1st edition of the competition of clinical cases related to the non-surgical clinical management of renal lithiasis[1]

- **Title:** Nephrocalcinosis as a manifestation of distal renal tubular acidosis.
- **Keywords:** lupus erythematosus, hypercalciuria, urinary pH.

1. Summary

A woman with Systemic Lupus Erythematosus (SLE) and distal renal tubular acidosis (DTRTA) presents a case of exacerbation of SLE during pregnancy together with nephritic colic with spontaneous expulsion of stones. Radiological tests show diffuse calcifications in both renal parenchyma suggesting, in the context of DRTA, nephrocalcinosis. Together with stabilization of the SLE and medical treatment aimed at correcting the metabolic disturbances, radiological and clinical stability of the lithiasic disease is achieved.

2. Introduction

SLE is an autoimmune disease that predominantly affects women of childbearing age. During pregnancy and postpartum, the risk of flares and thus the complications of SLE increases (1).

A rare association of SLE is DTRTA or type I. This is the inability of the collecting tubule to excrete hydrogenions (H+), which triggers systemic metabolic acidosis, urinary alkalosis and, consequently, increased bone resorption as a buffering mechanism. Thus, hypercalciuria secondary to resorption and hypocitraturia and hypokalemia secondary to metabolic acidosis occur (2, 3). Complete DTRTA is more frequent in childhood. However, incomplete DTRTA, a milder form without metabolic acidosis, usually occurs in adulthood (4, 5).

The clinical manifestation of DTRTA in adults is usually urinary lithiasis. However, nephrocalcinosis is an infrequent expression of DTRTA in adults, but rather typical of childhood, and consists of the accumulation of calcium phosphate crystals (CaP) in the renal tubules and renal parenchyma. Stone formation in DTRTA is mainly due to the presence of an alkaline urine pH and hypercalciuria (6, 3).

We present the case of a woman with SLE and DTRTA who after childbirth presented with nephrocalcinosis. Few cases have been published on this manifestation of DTRTA in adults.

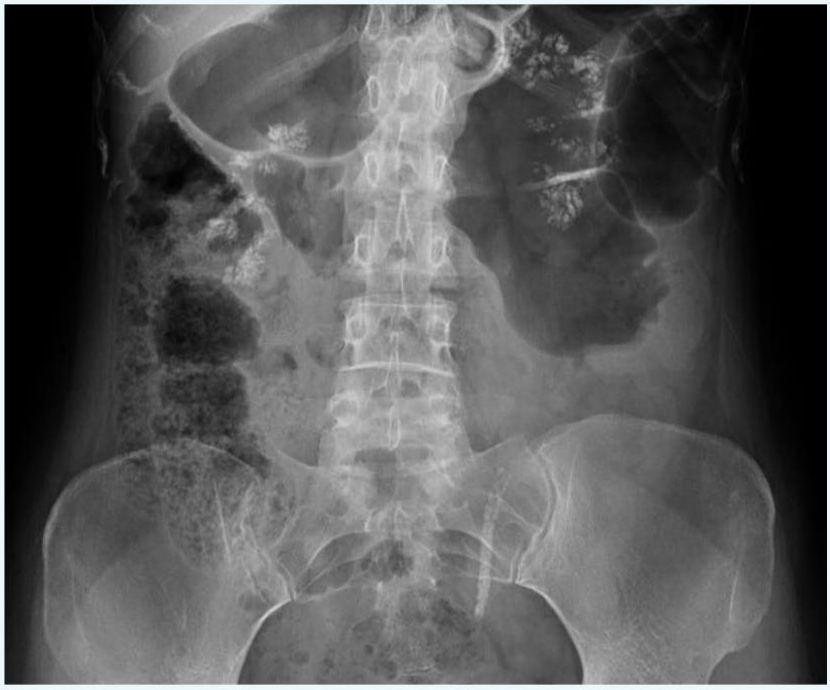
3. Description of the clinical case:

a. Relevant background:

The case is presented of a 36-year-old woman with SLE and incomplete DTRTA who during pregnancy presented an exacerbation of SLE and, secondarily, of DTRTA, progressing to a complete form. After delivery, the SLE stabilized and since then she reports spontaneous expulsion of small stones.

b. Diagnostic support studies and results:

1) Abdominal X-ray: macroscopic nephrocalcinosis and lithiasic street in left distal ureter.



