

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

Title: Combined medical approach for uric acid staghorn lithiasis. Case report.

Keywords: urolithiasis, uric acid, chemolysis, pH control

Authors: Laura Sánchez, Pau Sarrió, Carla Pérez

1. Summary

Objective: Medical treatment for uric acid lithiasis comprises two modalities: the stone formation prevention and chemolysis with curative intent. The aim of this work is to show the results of the combined medical treatment of uric acid lithiasis for the purpose of stone size reduction.

Methods: The case of a 54-year-old man is presented who, after presenting an episode of mild, self-limited hematuria, is diagnosed by CT scan with staghorn renal stone in the right kidney. The metabolic study shows hyperuricemia and hyperuricosuria. Given the normal renal function and the disappearance of the symptoms, it was decided to start combined therapy by alkalinizing the urine using Lit-Control pH Up, allopurinol and dietary measures.

Result: After four months of treatment, the patient presents with uremia and uricosuria within normal values, as well as a reduction in the stone size, completely disappearing the stone that was in the upper calyx of the right kidney.

Conclusions: The combined medical treatment for uric acid stones can dissolve the stone or reduce its size, avoiding or facilitating surgical treatment.

2. Introduction

Uric acid stones have a prevalence of 10-15% within the general population. An increase in prevalence has been described in the USA, probably due to the increase in patients with metabolic syndrome and other cardiovascular risk factors.¹

The composition of uric acid stones enables the possibility of using exclusive medical treatment with the intention of its dissolution and therefore its cure without requiring any other invasive procedures.

The formation of this type of lithiasis will depend mainly on the amount of purines metabolized by the body, whether they are supplied exogenously or endogenously, and above all, on urinary pH. The solubility of uric acid is pH dependent, being considered a soluble compound when urinary pH is above 6.5.²

Therefore, different dietary recommendations based on decreasing purines intake and the inhibition of enzymes that promote their formation, using hypouricemic drugs, will be necessary to decrease the concentration of uric acid excreted through urine.

3. Description of the clinical case

a) Relevant medical history

Case presentation of a 54-year-old male patient with a personal history of overweight, high blood pressure treated with enalapril + hydrochlorothiazide (20/12.5 mg/day) and erectile dysfunction treated with sildenafil 100 mg/week. The patient attends an appointment after presenting a single episode of mild self-limited hematuria. Denies any other associated symptoms.

b) Diagnostic support studies and results

A blood test is requested which levels of creatinine of 1.1 mg/dL, glomerular filtration rate calculated by the CKD-EPI formula of 72 ml/min and uricemia of 8.7 mg/dL (normal values of 3.40 to 7.00 mg/dL) are highlighted. In the urine sediment, a pH value of 4 and 130 red blood cells per field stand out.

Subsequently, it is decided to request a urine culture which results negative, and a renovascular ultrasound in which the probable presence of a staghorn stone in the right kidney is observed. After the ultrasound, an abdominal Computerized Axial Tomography (CT) scan without contrast is requested in which a staghorn stone lodged in the right kidney of 33 x 55 x 60 mm is observed with attenuation indices measured by Hounsfield units of 300. Mild ectasia of the lower calyces is observed. (Image 1)

c) Diagnosis

The patient is diagnosed with staghorn calculi in the right kidney.

d) Outcome

After obtaining the CT scan results, it is decided to request a 24-hour urine metabolic study. With a total diuresis of 980 ml/day a pathological finding is diagnosed, hyperuricosuria with levels of 957 mg/day (normal values less than 800 mg/day in men).

The patient does not experience another episode of hematuria and maintains a stable renal function.

The patient denies episodes of colic pain.

