2nd Edition of the Contest of Clinical Cases related to the non-surgical clinical management of kidney stones

Title: Oral chemolysis as an effective treatment in the resolution of uric acid kidney stones

Keywords: Nephrolithiasis, uric acid, oral chemolysis, urinary alkalinization, potassium citrate, theobromine

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1. Summary

Kidney stone disease is a very prevalent pathology that is on the rise, and between 10 and 15% have uric acid in its composition. A clear relationship has been established between the formation of this type of stones with the presence of an acid urinary pH. Therefore, the current treatment will be based on the use of urine alkalizers to prevent the crystallization of uric acid. Among the available treatments, the most used are those that include potassium as principal component of their formula, due to lower rates of synthesis of future calcium stones with this type of preparations. It also seems that the association of theobromine with this treatment will decrease this possible complication. We reviewed a clinical case from our center that presents uric acid nephrolithiasis resolved by medical treatment.

2. Introduction

The presence of renal stones is a common pathology in developed countries. Although the prevalence of these in the Spanish population is not clear today, there are several studies that conclude that during the last decades there has been an increase in it. In the PreLiRenE study published in 2016, conducted through a nationwide telephone survey, was observed a prevalence of urolithiasis of 14.6% with an incidence of 2.9%, and a recurrence rate of 52.8% (1).

These data should alert us to the importance of this pathology, since it is not only very frequent in the general population, but also on many occasions the same individual will suffer it repeatedly throughout his life.

Of all urinary system lithiasis, up to 10-15% will be uric acid (UA). Of the patients who present this type of stones, up to 79% will be men, being more frequent to suffer them in the decade of the 60s (2).

A clear relationship has been established between the formation of uric stones and a low urinary pH. Thus, for a correct treatment of this type of stones, it will be essential to know the urinary pH and correct it, ensure an adequate water intake and identify the metabolic alterations that lead to excessive uric acid production. The urinary pH is a determining factor for the precipitation of the UA crystals, therefore, the basis of the treatment will be the correction of the pH of the urine.

Hyperuricemia can be associated with hyperuricosuria (urinary excretion UA> 800mg/24h in men and UA> 750mg/24h in women), which leads to a deposit of uric crystals in the collecting tubules, generating inflammatory damage and progressive tubulointerstitial damage, so that glomerular filtration rate decreases, which can lead to chronic kidney disease (4).

Oral chemolysis has shown great efficacy in the treatment and prevention of uric calculi. We must not forget that we are facing a disease with a high recurrence rate and that correct pharmacological management could avoid multiple interventions.

3. Description of the clinical case

We present a clinical case of UA kidney stone resolved by dissolutive medical treatment.

This is an 83-year-old female patient with a personal history of poorly controlled hypertension. She was referred to our clinic by her primary care physician for microhaematuria with no other accompanying symptoms. A urine cytology was negative for malignancy, and a computerised axial tomography (CAT) scan showed a 17x 5 mm coral-shaped stone in the right kidney extending from the renal pelvis towards the lower calyces (500HU), with associated thickening and enhancement of the urothelium in the pelvis and proximal ureter in relation to inflammatory changes. Another 3 mm stone was identified in the right lower calyceal group. There was no dilatation of the excretory tract. Normal ureters. Bladder without findings. (Image 1). In the urine system, a pH of 5.0 and a sediment with uric acid crystals were observed.

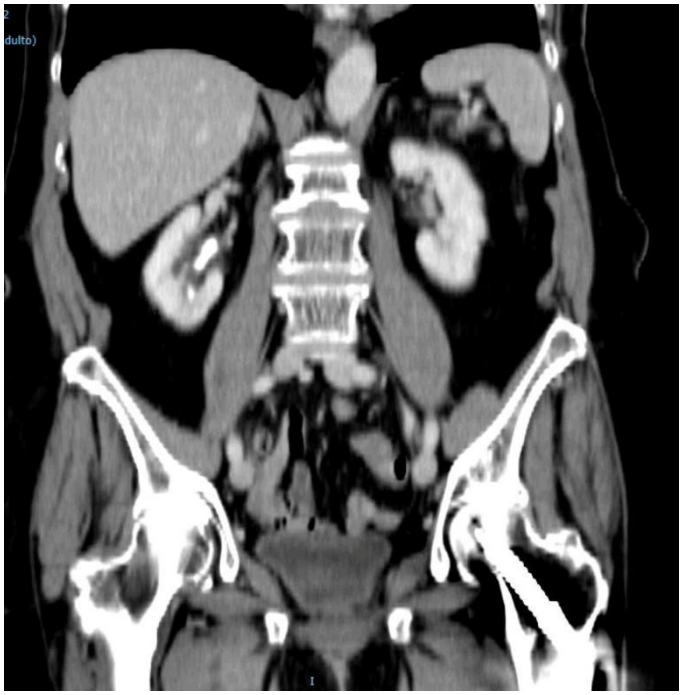

Image 1 CT image on the patient's arrival at our clinic. A 17x 5 mm right coralliform stone was found extending from the renal pelvis towards the lower calyces (500HU). Another 3 mm stone was identified in the right lower calyceal group.

