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

Title: Medical treatment of staghorn uric acid lithiasis with Lit-Control pH Up®

Key words (between 3 and 6): renal lithiasis, staghorn, uric acid, urinary alkalinization, Lit-Control pH Up, potassium citrate.

1. Summary

➔ **Objective:** To evaluate the utility of treatment with chemolysis in uric staghorn lithiasis in relation to a clinical case.

➔ **Method:** Clinical case report of a 65-year-old Caucasian female who is evaluated for pain in the right renal fossa of 10 days evolution, is presented. During her follow-up appointment, an abdominal/pelvic CT scan was requested where a right staghorn lithiasis of 4.5 cm x 3.2 cm is observed, occupying the upper, middle, and lower calyxes, with growth towards the renal pelvis, with an average density of 450 Hounsfield Units (HU). An alkalizing medical treatment was started using Lit-Control pH Up (potassium citrate, magnesium citrate and theobromine).

➔ **Result:** After being treated for three months, the resolution of the lithiasis was observed.

➔ **Conclusions:** Chemolytic treatment for uric acid lithiasis, even for staghorn stones, should be considered the first treatment option.

2. Introduction

Urinary lithiasis is a common problem. A study conducted by the *National Health and Nutrition Survey (NHANES)* estimated that 19% of men and 9% of women will develop urinary lithiasis by the age of 70[1]. Secondly, the prevalence increased from 3.8% during the period 1976-1980, to 5.2% during the period 1988-1994, reaching 8.8% between 2007-2010 among the North American population[1].

Some factors that contribute to an increase in the prevalence of lithiasis include the growing prevalence of obesity, rising temperatures, and due to the improvement and increased use of diagnostic imaging techniques[1].

Incidence depends on geographical, ethnic, nutritional and genetic factors. The risk of recurrence is basically determined by the disease or condition that causes the formation of lithiasis[2].

As for uric acid lithiasis, its described prevalence is between 5 and 10% of all urinary lithiasis in the United States and Europe. However, in warm weather, with arid climates, where people usually have a decreased diuresis and an acidic urinary PH, uric acid lithiasis can have a prevalence that rises to 40%[3].

3. Description of the clinical case:

a. Relevant medical history

This is a 65-year-old Caucasian woman, who has a history of obesity, hyperuricemia and high blood pressure (treated with enalapril).

b. Diagnostic support studies and results

- Abdominal/pelvic CT scan: an image compatible with right renal staghorn lithiasis that extends to upper, middle, and lower calyxes, with growth towards the renal pelvis (4.5 cm long x 3.2 cm wide) with a media of 450 UH, is observed. No other alterations are observed.

- Abdominal X-ray: non-specific air luminogram, bone structures within normal. There are no images suggesting urinary lithiasis.

- Blood testing:

    a. Blood count: 8.3 x 10e9/L leukocytes (65% neutrophils), Hb 13 g/dL, platelets 270 x 10e9/L, other parameters within normal

    b. Blood chemistry: glucose 107 mg/dL, **uric acid 7.8 mg/dL (hyperuricemia),** creatinine 0.75 mg/dL, glomerular filtration rate > 90 ml/min, sodium 139 mmol/L, potassium 3.86 mmol/L, LDL 220 mg/dL, HDL 40 mg/dL, TG 155 mg/dL

- Urine culture: negative.

- Urine sediment:

    a. Leukocytes: negative

    b. Nitrites: negative

    c. Density: 1.011 g/L

    d. Red blood cells: 27/microL

    e. pH: 5

c. Diagnosis

In images 1 and 2, the most representative axial and coronal sections of the CT scan are shown, in which the staghorn lithiasis can be observed in the right kidney.