2) 24h urinalysis: suggestive of incomplete distal renal tubular acidosis: pH 6.85, hypocitraturia, mild hypercalciuria (258 mg/24 hrs.), normal oxaluria, hypomagnesuria, hypokalemia.
3) Beta Crosslaps and Vit D within normality.
4) Densitometry: Spine: T-score -1; Femur: T score -2,1 (compatible with osteopenia).
5) Furosemide test: No acidification of urine, i.e., positive for DTRTA.

c. Diagnosis:

Four years after delivery the patient attended the emergency department for left renal colic, where an abdominal radiograph showed diffuse calcifications in the renal parenchyma of both kidneys and radiopaque occupation in the left distal ureteral tract. This finding suggests renal involvement in the form of nephrocalcinosis that probably occurred secondary to complete DTRTA during the SLE course in pregnancy. In addition, densitometry data show signs of osteopenia that could also be secondary to bone resorption during the full-blown DTRTA episode.

The 24h urinalysis at the time of our evaluation suggests a distal tubular acidosis, now incomplete, which is confirmed by furosemide test.

d. Treatment:

For the management of nephritic colic, a ureterorenoscopy (URS) was performed, with endoscopic lithotripsy of the ureteral lithiasis. During the URS the renal cavities were explored, showing multiple type II papillary calcifications or "plugs" with dilated collecting tubules and small hydroxyapatite stones inside.

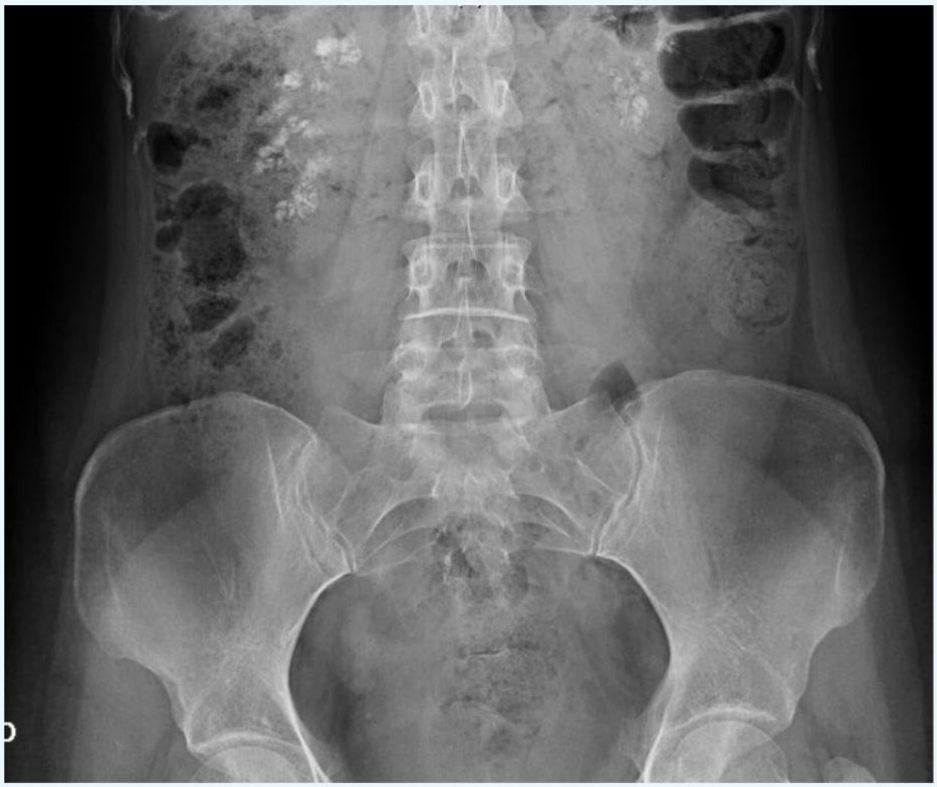
As for renal nephrocalcinosis, medical treatment was started with potassium citrate (Lit-Control pH Up®), phytate (Lit-Control pH Balance®) and dietary advice (abundant water intake and avoidance of a diet rich in protein).

e. Evolution:

After 12 months with well-controlled SLE and therapeutic compliance, the patient remains asymptomatic and nephrocalcinosis remains stable. The control metabolic study shows unchanged results with respect to the previous one, without reaching severe DTRTA values.

f. Clinical results:

1) Abdominal X-ray: stability/slight improvement of nephrocalcinosis



2) 24h urinalysis: suggestive of incomplete distal renal tubular acidosis pH 7'1, normocalciuria, hypocitraturia, hypomagnesuria and hypokalemia.