Therefore, it is decided to establish a combined therapy with curative intention. First, treatment for hyperuricemia and hyperuricosuria is initiated with Allopurinol 300 mg/day. Subsequently and based on the

attenuation indices in the imaging test and urinary pH, an urine alkalizing treatment is prescribed, using Lit-Control pH Up 2 capsules/day. Different dietary recommendations are also provided, which mainly include high water intake and decreasing the intake of animal proteins.

e) Clinical results

After four months of treatment, the patient remains asymptomatic. According to lab tests, uric acid is 6.9 mg/dL and renal function is stable. In the urinary metabolic study, uricosuria has decreased to a value of 657 mg/day. In the control CT scan the patient shows a reduction of the stone that currently measures 30 x 39 x 50 mm due to the disappearance of the component that occupied the upper calyx (Image 2).

4. Discussion

The formation of uric acid lithiasis depends on both genetic and environmental factors and in the latter dietary factors play a key role. Possible enzymatic alterations in the metabolism chain or excessive purines intake will determine the final concentration of uric acid in both blood and urine.

Seventy percent of the body's uric acid excretion is by through kidneys. The fact that urinary pH is below 5.5 provides an ideal medium for uric acid crystallization and the consequent formation of lithiasis, in fact it is the most influential factor for the development of this type of stone. Metabolic syndrome, primary gout or decreased urinary volume is associated with acidic pH. Therefore, if urinary pH is increased, it eases uric acid to become its base, urate, being considered a soluble component and with a lower crystallization capacity. This explains why this type of lithiasis can be prevented and even treated by correcting the urinary pH and taking dietary measures, without requiring surgical treatment.

The correction of this imbalance can be achieved by administering potassium citrate or sodium bicarbonate. Potassium citrate is a crystallization inhibitor that increases urinary pH. In this case, Lit-Control pH Up 2 capsules/day was used, a pharmacological compound that, apart from potassium citrate, contains other nutritional supplements such as lemon juice, magnesium citrate or zinc gluconate that also favor urinary alkalization.

It also contains theobromine, a compound present in cocoa, which has proven to be a powerful inhibitor of uric acid crystallization, reducing the size of the crystals formed ³.

Since dietary factors are also determinants, they play an important role within medical treatment. Dietary recommendations are based on high water intake and decreasing the intake of animal proteins, as it decreases the exogenous acid load and therefore improves urinary pH regulation. This last statement is related to metabolic syndrome and obesity, due to the excessive intake of high in protein processed components, which increase urinary pH and decrease the excretion of citrate to compensate for the imbalance, thus favoring an ideal medium for uric acid crystallization.⁴ In this case the patient is overweight, suffers from high blood pressure, and erectile dysfunction of probable vascular cause, so this type of recommendations would be appropriately indicated.

It is recommended to treat a patient with blood uric acid levels over 7 mg/dl in men and 6 mg/dl in women, to reduce uremia and therefore uricosuria.⁵ Hypouricemic drugs are mainly classified into two types: xanthine oxidase inhibitors (allopurinol or febuxostat) or uricosuric drugs (probenecid, benzbromarone). The recommended treatment for patients with uric acid stones is the first. In this case, allopurinol is chosen, a xanthine oxidase inhibitor that reduces serum and urinary urate. It is recommended to administer a dose of at least 300 mg/day. In the described case, treatment with allopurinol 300 mg/day was initiated due to increased blood uricemia (8.7 mg/dL) and hyperuricosuria (957 mg/day). After 4 months of treatment, the blood uric acid value is 6.1 mg/dL and uricosuria is 549 mg/day.

Finally, with the combined therapy using systemic chemolysis with Lit-Control pH Up 2 capsules/day, hypouricemic therapy with allopurinol 300 mg/day and dietary measures, a significant size reduction of the stone was achieved in a 4-month period. According to the European clinical guidelines, given the dimensions of the stone described in the case, a surgical treatment such as percutaneous nephrolithotomy, retrograde flexible ureteroscopy or extracorporeal shock wave lithotripsy, would be indicated⁶. Given the current situation due to the global pandemic caused by SARS-CoV2, the availability and frequency of surgical activity in many Spanish hospitals has been significantly reduced. The described patient presented only a single episode of mild self-limited hematuria, remaining asymptomatic the rest of the follow-up. It is for this reason and due to the characteristics of the lithiasis described, that it was decided to start a medical treatment aimed at resolving said lithiasis. The probability of presenting symptomatic episodes or requiring surgical treatment in patients with asymptomatic renal lithiasis is approximately 10-25%⁷.