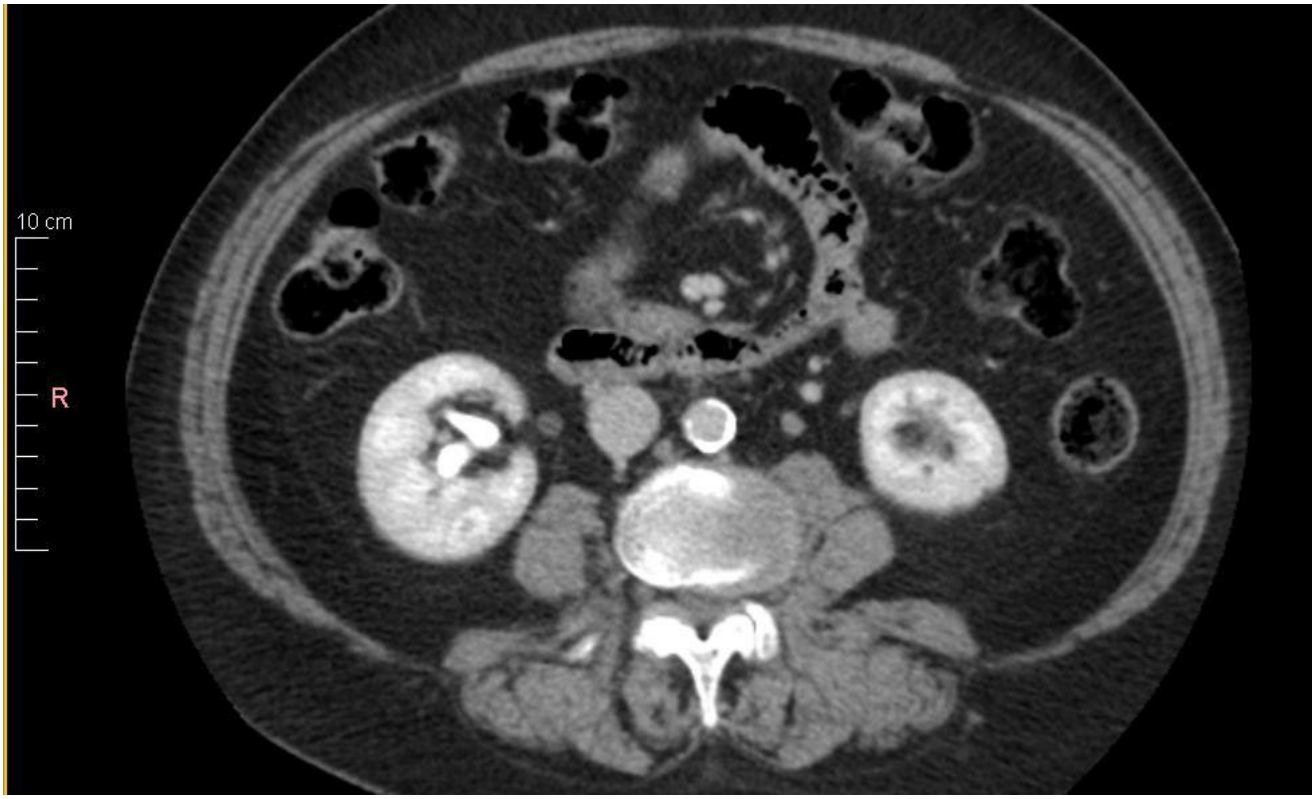

Image 1. Abdominal/pelvic CT scan: axial section.

