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VI Edition of the Clinical Cases Contest on non-surgical clinical management of Kidney Stones

Official template

Title: Successful Medical Dissolution of Bilateral Uric Acid (Anhydrous) Kidney Stones in a High-Risk Patient with Chronic Kidney Disease.

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Key words (3 to 6): Uric acid lithiasis, Uricite, Chemolysis, Urinary alkalization, Chronic renal failure, Theobromine.

1. Abstract (no longer than 150 words).

Objective: To describe the successful non-surgical management of massive, recurrent anhydrous uric acid renal lithiasis (uricite) in a complex patient with chronic kidney disease (CKD) and a history of multiple surgeries.

Clinical Case: A 75-year-old male with Stage G3b chronic kidney disease (CKD), essential thrombocythemia, and progressive bilateral stone burden. Following a metabolic workup that revealed persistently acidic urine (pH 5.0 - 5.5) and confirmed uricite stones, an initial treatment attempt with potassium citrate alongside a potassium binder was initiated but had to be discontinued due to hyperkalemia. Given this situation, treatment with theobromine and oral bicarbonate was instituted, accompanied by close monitoring of urinary pH.

Results: After 18 months of theobromine therapy, a computed tomography (CT) scan showed a dramatic reduction in the stone burden, with the disappearance of an obstructive ureteral calculus and the renal stones. The patient remained asymptomatic, with stable renal function and no electrolyte imbalances.

Conclusions: This case demonstrates the efficacy and safety of theobromine in achieving complete chemolysis of uricite stones through urinary alkalinization. It represents a crucial therapeutic alternative for patients with renal insufficiency in whom other alkalinizing measures are contraindicated, thereby avoiding repeated surgeries in high-risk patients.

2. Introduction

Uric acid (UA) lithiasis accounts for approximately 10-15% of all kidney stones (1). Its formation is strongly influenced by three factors: low urinary pH (<5.5), low urine volume, and hyperuricosuria (1). The anhydrous form (uricite) is less common and can be particularly dense. Unlike other types of stones, UA stones are unique in that they can be completely dissolved through pharmacological alkalinization of the urine to a pH of 6.5-7.0 (2), which forms the basis of chemolysis. We present a complex case in which a

meticulous, medically-managed approach—tailored due to renal insufficiency with a tendency toward hyperkalemia—achieved an objective and dramatic regression of a massive uricite stone burden, thereby avoiding additional surgical interventions in a patient with significant comorbidities.

3. Clinical Case description

a. Patient information / Medical records

A 75-year-old male with a medical history of Stage G3b chronic kidney disease (CKD) (baseline creatinine ~1.7 mg/dL), resected colon adenocarcinoma currently in complete remission, essential thrombocythemia, and long-standing recurrent renal lithiasis with multiple previous interventions (right percutaneous nephrolithotomy (PCNL), right retrograde intrarenal surgery (RIRS) for a 1.6 cm stone).

b. Diagnostic support studies and results

• **Stone Analysis:** Confirmed composition of Anhydrous Uric Acid (Uricite).

• **Laboratory Findings:** Chronic Kidney Disease (creatinine 2.05 mg/dL, eGFR 30 mL/min). Venous Blood Gas: Metabolic Acidosis (pH 7.26, Bicarbonate 16.2 mmol/L). 24-hour Urine: pH 5.5. Normouricemia.

• **Abdominopelvic CT scan (Prior to Theobromine):** Showed progressive stone disease with multiple bilateral lithiases and a 6 mm obstructive left ureteral stone causing Grade II hydronephrosis. See Figure 1.

