V Edition of the Clinical Cases Contest on

non-surgical clinical management of Kidney Stones

Official template

Title: Conservative management of renal lithiasis in a right solitary kidney patient with congenital pelvic renal ectopia and history of left upper urothelial tumor.

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1. Abstract (no longer than 150 words).

Objective: Managing lithiasis in patients with urinary anatomical anomalies is complex and often requires medical treatments that delay or even avoid active interventions and their potential complications.

Methods: A 68-year-old male diagnosed with a left upper urothelial tumor and congenital pelvic right ectopic kidney with associated multiple lithiasis (<4 millimeters). He underwent left nephroureterectomy in 2020, with no oncological disease on subsequent follow-ups. A metabolic study showed no abnormalities, with a urinary pH of 6. A CT scan in October 2023 revealed lithiasis progression, prompting the initiation of medical treatment with LitControl-PH-Balance, 1 tablet every 12 hours.

Results: A follow-up CT scan in October 2024 showed reduction in the size of the stones and no complications.

Conclusions: The use of crystallization inhibitors in patients with renal lithiasis and anatomical anomalies that complicate active treatment could beneficially influence the progression of lithiasis.

2. Introduction

The use of medical treatments to slow the progression of lithiasis through crystallization inhibitors that prevent the association of calcium salts in the urine is becoming more widespread. Substances such as phytic acid help to prevent the progression of lithiasis residues before or after active treatment, whether through various surgical modalities or extracorporeal shock wave lithotripsy (ESWL).

Managing renal lithiasis in patients with renal ectopia can be challenging due to the anatomical complexity, which hinders the implementation of any active treatment capable of achieving an acceptable stone-free rate. For this reason, in these patients, early initiation of medical treatment with crystallization inhibitors to delay lithiasis progression and reduce potential complications associated with active treatment is of particular importance.

3. Clinical Case description

We present the case of a 68-year-old male with notable personal history of controlled hypertension (treated with two medications) and a deep vein thrombosis episode in 2016, managed with acenocoumarol. He was followed up by urology for a left upper urothelial tumor in the superior calyceal group of the left kidney and congenital ectopic right kidney with pelvic localization, associated with multiple renal calyceal stones less than 4 millimeters.

Due to the inability to perform conservative treatment for his tumoral disease because of its infiltrative appearance on uroCT, he underwent a left nephroureterectomy with laparoscopic distal ureteral resection in August 2020, with no complications.

The pathology report revealed a high-grade papillary urothelial carcinoma of the renal pelvis and upper calyx, with associated lymphovascular invasion (pT3NxMx), and free resection margins. Adjuvant chemotherapy with Carboplatin and Gemcitabine was administered due to renal function deterioration after surgery, completing the regimen in January 2021. The patient is currently disease-free, with annual follow-up via urine cytology, cystoscopy, and uroCT.

Regarding his lithiasis pathology, a metabolic study was performed, showing no significant abnormalities, with a urinary pH of 6. Follow-up CT in October 2023 showed progression of the right posterior-inferior and mid-calyceal renal stones to up to 6mm and >1000 HU.