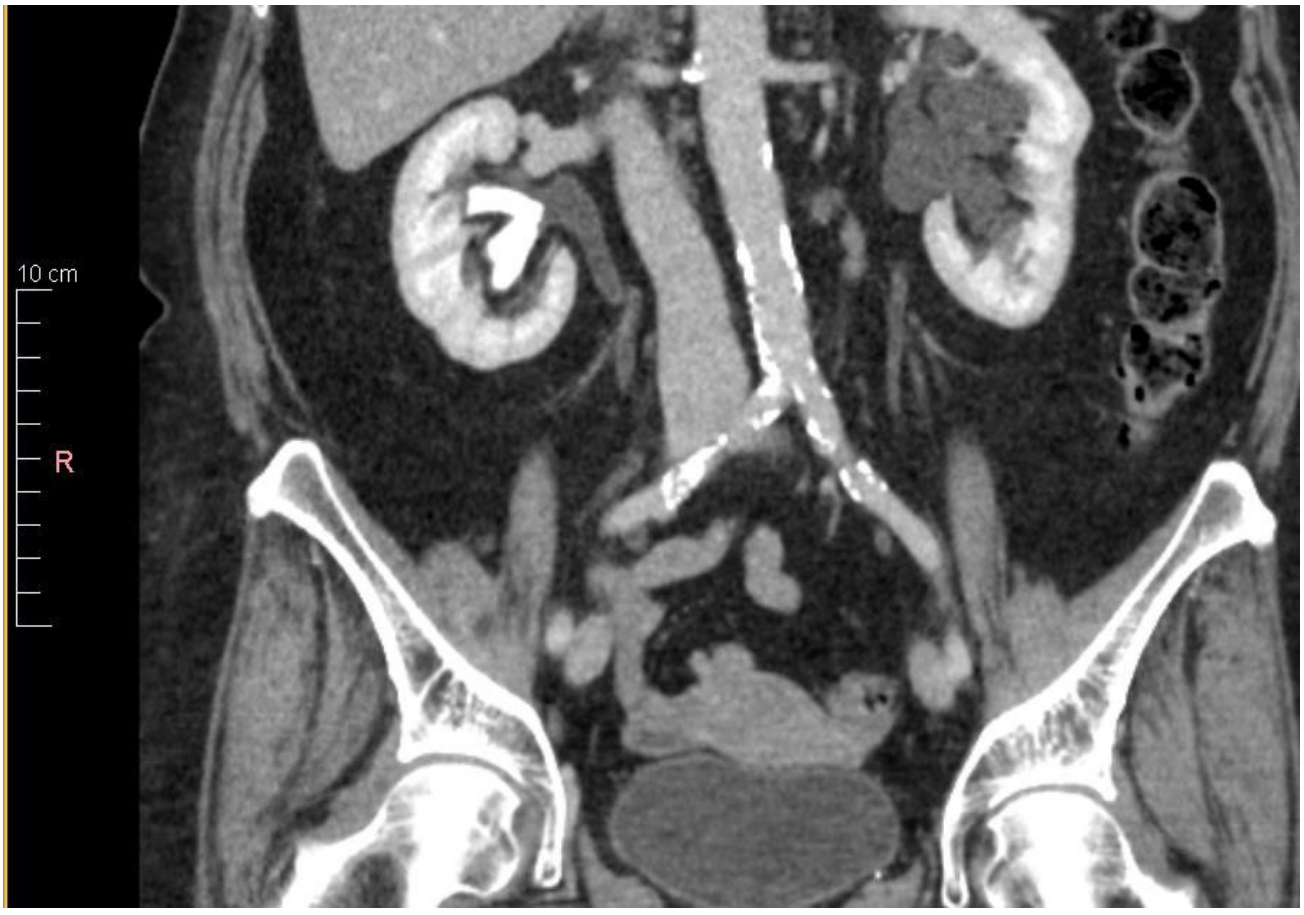

Image 2a. Abdominal/pelvic CT scan: coronal section.

