VI Edition of the Clinical Cases Contest on

non-surgical clinical management of Kidney Stones

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Title: "When Acidification Makes the Difference: Preventing Struvite Stone Recurrence After Cutaneous Ureterostomy"

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1. Abstract

Objective: To report a complex urological case where urinary acidification effectively prevented recurrent struvite lithiasis.

Material and Methods: A 71-year-old male with prior right nephroureterectomy (2002) for Wünderlich syndrome secondary to renal pelvic tumor and radical cystectomy with left ureterectomy and cutaneous ureterostomy (2019) due to multifocal papillary urothelial carcinoma presented with struvite stones and recurrent struvite crystalography. Urinary acidification therapy (Lit-Control pH Down®) along with prophylactic antibiotics were initiated.

Results: Crystallographic urine analysis before treatment confirmed struvite crystal presence. After antibiotic treatment and acidification, no struvite crystals were detected, and the patient remained free of lithiasis.

Conclusions: Urinary acidification effectively inhibited struvite crystallization in this high-risk patient, preventing further infectious lithiasis. This case supports the role of urinary pH modification as a preventive strategy against infection-related stone formation in patients with complex urological conditions.

2. Introduction

Infection-related struvite stones (magnesium ammonium phosphate) account for a clinically important subset of urolithiasis and are almost always associated with colonization by urease-producing microorganisms. Urease catalyses the hydrolysis of urea into ammonia and CO^2, leading to a marked increase in urinary pH and ammonium concentration; the resultant alkaline chemical medium favours nucleation and rapid growth of struvite crystals. This biochemical process explains the typical fast enlargement of infection stones and their

frequent occupation of the renal collecting system. (1)

Classic agents such as *Proteus, Klebsiella, Pseudomona, Morganella, Serratia* and some *Staphylococcus* species express potent urease activity and form structured biofilms that act as a scaffold for mineral deposition. Biofilm formation on urothelial surfaces or exogenous devices (stents, catheters, etc.) concentrates urease activity locally, promotes micro-environments of high ionic supersaturation, and protects bacteria from host defences and antibiotics, perpetuating stone growth and infection (2, 3).

Therapeutically, the pillars of management are eradication of infection, complete removal of stone burden and prevention of recurrence. Adjunctive strategies aimed to alter the urinary conditions, like urine acidification to lower pH and reduce struvite supersaturation, have limited clinical evidence. Recent reviews and guideline summaries emphasize individualized approaches in high-risk patients (urinary diversion, chronic catheterization), combining targeted antimicrobials, rigorous device/stoma care and consideration of pH-modifying agents when appropriate (4, 5).

Patients with complex urinary anatomy, such as those with cutaneous ureterostomies or permanent indwelling catheters, face additional challenges. They have increased risk of recurrent infection stones, difficult stone clearance, and require careful long-term monitoring. The following case illustrates how these complexities can be addressed through a combination of **crystallographic monitoring** and targeted urinary acidification therapy along with antibiotics.

3. Clinical Case description

a. Patient information / Medical records

We present the case of a 71-year-old male with no known drug allergies and a medical history of hypertension and dyslipidaemia, currently treated with Enalapril 5 mg and Simvastatin 20 mg.

Past surgical and oncological history:

- **2002:** Right nephroureterectomy for Wunderlich syndrome secondary to a urinary tract tumour (*pT1N0M0*).
- **2019:** Radical cystectomy with pelvic lymphadenectomy, left ureterectomy, and cutaneous ureterostomy for multifocal papillary urothelial carcinoma (*pT3N0M0*, carcinoma in situ). A permanent ureteral stent was placed. He undergoes catheter replacement every 4-6 months.

Since the urinary diversion, the patient has experienced **recurrent urinary tract infections (UTI).** He remains under regular follow-up in the Urology and Oncology departments, with frequent laboratory and imaging evaluations.

b. Diagnostic support studies and results

Initial study between UTI episodes

- Blood biochemistry: Creatinine 1.72 mg/dL, **eGFR 41 ml/min**, Hb 12.5 g/dL, Na 139 mEq/L, K 4.4 mEq/L, Cl 101 mEq/L, BUN 12 mg/dL.
- Urinalysis: Density 1.020 g/dL, **pH 8.0**, negative glucose, urobilinogen, protein and ketones, **positive nitrites**, **leukocytes 100-200 pc**, red blood cells 10-20 pc.
- Urine culture: *Klebsiella pneumoniae* (pan-susceptible strain).

- CT scan (07/2022): Incidental finding of **single 5 mm calculus located in the middle calyceal group of the left kidney**.

c. Diagnosis and treatment

The patient, with a permanent cutaneous ureterostomy with a permanent ureteral stent, experienced recurrent episodes of complicated urinary tract infection.
Two hospital admissions were required for intravenous antibiotic therapy, followed by replacement of the ureteral stent due to persistent positive urine cultures.

Between infection episodes, serial quantitative urine crystallography consistently demonstrated **abundant magnesium ammonium phosphate (struvite) crystals** and a persistently **alkaline urinary pH**.