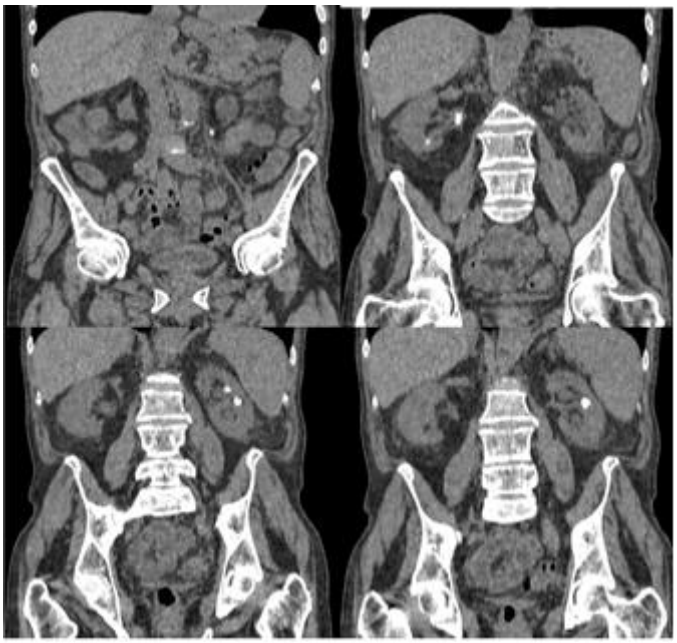

Figure 1. CT image revealing the bilateral nephrolithiasis and an associated obstructive left ureteral calculus.

• **Abdominopelvic CT scan (On Theobromine):** Resolution of the hydronephrosis and disappearance of the ureteral stone and renal calculi. See Figure 2.

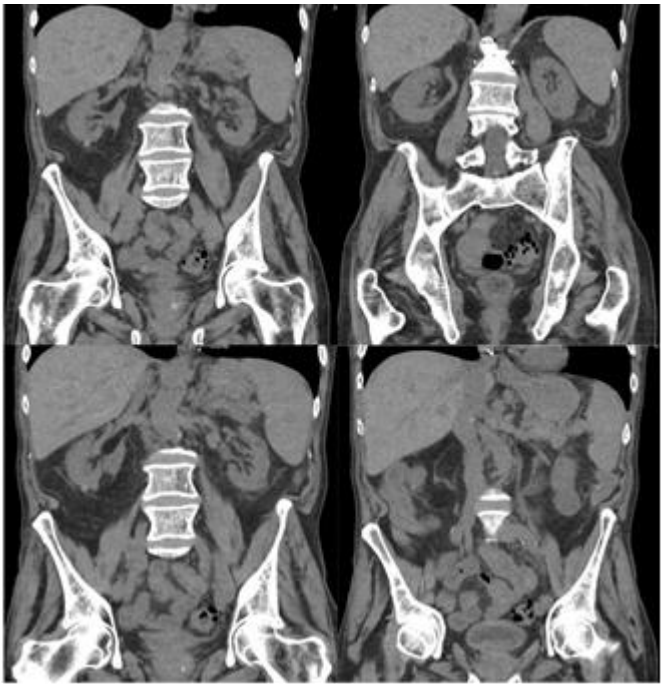

Figure 2. CT image demonstrating complete resolution of the previously documented nephrolithiasis.

c. Diagnosis

- Bilateral Recurrent Renal Lithiasis of Anhydrous Uric Acid (Uricite).
- Stage G3b Chronic Kidney Disease.
- Hyperchloremic Metabolic Acidosis.
- Persistent Acidic Urine (Primary Lithogenic Risk Factor).

d. Treatment

A staged medical chemolysis protocol was implemented:

Initial Treatment: Alkalinization therapy was initiated with potassium citrate co-administered with a potassium-binding agent. However, this regimen was discontinued due to the development of hyperkalemia (K: 6.7 mEq/L) in the context of his pre-existing chronic kidney disease.

Definitive Treatment: Given the contraindication of potassium citrate, the therapeutic strategy was switched to theobromine, supplemented with oral sodium bicarbonate 1g every 8 hours. This potassium-sparing alkalinizing combination was used to raise and maintain the urinary pH within the target range (6.5 - 7.0), thereby preventing uric acid crystallization.

Hydration: Fluid intake was optimized within the limits tolerated by his renal function.

Monitoring: This involved periodic self-monitoring of urinary pH using dipsticks and close follow-up of renal function and electrolytes (especially potassium).

e. Evolution and progress

The patient tolerated theobromine treatment well, with no reports of gastrointestinal adverse

effects or episodes of hyperkalemia. He experienced no further episodes of renal colic. Renal function remained stable (creatinine 2.0-2.4 mg/dL). The follow-up CT scan confirmed the success of the chemolysis.

f. Clinical results

Primary Outcome: Complete chemolysis confirmed by CT imaging, evidenced by reduction in total stone volume and resolution of the obstruction.

Secondary Outcomes: Absence of renal colic, stabilization of renal function, and excellent treatment adherence.