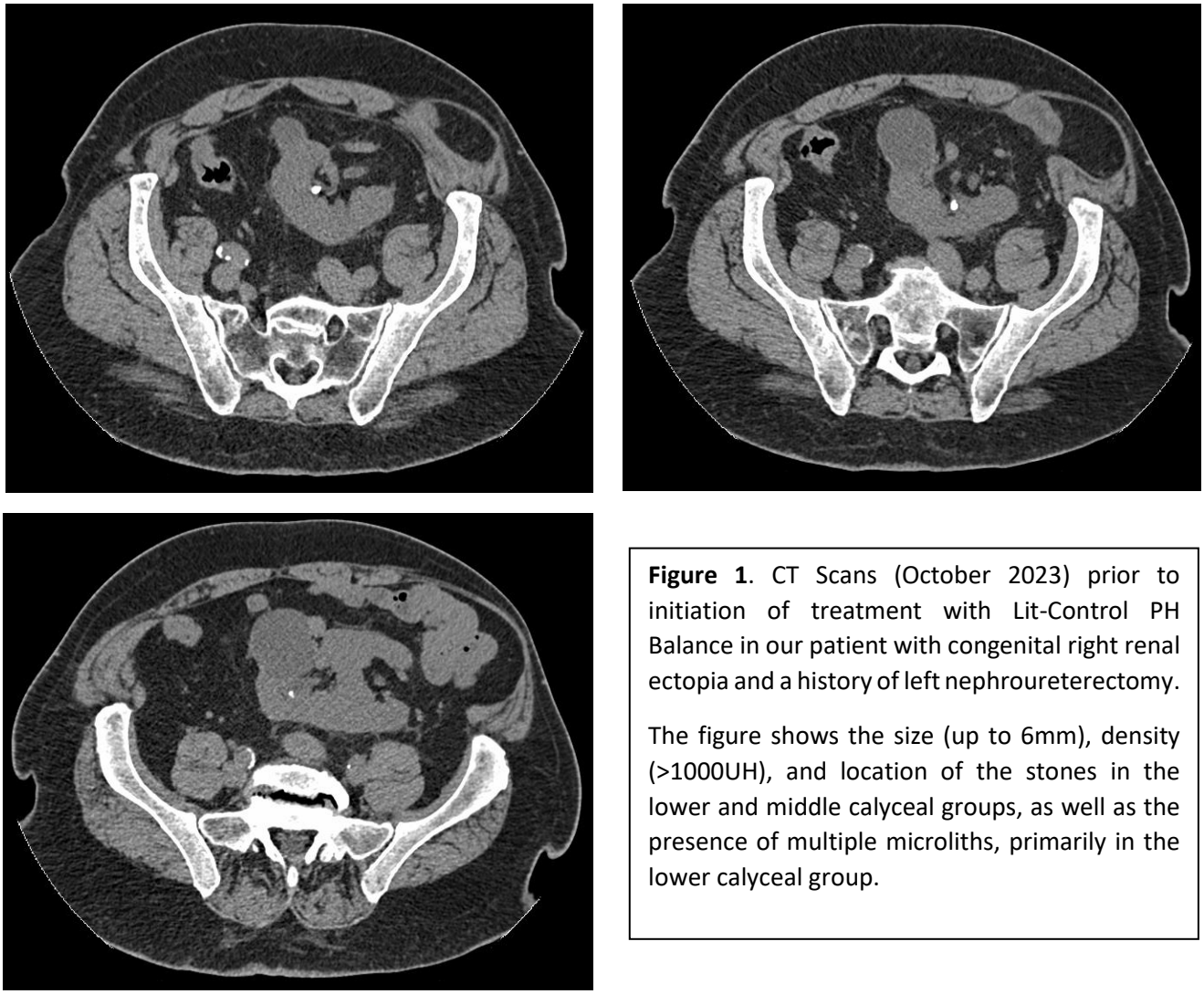

Figure 1. CT Scans (October 2023) prior to initiation of treatment with Lit-Control PH Balance in our patient with congenital right renal ectopia and a history of left nephroureterectomy.

The figure shows the size (up to 6mm), density (>1000UH), and location of the stones in the lower and middle calyceal groups, as well as the presence of multiple microliths, primarily in the lower calyceal group.

Given the patient's medical history of chronic kidney disease (CKD) stage 3b and anticoagulation for deep vein thrombosis, along with the absence of symptoms and the anatomical complexity of the right urinary tract, which made active treatment via surgery or extracorporeal shock wave lithotripsy (ESWL) challenging, a decision was made to initiate medical treatment with LitControl PH Balance (1 tablet every 12 hours). This treatment, primarily composed of phytic acid and magnesium, acts as crystallization inhibitors.

The patient's progress after starting the LitControl PH Balance treatment was favorable, showing a reduction in the size of the right calyceal stones from 6mm to 4mm, and the disappearance of the smaller stones. Additionally, spontaneous urine cytology remained negative, and cystoscopy revealed no findings in the latest follow-up in October 2024.