If the described patient presented symptoms or test results alterations at some point, the indication for surgical treatment would be considered. In any case, the size reduction of the stone may facilitate any indicated technique in the future.

It would be interesting to evaluate the option of monitoring the patient's urinary pH to optimize the treatment and achieve better clinical results. The pH monitoring had been performed using test strips due to their low cost and how easy to use they are, although it has been shown that due to their lack of precision these are insufficient to make clinical or therapeutic decisions⁸. The current gold standard for pH monitoring is by using pH electrodes or pH meters. An automatic device designed to allow the patients themselves to monitor urinary pH at home has recently been patented, which is a convenient and accurate option for obtaining the values that will determine therapeutic decisions⁹.

5. Conclusions and recommendations

The solubility of uric acid at certain urinary pH facilitates the dissolution of stones present in the urinary track. Systemic chemolysis by alkalizing urine is an essential therapeutic pillar for size reduction or total dissolution of the stones. Urinary pH monitoring facilitates the adjustment of the treatment doses necessary to achieve the established objective.

It is essential to identify patients with metabolic syndrome and cardiovascular risk factors related to insulin resistance to establish a series of dietary recommendations to reduce the amount of purines intake.

Performing blood and urine metabolic studies will help optimize the treatment for patients with kidney stones, allowing to diagnose and treat metabolic disorders that perpetuate lithiasis formation, in this case composed of uric acid.

Combined medical therapy for uric acid stones can achieve the reduction of the size of the stone or even its full resolution, avoiding or facilitating surgical procedures whenever indicated.



Image 1



Image 2

6. Bibliographic references

1. García MP, Luis Yanes MI. Litiasis renal. Lorenzo V, López Gómez JM (Eds) Nefrología al Día. <https://www.nefrologiaaldia.org/es-articulo-litiasis-242>
2. Rodman JS, Williams JJ, Peterson CM. Dissolution of uric acid calculi. J Urol. 1984 Jun;131(6):1039-44.
- *3. Grases F, Rodriguez A, Costa-Bauza A. Theobromine Inhibits Uric Acid Crystallization. A Potencial Application in the Treatment of Uric Acid Nephrolithiasis. PLoS ONE. 2014;9(10):e111184.
- *4. Sakhaee K. Epidemiology and Clinical Pathophysiology of Uric Acid Kidney Stones. J Nephrol. 2014;27(3):241-245.
- **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 29 septiembre 2020).

6. Srisubat A, Potisat S, Lojanapiwat B, Setthawong V, Laopaiboon M. Extracorporeal shock wave lithotripsy (ESWL) versus percutaneous nephrolithotomy (PCNL) or retrograde intrarenal surgery (RIRS) for kidney stones. *Cochrane Database Syst Rev.* 2014 Nov 24;(11):CD007044.

7: Burgher A, Beman M, Holtzman JL, Monga M. Progression of nephrolithiasis: long-term outcomes with observation of asymptomatic calculi. *J Endourol.* 2004 Aug;18(6):534-9.

8. Kwong, T, Robinson, C, Spencer, D, Wiseman, OJ, Karet Frankl, FE. Accuracy of urine pH testing in a regional metabolic renal clinic: is the dipstick accurate enough? *Urolithiasis.* 2013;41:129–132.

*9. Grases, F, Rodriguez, A, Berga, F. A new device for simple and accurate urinary pH testing by the Stone- former patient. *Springerplus.* 2014;3:209.