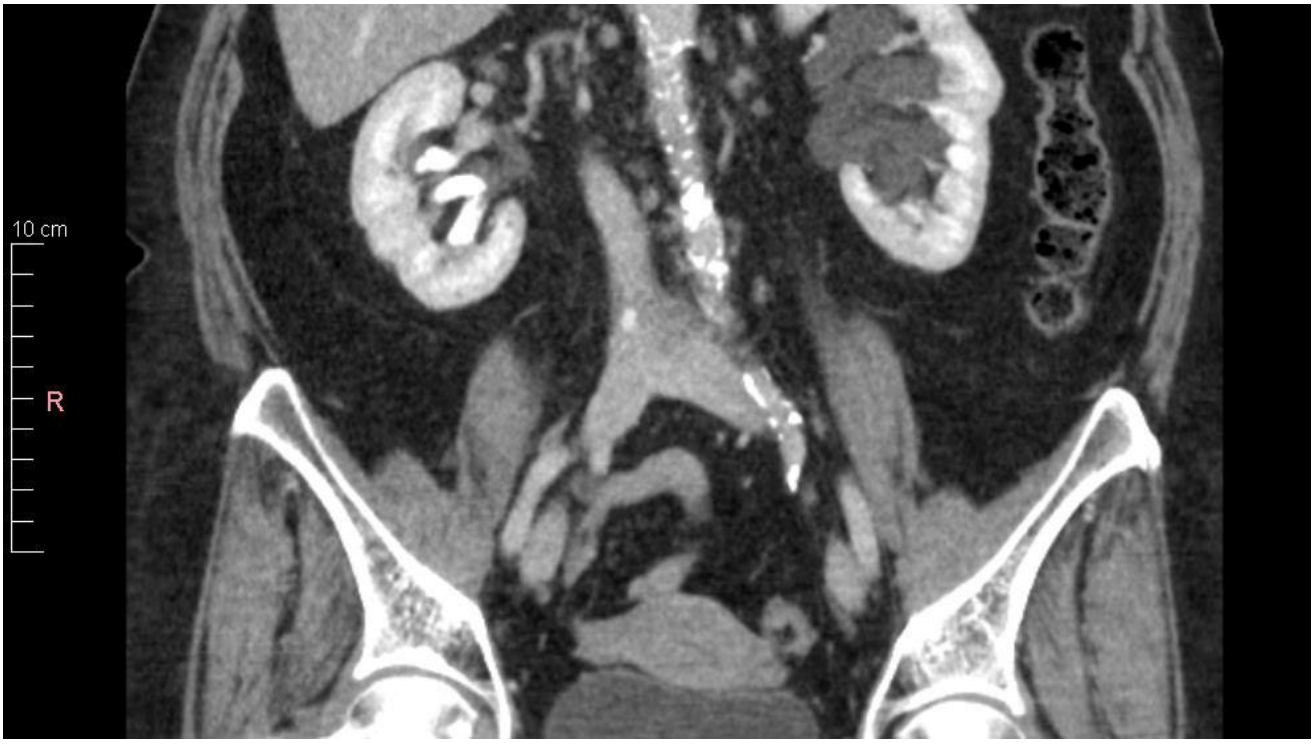

Image 2b Abdominal/pelvic CT scan: coronal section.

d. Treatment

In April 2022, the patient began medical alkalizing treatment using Lit-Control pH Up® (potassium citrate, magnesium citrate and Theobromine), taking 1 capsule every 6 hr., aiming to maintain a > 5.5 urinary pH.

e. Progress and monitoring

After two weeks of follow-up, urinary pH was > 5.5 and with an excellent tolerance to the administered medication. In image 3, a renal ultrasound is shown, requested after three months, in which a residual 2 mm lithiasis can be observed in the lower calyx of the right kidney. During the subsequent follow-up, 4 months after starting the treatment, the lithiasis was completely resolved.

f. Clinical results

Urinary pH remained in range throughout the follow-up. The patient monitored urinary pH using test strips. After the complete dissolution of the lithiasis, preventive treatment has been continued, reducing the dose to 1 capsule every 12 hr.

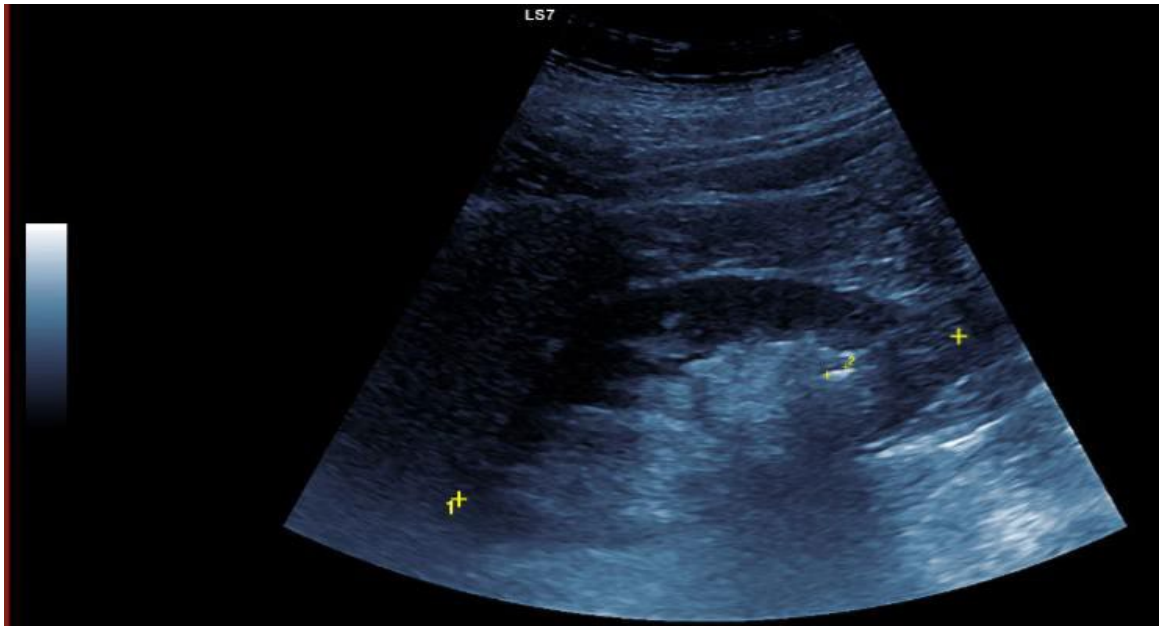

Image 3. Renal ultrasound: a 2 mm lithiasis is observed in the lower calyx of the right kidney.