4. Discussion

This case provides a paradigmatic illustration of the efficacy of targeted medical management in uric acid lithiasis, a condition whose prevalence is increasing globally, closely linked to the epidemic of obesity, metabolic syndrome, and type 2 diabetes (1). The pathophysiology of uric urolithiasis is based on three pillars: persistently acidic urinary pH (<5.5), low urine volume, and hyperuricosuria (2,3). In our patient, the confirmation of uricite composition and the documentation of a consistently acidic fasting urinary pH (5.5) identified the principal lithogenic factor and, therefore, the therapeutic target.

However, the therapeutic strategy required adjustment based on patient safety. The initial treatment with potassium citrate, despite being used concomitantly with a potassium-binding agent, induced hyperkalemia, a known and potentially serious complication in patients with renal insufficiency, which necessitated discontinuation of the treatment.

The alternative alkalinization strategy with sodium bicarbonate and theobromine was crucial for several reasons: 1) It achieved effective urinary alkalinization into the target range for uricite dissolution (pH >6.5) without the risk of hyperkalemia, as its formulation contains no potassium salts; 2) Theobromine possesses a mild diuretic effect that may be contributory; and 3) It allowed for the continuation of the medical chemolysis strategy, which is the cornerstone of treatment (3), in a patient for whom the standard option was contraindicated. The study by Costa-Bauzá et al. (4) demonstrates that theobromine and its main metabolites (7-methylxanthine, 3-methylxanthine, and 3,7-dimethyluric acid) directly inhibit uric acid crystallization by interacting with it in solution, significantly delaying its nucleation and modifying crystal morphology. It is crucial to highlight that the authors observed that individuals with high-risk urinary parameters (supersaturation >2) did not develop crystals when they had high urinary concentrations of theobromine and its metabolites—a situation perfectly aligned with the results in our case. Therefore, theobromine not only alkalinizes the urine but also exerts a direct and complementary inhibitory effect on uric acid crystallization, which explains the spectacular chemolytic response we achieved.

Our results, with a reduction in total stone burden objectified by CT, are consistent with these findings and underscore that this approach should be considered a first-line option, especially in patients at high surgical risk or with contraindications to citrate use, such as those with CKD.

Close monitoring of urinary pH emerges as the critical success factor, as highlighted by Ungerer et al. (5). The use of dipsticks by our patient, while effective, could be optimized. mHealth technology, such as the smart pH meter Lit-Control®, connected to a mobile application, has been shown in recent studies to have high accuracy, acceptability, and short-term adherence (87.6% compliance), facilitating immediate feedback and dose adjustment of alkalinizing agents (6, 7). Implementing this technology could have refined metabolic control in our case and is a clear example of necessary innovation, enabling more personalized and preventive medicine (6). Furthermore, using the myLit-Control® App for recording pH and fluid intake would have been an ideal tool to optimize adherence and fine-tune treatment adjustment, as recommended by recent publications (7,8).

Long-term adherence to pH monitoring and medication is the Achilles' heel of this treatment, as observed in studies where the use of health apps declined significantly after the first year (5, 8). Additionally, the risk of excessive alkalinization (pH >7.0) could predispose patients to the formation of calcium phosphate stones (9,10), reinforcing the need for precise and continued monitoring.

In conclusion, this case demonstrates that targeted medical chemolysis is a highly effective and safe strategy for uric acid stones, even in complex clinical scenarios. The radiological evolution is incontrovertible proof of its efficacy. Future initiatives should routinely integrate stone composition analysis and the use of technologies, such as smart pH meters, to optimize treatment adjustment, improve patient adherence, and consolidate the role of medical management as the cornerstone of treatment for this condition.

5. Conclusions and recommendations

- Stone composition analysis is the cornerstone for guiding effective and targeted medical therapy.
- Anhydrous uric acid stones (uricite) are highly amenable to dissolution through pharmacological urinary alkalinization.
- Theobromine is an effective and safe agent, representing a first-line alternative for patients with chronic kidney disease or at risk of hyperkalemia, in whom potassium citrates are contraindicated. Close monitoring of urinary pH is a fundamental pillar for success.
- This medical management approach should be prioritized in patients at high surgical risk or with recurrent stone disease, as it avoids the morbidity associated with surgical procedures

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