On follow-up CT scan in July 2022, a single 5 mm calculus was identified in the middle calyceal group of the left kidney, consistent with infection-related lithiasis.

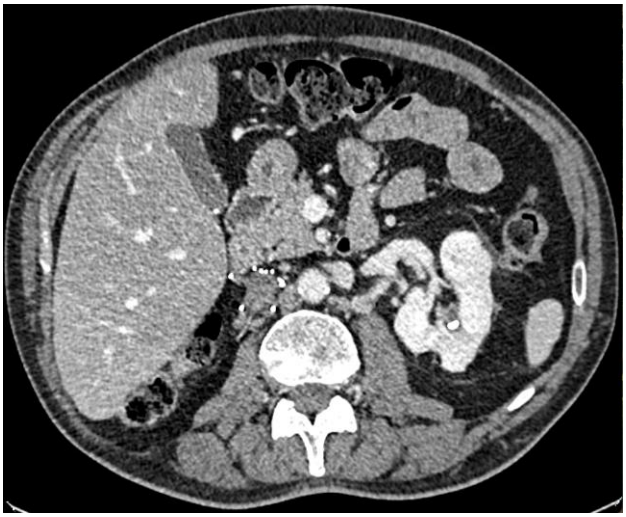


Fig. 1. CT scan showing 5mm struvite infective lithiasis in the left MCG.

d. Treatment

Given the recurrence of complicated urinary tract infections, long-term prophylactic antibiotic therapy was initiated, according to urine culture sensitivity results. The selected regimen consisted of **trimethoprim - sulfamethoxazole 40/200 mg** administered **three times per week**

To address the persistently alkaline urinary environment and inhibit further struvite crystallization, urinary acidification therapy was added with **L-methionine (Lit-Control pH Down®, Devicare) twice daily**. This treatment aimed to maintain an acidic urinary pH and thus reduce the risk of infection-related stone formation.

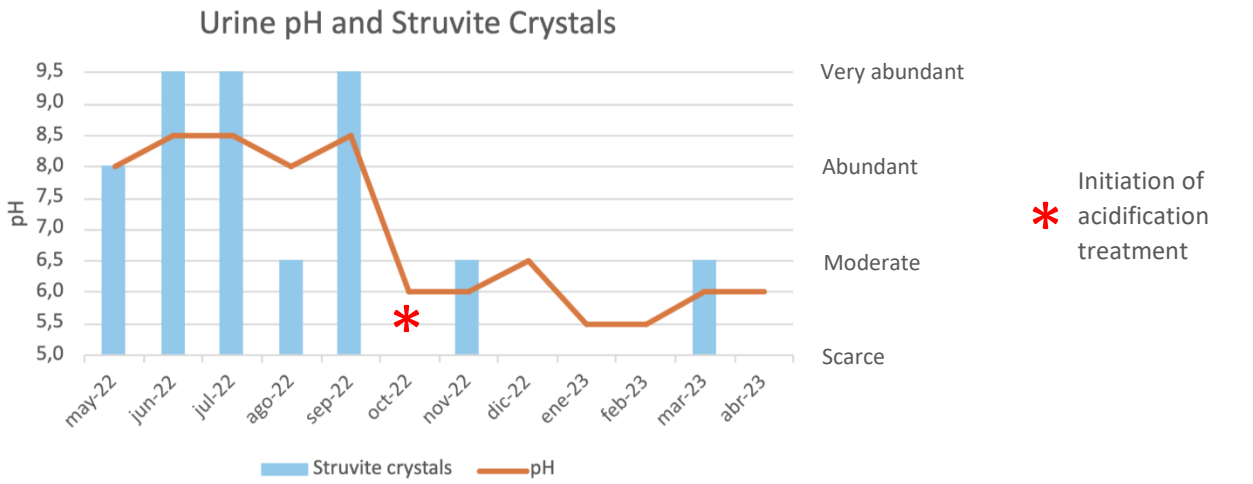
Additionally, scheduled catheter replacements were programmed every 4 months to minimize biofilm formation and bacterial colonization of the urinary tract. To prevent catheter encrustation, treatment with Canoxidin® (Devicare) was initiated.

e. Evolution and progress

The patient underwent regular follow-up with **periodic urine crystallography** and **routine CT scans** performed as part of surveillance for his underlying oncological disease.

During this follow-up, the patient spontaneously expelled the previously detected 5 mm calculus from the middle calyceal group of the left kidney in the subsequent CT-scan control. He continued antibiotic **prophylaxis** with trimethoprim-sulfamethoxazole and urinary acidification therapy with L-methionine (Lit-Control pH Down®, Devicare).

After initiating acidification therapy, subsequent urine pH measurements consistently remained below 6.0, indicating **effective urinary acidification**. This biochemical improvement was directly correlated with a marked reduction in struvite crystal formation observed on serial quantitative crystallography.



	may-22	jun-22	jul-22	aug-22	sep-22	oct-22	nov-22	dec-22	jan-23	feb-23	mar-23	apr-23
pH	8,0	8,5	8,5	8,0	8,5	6,0	6,0	6,5	5,5	5,5	6,0	6,0
Struvite crystals	Abundant	Very abundant	Very abundant	Moderate	Very abundant	Scarce	Moderate	Scarce	Scarce	Scarce	Moderate	Scarce

Fig. 2. Table and graphic representation of the evolution of urine pH and struvite crystals in crystallography. After acidification treatment was initiated in October 2022, a marked reduction un urinary pH and qualitative amount of struvite crystals in urine crystallography is depicted.