In view of these findings, it was suspected that the stone in our patient was uric acid and treatment was started to alkalinise the urine with sodium bicarbonate, with strict control of her blood pressure; and a control abdominal X-ray and ultrasound scan were requested.

After 3 months, we reviewed the patient, who remained asymptomatic, with no episodes of urinary tract infection or renal colic. She reported having stopped taking bicarbonate due to poor blood pressure control. Urine systemic analysis showed a persistent pH of 5 with microhaematuria. The X-ray did not show radiopaque images compatible with stone disease, and the ultrasound confirmed the presence of the stone, visualising an echogenic image in the interpolar region of the right kidney with a 13 mm posterior acoustic shadow, in relation to stone disease without repercussion of the excretory tract. Dietary measures were started with uric restriction in the diet and lemon juice.

A new check-up was performed 3 months later, during which the patient remained asymptomatic. A new CT scan was requested, showing that the coralline calculi in the renal pelvis and lower calyces of the right kidney had slightly increased in size, particularly the portion extending to the calyces. A slight dilatation of the upper calyceal group was also observed, which was not identified in the previous study (Image 2).

Image 2. CT image showing enlargement of the chorionic calculi in the renal pelvis and lower calyces of the right kidney.

At this point, it was decided to start treatment with Lit-Control® pH Up two pills a day and a new review was requested in 3 months' time. This treatment was well tolerated and did not need to be discontinued. A new control CT scan was requested, in which we observed complete resolution of the stone present in the right kidney in the previous study, without observing pyelocaliceal dilatation or other kidney stone. (Images 3A and 3B).

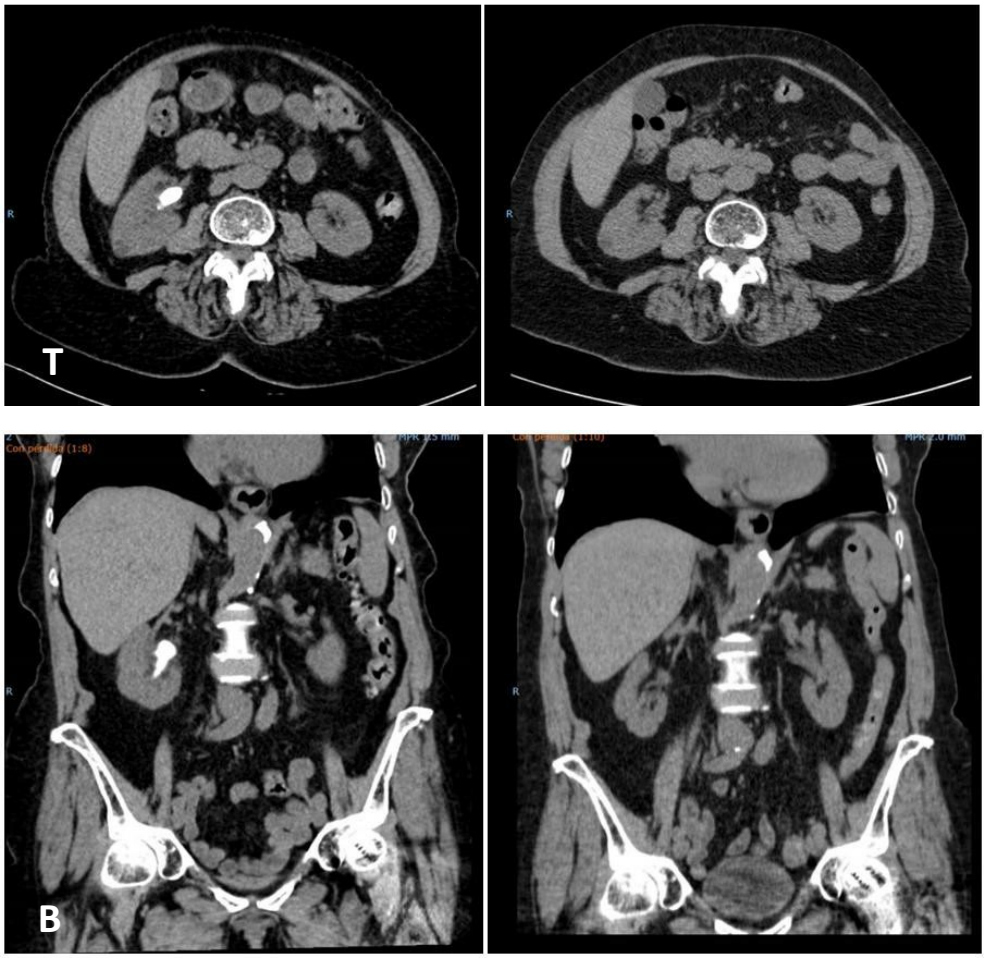

Image 3. A) Axial section. B) Coronal section. On the left, CT image prior to starting treatment with Lit Control pH Up. A coralliform lithiasis image can be seen in the right kidney. On the right, control CT scan after 6 months of treatment, showing complete resolution of the renal lithiasis.

