

1st Edition of the Clinical Cases Contest related to the non-surgical clinical management of renal lithiasis.

Title: Chemolysis in uric acid nephrolithiasis: case report.

Keywords: Urinary lithiasis. Uric acid. Potassium citrate. Chemolysis.

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1. Summary

Objective: Clinical case presentation of a patient with large kidney stones treated with chemolysis in daily clinical practice.

Method: Clinical case presentation of a 50-year-old patient with uric acid kidney stones, in which medical treatment with potassium citrate is prescribed to treat the stones.

Results: After chemolytic treatment and undergoing surgery for one of his kidneys due to obstruction of the urinary tract, clinical resolution is achieved.

Conclusions: Chemolytic treatment should be considered as a valid alternative to surgery, as already included in several guidelines, especially in patients with lithiasis less than 20 mm.

2. Introduction

Kidney stones are mineral deposits that normally develop in the calyces of the kidney and are usually related to the presence of a certain substance in urine in concentrations higher than expected, causing the substance to precipitate [1]. These stones can appear at various locations of the urinary tract, from the renal calyces to the urethral meatus, in some locations they appear because of formation, and in others after moving through the urinary system. The most common compound in lithiasis is calcium oxalate, which represent, along those formed of calcium phosphate, approximately 80% of all lithiasis. 10% correspond to stones composed of struvite (related to urease-producing bacteria), 9% to uric acid, and 1% to other substances [2].

Nephrolithiasis is a common pathology with an approximate prevalence between 2% and 15% worldwide, and being more frequent in men than in women [3].

In the United States, its prevalence varies between 5% in women and 12% in men, being more frequent in Caucasian individuals [4,3].

The diagnosis is usually given after a renal colic episode, either after the stone is passed or after performing an imaging study, being the computerized tomography without contrast the most sensitive and specific study [1]. The complete diagnosis, however, is not achieved until the stone is analyzed, either after it is passed or after it is extracted or fragmented through surgery.

The treatment for kidney stones can be medical or surgical. Surgical treatment can be performed by extracorporeal lithotripsy, ureteroscopy or percutaneous nephrolithotomy. Medical treatment consists of the combination of medical expulsive therapy, such as hydration, analgesic drugs, and β -adrenergic receptor antagonists such as Tamsulosin; as well as the administration of drugs with chemolytic activity for certain cases.

3. Description of the clinical case

a) Diagnostic support studies and results

Clinical case presentation of a 50-year-old male patient, who was monitored in the outpatient Urology service of our hospital due to recurrent renal colic, with spontaneous expulsion of lithiasis.

In February 2019, an abdominal CT scan was performed (Image 1) in which two stones of 14 and 17 mm were observed in the lower calyx of the left kidney, in addition to another 20 mm stone in the renal pelvis of the same kidney. In the right kidney, a 12mm stone is described in the lower calyx, as well as another 6mm stone in the renal pelvis. The composition of these stones is assumed thanks to the analysis of those stones that were previously passed, these being formed of uric acid crystals, it was also assumed indirectly by the radiodensity of the stones observed in the CT, which is approximately 500 Hounsfield units.

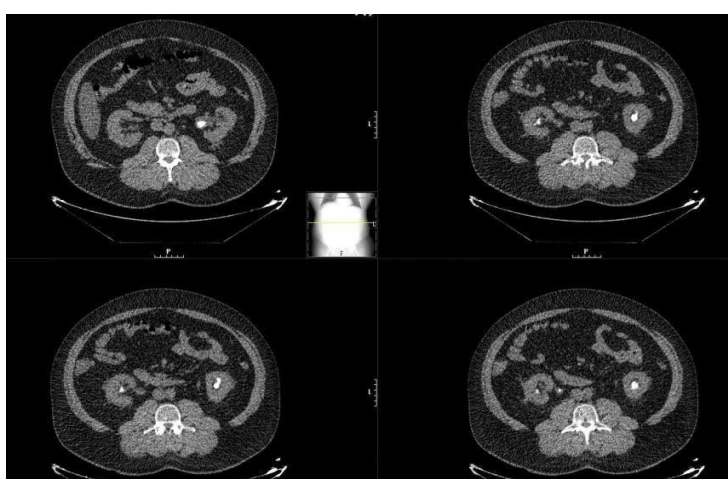


Image 1: Abdominal CT scan performed in February 2019

b) Diagnosis

The patient is diagnosed with bilateral, non-obstructive renal lithiasis. Given the high suspicion that these stones are composed of uric acid, a 24-hour urine analysis is performed, thus ruling out the presence of hyperuricosuria.