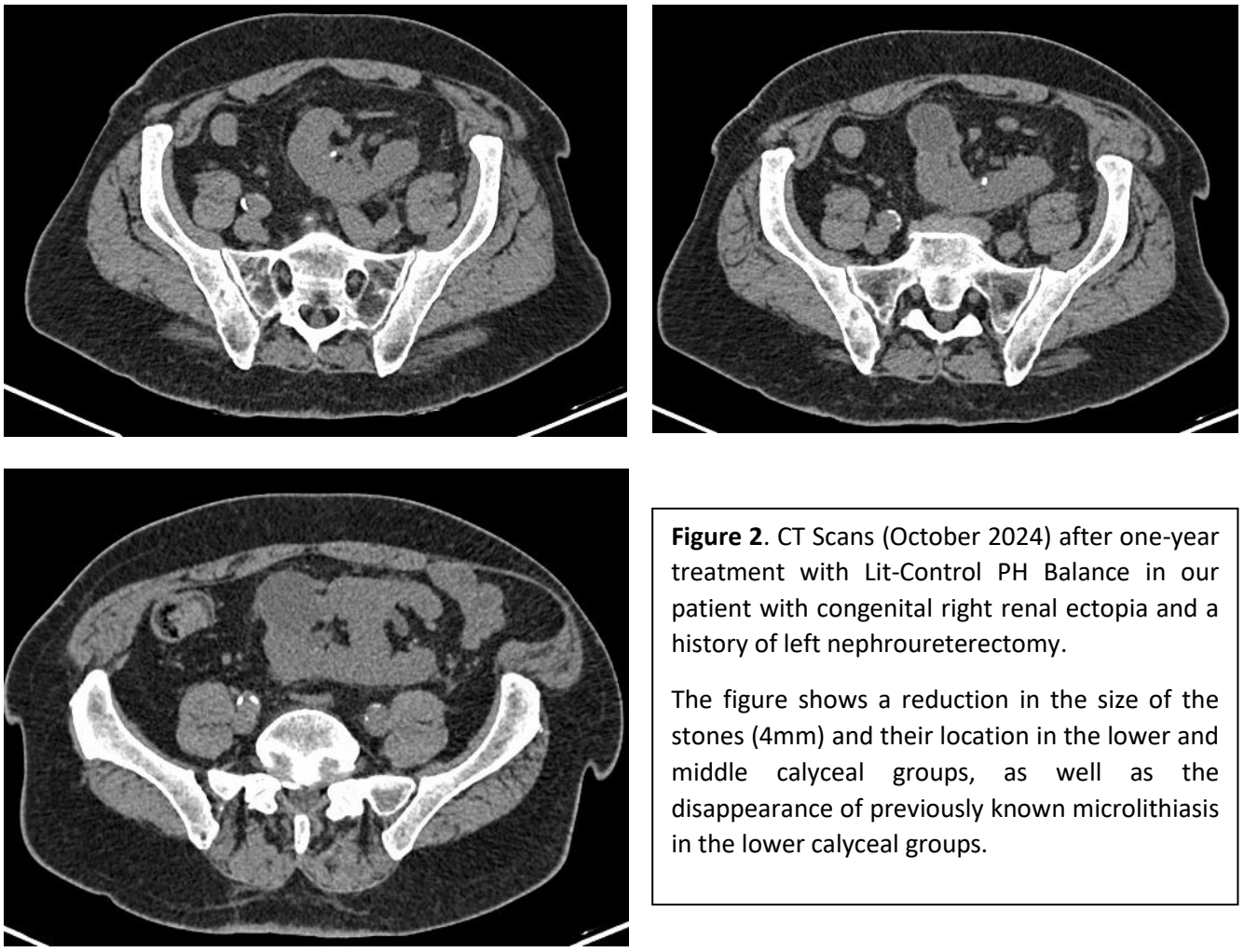

Figure 2. CT Scans (October 2024) after one-year treatment with Lit-Control PH Balance in our patient with congenital right renal ectopia and a history of left nephroureterectomy.

The figure shows a reduction in the size of the stones (4mm) and their location in the lower and middle calyceal groups, as well as the disappearance of previously known microlithiasis in the lower calyceal groups.

4. Discussion

Urothelial Tumors:

Urothelial carcinomas of the upper urinary tract (UTUC) account for 5-10% of all urothelial tumors. Their incidence has increased in recent decades due to better detection methods and increased survival rates of bladder cancer. UTUC is more common in men aged 70-90 years. Approximately two-thirds of UTUC patients present with invasive disease at the time of diagnosis.

The main environmental risk factor identified is tobacco use. A history of bladder cancer is associated with a higher risk of developing UTUC. Genomic characterization of UTUC may provide valuable information regarding the risk of recurrence in the bladder and other associated tumors.

Most urothelial tumors are of the urothelial carcinoma type. Classification is based on histological grade, which informs clinical decision-making (WHO classification 1973 and 2004/2016), as distinguishing between invasive, non-invasive tumors or flat lesions can be challenging due to limitations in obtaining tissue samples. Staging is based on the TNM classification system.

The most common symptoms are hematuria (70-80%) and flank pain (20-32%). Diagnosis is typically confirmed by uroCT (sensitivity 92%, specificity 95%) and chest-abdomen-pelvic CT with intravenous contrast to rule out metastases at diagnosis. Cystoscopy is essential to exclude concomitant bladder tumors, and abnormal cytology may indicate high-grade UTUC when cystoscopy is normal, and there is no carcinoma in situ (CIS) in the bladder or prostate urethra. Flexible ureteroscopy (URS) confirms the diagnosis by mapping suspicious areas of the urothelial tract, although it is not indicated in cases where imaging studies reveal tumors that are not amenable to endoscopic treatment due to the risk of tumor dissemination. URS can determine the tumor grade in more than 90% of cases with a low false-negative rate.

Given the difficulty in clinically evaluating the stage of UTUC, stratifying the risk of progression into low and high-risk groups is useful. This helps identify patients who may benefit from conservative kidney-preserving treatments and those who require radical treatment. High-risk factors to consider include multifocality, tumors >2 cm, high-grade cytology or biopsy, hydronephrosis, infiltrative appearance on CT, history of invasive bladder tumors, or certain histological subtypes.

