of potassium citrate) lithiasis formation and episodes recurrence of expulsive renal colic are significantly decreased and high rates of complete stone dissolution are achieved (2). Allopurinol, on the other hand, a xanthine oxidase inhibitor, prevents the degradation of purines to uric acid. Becker G collects several prospective studies where the use of allopurinol in patients with hyperuricosuria and/or hyperuricemia, along with high fluid intake was effective for preventing the formation of uric acid stones and reduced the frequency of stone removal (2).

Elsawey et al prospectively evaluated the efficacy and success predictors of oral alkalization therapy in patients with radiolucent kidney stones. They combined 3L of daily water intake, diet modifications and 60 mEq/d of potassium citrate to maintain urinary pH between 6.2 and 6.8. In patients with hyperuricemia, allopurinol 300 mg/d was also prescribed. The dissolution of the stones was evaluated through CT scans without contrast. After 3 months, out of the 182 patients 53.3% of them achieved complete dissolution, 35.7% partial response and 11% showed no response. Poor glycemic control and lithiasis density were independent predictors for non-dissolution of stones after 3 months of treatment. Initial response (3 months) to oral alkalization, lower density of the stones, and higher urinary pH 12 weeks after treatment were independent predictors of stone dissolution after 6 months of treatment (4).

It is worth mentioning that the duration of urinary alkalization treatment is not clear nor established. Regardless of the size of the stone, oral alkalization is an effective treatment method

for uric acid kidney stones and, although there are no randomized clinical trials, we have prospective trials that support its use. Based on scientific evidence, the patient was treated with abundant water intake, urinary alkalization, and allopurinol, with excellent results.

5. Conclusions and recommendations

- An adequate diagnosis and lithiatic characterization are essential to offer the patient the best therapeutic management.
- The treatment for uric lithiasis should be based on different combined measures: sufficient water intake to ensure a diuresis above 2L a day, diet regularization, urinary alkalization, hyperuricemia/hyperuricosuria treatment and control of lower urinary tract infections.
- Although there are no randomized clinical trials on which alkalizing oral chemolysis is based, prospective trials support its use in urinary lithiasis that are composed of uric acid.
- We must offer treatment with alkalizing oral chemolysis to patients with lithiasis composed of uric acid +/- allopurinol for patients with hyperuricemia and/or hyperuricosuria, maintaining a urinary pH above 7.

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

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