c) Treatment

Due to the size of the stones and their composition, it was decided to propose chemolytic treatment and successive follow-ups to assess their evolution. Potassium citrate is prescribed in the form of extended-release tablets, with a dosage of two tablets (20 mEq of potassium citrate) every 8 hours.

d) Outcome

Based on the proposed treatment, imaging follow-up by CT scan is performed in June 2019. An increase in the lithiatic mass in both kidneys was observed, showing a 25 mm stone in the left renal pelvis and another 16 mm stone in the right renal pelvis, which previously measured 20 mm and 6 mm, respectively. The stone located in the lower calyx of the left kidney showed no changes in size, remaining at 14 and 17 mm. On the other hand, the stone located in the lower calyx of the right kidney disappeared.

After further interrogation, the patient acknowledges taking only half of the prescribed dose of potassium citrate, since he is diabetic and refers decompensations in blood glucose levels, which he associated to the prescribed treatment. Due to the increase in the size of the stones, mainly in the left kidney, a change of approach is proposed, and it is decided to perform percutaneous surgical treatment on said kidney, maintaining the prescription of potassium citrate at a dose of twenty mEq every 8 hours. Blood and urine lab tests are performed, detecting urinary pH of 5.5 and decreased renal function, along with creatinine 2.4 mg/dl (reference values 0.7-1.3), no signs of obstructive uropathy were observed in the CT scan, therefore an appointment with nephrology is scheduled, to which the patient does not attend.

During the next follow up, at the beginning of July 2019, an elevation of creatinine values up to 3.5 mg/dl was observed; as well as a persistent urinary pH of 5.5. The patient acknowledges continuing to take 10 mEq every 8 hours. In the ultrasound performed in the consultation, right hydronephrosis is observed, with normal left kidney. Due to the ultrasound findings and the alteration of renal function, urinary derivation of the right kidney using a double J stent is decided, as well as a surgery change to a right ureterorenoscopy, which is performed that same month.

One month after surgery, the patient showed renal function improvement, with creatinine levels of 1.75 mg/dl. Treatment is changed, prescribing potassium citrate/citric acid complex at a dosage of 20 mEq every 8 hours, bioequivalent drug to the one prescribed previously but in the form of granulate for oral suspension. Likewise, the patient is faced with the need to perform periodic pH controls, with the aim of maintaining pH levels approximate to 7. It is decided to extend the treatment with allopurinol.

In September 2019, a control CT scan was performed, and an almost complete resolution of renal lithiasis was observed. An 8 mm stone in the renal pelvis of the left kidney is described, which previously measured 25 mm, and a 3 mm lithiasis in the lower calyx, previously presenting two stones of 14 and 17 mm. In urinary pH control, a pH of 7.0 is detected. Given the radiological findings, it was decided to maintain the scheduled treatment, the patient was evaluated once again in November, ultrasound showed no signs of renal dilation. A new CT scan was performed in March 2020 (Image 3), finding a single 5 mm lithiasis in the lower pole of the left kidney. Currently, the patient continues to be treated with potassium citrate/citric acid complex and routine urinary pH home checks using Lit-Control® pH Meter.



Image 2: CT scan performed in February 2020

e) Clinical results

After appropriate treatment, a substantial decrease in the number and size of kidney stones was observed, achieving the practical resolution of the initial issue.

f) Relevant medical history

The patient presented as underlying disease high blood pressure, dyslipidemia, obesity, and paroxysmal atrial fibrillation to treatment with oral anticoagulants.

In 2013 the patient consulted the Urology department for the first time for the same issue, after passing urinary stones spontaneously, which are later analyzed and are formed of uric acid. Medical treatment with potassium citrate/citric acid complex is prescribed, at the doses mentioned above. At that time, the patient does not take the prescribed medication and he misses follow-up.

As a result of a different urological issue, an abdominal CT scan is performed in 2017, showing large lithiasis in both kidneys. In the left kidney he presented four stones of 40, 19, 20 and 13 mm each in the renal pelvis; and in the right kidney two stones of 26.9 and 17.9 mm were found, also in the renal pelvis. Based on the radiological findings, surgical treatment of kidney stones is decided performing percutaneous nephrolithotomy in both kidneys.