Localized low-risk disease can be managed conservatively with kidney preservation through endourological ablative techniques, such as retrograde ureterorenoscopy or percutaneous access, but this requires strict follow-up due to the risk of tumor dissemination. Other conservative techniques include segmental ureterectomy or intravesical instillations. High-risk localized disease is typically treated with radical nephroureterectomy with intravesical ureteral resection via various techniques. Both laparoscopic and open approaches have similar results, but the latter is preferred in T3/T4 tumors. Lymphadenectomy appears to impact survival in non-metastatic infiltrating tumors.

Adjuvant intravesical instillation with Mitomycin C post-surgery reduces the risk of intravesical recurrence, and adjuvant chemotherapy with platinum compounds improves survival in patients with infiltrating disease or affected lymph nodes.

In cases of metastatic disease, treatment options include chemotherapy, immunotherapy, and, in some cases, palliative surgery.

During follow-up, the goal is to detect associated complications, recurrences, new primary urothelial tumors, and regional or distant metastasis. For patients undergoing conservative treatment, a second endourological surgery for revision is required within 6-8 weeks, in addition to regular follow-ups with urine cytology, cystoscopy, and uroCT.

In our patient's case, close monitoring of his underlying oncological disease allowed us to detect the progression of lithiasis in his remaining ectopic kidney and initiate medical treatment before complications or the need for invasive treatments arose.

Renal Ectopia:

Renal development is complex and involves several stages: pronephros, mesonephros, and metanephros. Initially, the kidney is located at the sacral level, later ascending to the upper lumbar vertebrae and rotating

along its axis. Renal localization outside of its normal position is termed renal ectopia. It is a rare condition, predominantly seen in women and on the left side. Ectopic kidneys can be located in the pelvic, lumbar, thoracic, or contralateral areas and are often associated with malrotation, leading to an anterior positioning of the renal pelvis.

Ureteral ectasia, present in up to 57% of ectopic kidneys due to malrotation, vesicoureteral reflux, and abnormal vascularization, is linked to a higher incidence of lithiasis and difficulty in its elimination.

The treatment of renal lithiasis in ectopic kidneys, particularly those with pelvic localization, presents unique challenges. Procedures such as extracorporeal shock wave lithotripsy (ESWL), open surgery, ureteroscopy (URS), and percutaneous approaches are viable treatment options.

ESWL in patients with renal ectopia has reported stone-free rates ranging from 30-100%, with factors such as stone size, density, and renal position playing a critical role.

Regarding surgery, both rigid and flexible URS present challenges in achieving endoscopic access, as does percutaneous nephrolithotomy, due to the kidney's location behind the peritoneum and adjacent to the sacrum.

Given our patient's medical history of renal function deterioration (CKD stage 3b) and anticoagulation therapy for deep vein thrombosis, along with an ectopic right kidney in the pelvis and calyceal lithiasis up to 6mm in size, we opted to begin with medical treatment rather than active intervention due to the complexity of the renal anatomy.

Renal Lithiasis and Medical Treatment:

Numerous studies have been conducted to investigate the factors involved in lithiasis formation. Literature highlights the crystallization-inhibiting properties of calcium oxalate monohydrate and calcium phosphate through compounds such as citrate, pentosan polysulfate, and phytic acid. Additionally, zinc sulfate seems to enhance this inhibitory capacity.

Oral administration of phytic acid to patients with lithiasis aims to prevent calcium absorption from the diet, thereby reducing calcium excretion in urine, while promoting phytic acid excretion to prevent calcium salt crystallization.

Studies have shown that, in the absence of crystallization inhibitors, the growth of residual fragments after ESWL occurs within the first 24 hours, even in the presence of normocalciuric and normooxaluric urine, with a clear beneficial effect when crystallization inhibitors are present. Therefore, the use of effective prophylactic therapies to prevent renal stone recurrence after active treatments, especially when residual stones persist, is of great importance.

For this reason, to prevent the progression of lithiasis in our patient without resorting to active treatment due to the renal anatomical complexity, we decided to initiate treatment with LitControl PH Balance (1 tablet every 12 hours), composed of phytic acid, polyphenols, magnesium, vitamin A, and zinc, aimed at inhibiting calcium crystallization without altering urinary pH. The results have thus far been satisfactory, with the patient remaining asymptomatic and follow-up CT after one year showing a reduction in stone size from 6mm to 4mm, along with the disappearance of smaller stones.

5. Conclusions and recommendations

Managing lithiasis in patients with anatomical anomalies such as renal ectopia is complex and requires proper diagnostic approach and follow-up.

The decision to pursue active treatment will depend on lithiasis progression, clinical presentation, and patient preferences. This can be a real challenge in cases where the urinary tract anatomy is significantly altered.

Regarding medical treatment, the use of crystallization inhibitors such as phytic acid to prevent the aggregation of calcium salts could be beneficial, especially in these patients, as it may delay the need for active treatment and the associated complications.

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