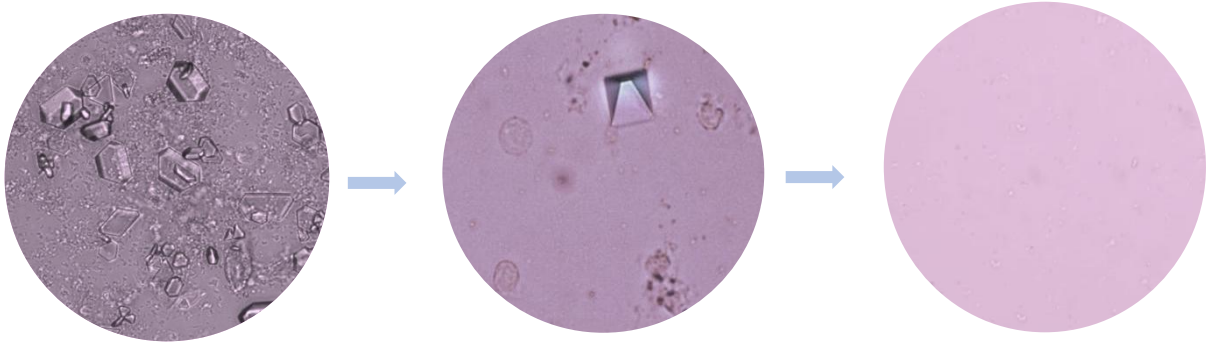


Fig. 3. Urine crystallography before and after initiating urine acidification therapy with L-methionine. The first image, taken two months prior to treatment, shows the characteristic cubic morphology of struvite crystals. The second image, obtained one month after starting acidification, depicts a marked reduction in crystal formation. The final image, taken six months after treatment initiation, shows complete absence of struvite crystals

f. Clinical results

Despite the risk factors for developing new infective stones, follow-up CT imaging demonstrated **no new lithiasis or signs of urinary tract infection**. The patient remained clinically stable, with no further episodes of febrile urinary infection and preserved renal function during long-term follow-up.

4. Discussion

Struvite lithiasis remains a significant therapeutic challenge in patients with chronic urinary tract infections and altered urinary anatomy, such as this patient, with cutaneous ureterostomy and indwelling catheters. The classical management pillars (eradication of urease-producing bacteria and complete stone clearance) are often insufficient in this type of patient, when persistent colonization, biofilm formation, and sustained alkaline urine coexist. (6,7)

In this context, urinary acidification using L-methionine represents a physiochemically rational adjunctive strategy (8,9). L-methionine is metabolized to sulfuric acid, which lowers urinary pH and reduces the concentration of ammonium, magnesium, and phosphate ions necessary for struvite nucleation. At urinary pH values above 7.0, urease-producing bacteria increase ammonia and bicarbonate concentrations, thereby elevating struvite supersaturation. By maintaining the pH below 6.0, L-methionine impairs this process and inhibits both crystal growth and bacterial urease activity.

Human studies have demonstrated that single doses of L-methionine (approximately 1,500 mg) can effectively reduce urinary pH to between 5.9 and 6.3, decreasing the relative supersaturation of struvite by roughly 30–35% (9). Similarly, long-term follow-up of former struvite stone formers treated with urinary acidification (L-methionine and other agents) showed a reduction of mean urinary pH from 7.5 to 5.5 and a 10% recurrence rate after 10 years (10).

In this patient, combining targeted antibiotic prophylaxis for persistent bacterial colonization, scheduled catheter replacement, and sustained urinary acidification with L-methionine (Lit-Control pH Down®, Devicare) maintained the urinary pH consistently below 6.0. This biochemical change correlated with the disappearance of struvite crystals on serial quantitative crystallography. These results show that even in patients with permanent urinary devices and chronic colonization, modification of the urinary environment can effectively interrupt the cycle of infection and stone formation. Canoxidin® (Devicare), with L-methionine in its composition along with other inhibitors of crystalisation, has shown good outcomes in prevention of incrustation in long term catheterisation of the urinary tract, and its addition has contributed positively in our patient catheter management.

The present case is of particular interest, as it involves a patient with multiple risk factors that make management especially challenging. Nevertheless, it illustrates how the complex pathophysiological mechanisms underlying infection-related stone formation can be effectively counteracted by a simple yet targeted intervention: urinary acidification.

5. Conclusions and recommendations

This case highlights the clinical and mechanistic rationale for urinary acidification with L-methionine as a preventive approach against infection-related lithiasis in complex urological patients. Close monitoring of urinary pH, renal function, and electrolytes is essential to ensure both safety and therapeutic efficacy.

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