The initial study was completed after obtaining parathyroid hormone (PTH), electrolytes levels and 24h urine, showing a slight elevation of PTH, with values of 86.23 pg/ml (reference values 15.0-65.0), in addition to hypocitraturia, presenting 19.20 mg/24h (reference values 268.71 – 1238.00 mg/24h). It is decided to prescribe potassium citrate/citric acid complex again and an appointment with endocrinology is scheduled. Several urinary pH measurements are performed, coinciding with patient visits to the emergency room, with persistent values of 5.5.

From the endocrinology department, new values of PTH, vitamin D, calcium, phosphorus, and 24-hour calciuria are requested; a probable hyperparathyroidism secondary to vitamin D deficiency is diagnosed, as a result of poor sun exposure, low dairy intake and obesity. Type 2 diabetes mellitus with poor metabolic control is diagnosed after being evaluated by endocrinology.

In December 2017, left percutaneous nephrolithotomy was performed without incidents, a sample of the stone was sent of its analysis, results showed it was composed of uric acid. The prescription of potassium citrate/citric acid complex is maintained, the patient underwent surgery for the right kidney in April 2018, also without incidents.

4. Discussion

In this case, the practical resolution of the patient's kidney stones with medical treatment is exposed. However, this resolution was achieved once the patient underwent a procedure that eliminated the stones of the right kidney, as the patient showed no results after being treated with drugs in the first place. During this section, an attempt will be made to respond to this delay in the results, as well as to evaluate whether the treatment process was correct.

After the imaging diagnosis, it is decided to treat the patient conservatively with potassium citrate. This drug alkalizes urine, increasing the solubility of uric acid, which favors the dissolution of stones and hinders the precipitation of uric acid, with the consequent formation of stones. According to both European and American clinical guidelines, this drug is indicated for the treatment of uric acid stones, as well as for the prevention of calcium oxalate stones [5,6]. On the other hand, it is worth questioning whether surgical treatment should not have been decided in the first place. Again, according to the current evidence, the surgical approach seems more appropriate for larger stones [5] and, consequently, when performing a radiological control and an increase in the lithiasis mass is observed, a change in therapeutic strategy is decided.

In view of the initial results, we could consider that the treatment lacks effectiveness. In the CT scan, an increase in the number of lithiasis is observed, despite the disappearance of the 12 mm stone described in the lower calyx of the right kidney. We cannot rule out the fusion of this stone with the one previously diagnosed, located in the renal pelvis. The absence of response to the treatment, also determined by the failure to alkalize the urine, could be related to the lack of adherence to the treatment acknowledged by the patient. The effect of potassium citrate on glucose levels reported by the patient is not reflected in the drug leaflet, nor is there clear evidence in the literature regarding it.

We should also consider the possibility of different intestinal absorption existing between the two presentations of potassium citrate. According to the experience in our department, sometimes patients treated with potassium citrate tablets report complete expulsion of the tablet with stool. In the specific case of this patient, this assumption cannot be confirmed, since he was not questioned about it, but it must be considered when assessing the cause for the effectiveness difference of the treatment between two different progress times.

As for the other drug prescribed during follow-up, allopurinol is included in the guidelines if the patient presents with hyperuricosuria, without this being the first-line treatment [6,7]. In this case, a 24-hour urine study is performed to determine the presence or absence of this alteration, which is ruled out. The guidelines insist that the use of allopurinol to decrease uric acid excretion does not prevent the formation of stones in patients with persistently acidic urine [6]. On the other hand, it is mentioned that in those patients who continue to form stones despite treatment, or who do not reach adequate pH levels, as in this case, allopurinol may be beneficial [8].

Finally, it is worth mentioning the existing relationship between diabetes and obesity with the formation of uric acid stones. In diabetes, like the metabolic syndrome, insulin resistance onsets, which causes an alteration in the formation of ammonium at the renal level.

This results in an acidic pH urine, which favors the precipitation of uric acid crystals. In diabetic patients the percentage of uric acid stones represents between 30 and 40% all stones, much higher compared to the non-diabetic population [8].

Obesity, understood as a body mass index higher than 30, is also related to the formation of these stones because those with a higher body mass index excrete more uric acid, there is also an inverse relationship between body mass index and urinary pH, as well as a direct relationship between this index and urinary uric acid saturation [9].

5. Conclusions and recommendations

Medical treatment for stones aimed at chemolysis should be considered a valid option as an alternative to surgery, as mentioned in the guidelines, especially in patients with lithiasis smaller than 20 mm. The composition of the stones, their size, the appropriate prescribed drug, as well as the patient's adherence to the treatment are determining factors for the therapeutic success of the treatment.

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