4. Discussion

Formation of uric acid lithiasis is usually associated with hyperuricosuria or acidic urinary pH. Hyperuricosuria has traditionally been defined as a urinary excretion of uric acid over 750 mg (4.5 mmol) for women or more than 800 mg (4.8 mmol) for men, in a 24-hr. period[3]. However, acidic urinary pH (< 5.5) plays a major role in the formation of uric acid lithiasis since the solubility of uric acid decreases and precipitates, although uricosuria is normal[3].

In this clinical case, the patient had hyperuricosuria associated with low urinary pH, so both risk factors for the formation of uric acid lithiasis and its recurrence were present.

As for the specific medical management of uric acid lithiasis, given its high probability of dissolution by alkalizing urine (with potassium citrate or sodium bicarbonate), the need for invasive procedures is usually ruled out. There are three therapeutic tools to treat and prevent the formation of uric acid lithiasis[4].

- Urine alkalization
- Increased water intake
- Decreasing the production of uric acid by reducing the intake of purines and using xanthine oxidase inhibitors.

Xanthine oxidase inhibitors are prescribed once uric acid lithiasis recurs despite adequate urinary alkalinization (due to excess urinary uric acid excretion > 1000 mg or 6 mmol per day), when uricemia levels are elevated and when urinary alkalinization cannot be opted for[4].

Therefore, in this case, urinary alkalization treatment was initiated using **Lit-Control pH Up®**, which contains potassium citrate, magnesium citrate and Theobromine (uric acid crystallization inhibitor), since xanthine oxidase inhibitors is not recommended for treatment initiation.

There are no randomized clinical trials evaluating the efficacy of urinary alkalinization in the recurrence or dissolution of uric acid lithiasis[5]. However, there are observational studies that prove it. The

objective is a > 5.5 pH. A > 6.2 pH offers little benefit in terms of dissolution of uric acid lithiasis, increasing the risk of formation of calcium phosphate (precipitates at > 6.2 pH) or struvite (precipitates with pH > 6.7) lithiasis [5].

The only randomized clinical trials evaluating the effect of xanthine oxidase inhibitors in patients with nephrolithiasis were carried-out with calcium lithiasis (not uric acid) and hyperuricosuria[6].

Initial treatment for this type of lithiasis should be aimed at increasing urinary pH and inhibiting crystal aggregation. The combination of potassium and magnesium citrate increases urinary pH and inhibits the aggregation of urinary crystals of different nature[7]. The association of theobromine in the same product achieves the specific inhibition of uric acid crystals, thus acting on the two most important factors involved in the mechanism of aggregation and formation of uric lithiasis.

Another aspect to consider is prevention after lithiasis dissolution. Keeping treatment at lower doses effectively prevents lithiasis recurrence in these patients, by inhibiting the etiopathogenic mechanism of formation of this type of lithiasis. Consequently, controlling uricemia levels, keeping urinary pH between ranges of 5.5 and 6.2 and an inhibition of the aggregation of uric acid crystals are key aspects when avoiding the recurrence of lithiasis.

Daily urinary pH control is important to achieve maximum effectiveness of the treatment. Although test strips have been classically used, they have proven to be an inaccurate measuring method[8].

With the arrival of electronic pH measuring devices on the market, these have proven to be more accurate, reliable and easy to interpret[9], the main advantage for the patient offered by these devices is an easy interpretation of the effectiveness of the treatment, which implies immediate feedback of the result, which usually translates into a better patient adherence to therapeutic indications. Therefore, for this type of lithiasis, the combination of specific treatment for uric lithiasis and exhaustive pH control guarantees a high rate of effectiveness.

5. Conclusions and recommendations

Uric acid lithiasis has a high probability of recurrence, over 50%, for that reason it is relevant to carry out both therapeutic and preventive actions in the long term[10]. Mainly, an adequate water intake is recommended to the patient, along urinary alkalization and inhibition of crystal aggregation.

The initial treatment of choice should be chemolysis of uric lithiasis, including staghorn lithiasis. If adequate urinary alkalinization is achieved, large pure uric acid lithiasis can be dissolved, thereby avoiding invasive endoscopic procedures (retrograde or antegrade) to fragment said lithiasis, and all the complications that could occur.

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

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