At the 4-month follow-up visit, the patient remained asymptomatic. She had a sterile urine culture, an abdominal X-ray with no abnormalities and an ultrasound scan with no evidence of stones.

4. Discussion

The prevalence of uric acid stones varies according to age, gender, race, and environmental factors; a higher prevalence has been seen in male patients over 65 years of age, as well as in non-Hispanic races. Studies in the United States show that from 5 to 40% of all kidney stone cases are due to uric acid stones (3).

In addition, they report that the annual cost associated with kidney stones has risen dramatically, from 1.3 billion dollars in 1994 to 2 billion dollars in 2000, with 971 million dollars in hospital costs, 607 million dollars in outpatient costs and 490 million dollars in emergency department costs.

Due to the increase in the population suffering from diabetes and obesity and dietary changes, the prevalence of this disease is on the rise, with an estimated increase of costs of $1.2 trillion by 2030 (3).

Regarding the risk of progression to chronic kidney disease, there is no consistent data in the literature. A case-control study published in 2009 based on a cohort from Olmsted County, Minnesota, showed that stone-forming patients were more likely to have chronic kidney disease compared to control subjects (HR, 1.67; 95% CI, 1.48–1.88), although they failed to observe an increased risk of end-stage renal disease (ESRD) in these types of patients (4).

However, years later a study based on a cohort from Canada was published in which an increase in the incidence of ESRD was seen in those patients who had one or more episodes of renal colic (HR, 2.16; 95% CI, 1.79–2.62) compared to those without a history of stones (5).

Therefore, we are faced with a very prevalent pathology, which is on the rise, and which can lead to ESRD. There are various therapeutic options available, including lifestyle changes, medical treatment to reduce uric acid production and excretion, medical treatment to achieve greater urinary alkalinisation and, finally, surgical management. Of these, the treatment currently considered most effective is urinary pH modification, aiming to achieve pH levels between 6 and 6.5.

With regard the medical management aimed at acting on the urinary pH, the most used drug today is potassium citrate (K +), although we also find sodium citrate (Na +) and sodium bicarbonate.

Regarding the use of Na+ or K+ based formulations, there are no clear recommendations. Classically, Na+ based alkalinising agents have been considered to produce a secondary increase in renal calcium excretion, increasing hypercalciuria and thus promoting calcium stone synthesis (6). However, an international study by López-García's group published in 2019 found no difference in the prevalence of hypercalciuria when comparing treatments containing Na+ formulations with those containing K+ (7).

In what does seem to be a clear association is that the intake of Na + in the different formulations favours the urinary excretion of the same, which leads to reabsorption of citrate, favouring hypocitraturia. Citrate acts as an inhibitor of crystallisation, so that a decrease in citrate may contribute to the development of future stones (6).

In addition to the above, we must take into account the possible side effects derived from taking these compounds.

Excessive sodium bicarbonate intake leads to an increase in extracellular volume, so special care should be taken in patients with hypertension, a history of decompensated heart failure with decreased ventricular function, and liver cirrhosis (8).

Due to these reasons, the use of potassium-based salt formulations is preferred over those that are based on sodium, since they allow to correct the urinary pH while helping to correct hypocitraturia, without increasing the risk of formation of calcium component stones.

The treatment that our patient has received includes a combination of different molecules among which potassium citrate, magnesium citrate and cocoa dry extract (40% theobromine) stand out.

In this context, the combination of potassium citrate with theobromine suggests greater efficacy in the treatment and prevention of uric acid stones in preliminary studies. Theobromine is a molecule present in cocoa, which belongs to the family of xanthine alkaloids. In vitro studies have shown strong inhibition in the crystallization of uric acid, especially at pHs between 5 and 5.5 (9). With this molecule we could solve the problem of excessive alkalinization of the pH above 6.2 with the treatment of citrate alone, since the exclusive use of citrate poses a risk for the precipitation of calcium phosphate salts, which could lead to the formation of another type of calculi. Therefore, the use of a urine alkalinizer, such as citrate, together with an inhibitor of UA crystallization, such as theobromine, could allow to reduce the doses of alkali, so that we would prevent reaching a high pH and the future synthesis of calcium stones (10).

5. Conclusions and recommendations

Uric acid stones lead to a decrease in the quality of life of patients and a very high socio-health expenditure due to the presence of repeated renal colic and multiple visits to the hospital, added, sometimes, to the need for repeated interventions. The treatment of the same with alkalinizers of the urine has shown great efficacy in its resolution and prevention, assuming a safe and well-tolerated drug in the long term.

6. References

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