3) Analysis of calculus: hydroxyapatite

4. Discussion

There are cases of DTRTA in which there is no metabolic acidosis or important biochemical alterations, however, the patient presents urine pH higher than 6 in repeated determinations and recurrent episodes of lithiasis. In these cases, the presence of incomplete DTRTA should be suspected (4). In the present case, the patient had high urinary pH in successive analyses without presenting metabolic acidosis or severe biochemical alterations, suggesting incomplete DTRTA. However, during pregnancy she presented an exacerbation of SLE together with an aggravation of DTRTA, presenting metabolic acidosis that was confirmed by blood gas analysis. These data suggest an episode of complete DTRTA that caused an increase in bone resorption, causing osteopenia and also hypercalciuria and alkaline urinary pH that led to nephrocalcinosis. Both osteopenia and nephrocalcinosis were diagnosed sometime after delivery, with stabilized SLE and again incomplete DTRTA (no metabolic acidosis, normocalciuria compensated with potassium citrate and with a maintained alkaline urinary pH).

In addition, the lithiasic debris analyzed after URS was hydroxyapatite, the most frequently analyzed stone in patients with DTRTA.

The mainstay of treatment of DTRTA, since it is not possible to modify urinary pH, consists of reducing calcinuria to hinder hydroxyapatite crystallization. Therefore, the main treatment is potassium citrate is potassium citrate, which acts as a calcium chelator. It is true that it can also alkalinize the urine, but the overall effect is to reduce the risk of crystallization in patients with DTRTA by reducing calcinuria, since the urinary pH in these patients is already alkaline and cannot be acidified. In the case presented, phytate supplementation was also added to the treatment, which inhibits the crystallization of calcium phosphate and inhibits the crystalline growth of calcium oxalate stones (7). Likewise, phytate acts as an inhibitor of bone resorption (8), thus decreasing the outflow of calcium in the bone and, consequently, calcinuria. Finally, the compound administered has magnesium in its composition, correcting the hypomagnesuria presented in the metabolic study.

The prognosis of nephrocalcinosis depends on the underlying pathology, in this case the evolution of SLE and the control of DTRTA. However, when nephrocalcinosis is detected radiologically (macroscopic nephrocalcinosis) it is hardly reversible, but improvement can be achieved (6). As we have shown, after 12 months of treatment and with stable SLE, the patient is asymptomatic but the radiological image shows no changes and, if there are any, they are slight.

The approach we propose in this case is to perform strict follow-up and metabolic management, and only perform endoscopic treatment in the event of nephritic colic due to non-expellable stones.

5. Conclusions and recommendations

DTRTA can be secondary to several systemic diseases other than SLE, such as amyloidosis or Sjögren's syndrome, but it can also be secondary to drugs or be idiopathic in origin. On the other hand, a DTRTA can sometimes be symptomatic before the debut of a systemic disease. Therefore, it is advisable to rule out DTRTA in patients with lithiasic involvement as it may be the first sign of an autoimmune disease.

It is also important to rule out this involvement in patients with lithiasis since the basis of treatment is medical and may prevent unnecessary intervention. A patient with renal lithiasis affected by undiagnosed DTRTA has a high probability of recurrence and, secondarily, of a high number of invasive procedures.

Finally, nephrocalcinosis should be understood as a diffuse and bilateral tubulointerstitial pathology, so invasive treatment is unlikely to be successful. Hence its importance in the rigorous management of systemic and urinary metabolism.

6. Bibliographic references

1. Clowse ME, Jamison M, Myers E et al. A national study of the complications of lupus in pregnancy. Am J Obstet Gynecol. 2008 Aug;199(2):127.e1-6.

2. Li S, Liou LB, Fang JT and Tsai WP. Symptomatic renal tubular acidosis (RTA) in patients with systemic lupus erythematosus: an analysis of six cases with new association of type 4 RTA. Rheumatology 2005;44:1176–1180 **

3. Guimerà J, Martínez A, Tubau V et al. Prevalence of distal renal tubular acidosis in patients with calcium phosphate stones. World J Urol. 2020 Mar; 38 (3):789-794 **

4. Pongchaiyakul C, Domrongkitchaiporn S, Stitchantrakul W, et al. Incomplete renal tubular acidosis and bone mineral density: A population survey in an area of endemic renal tubular acidosis. Nephrol Dial Transplant. 2004;19:3029-33

5. Cano-García MC, Girón-Prieto MS y Arrabal-Polo MA. Distal renal tubular acidosis: Diagnosis at an urologic unit. Rev Mex Urol. 2016;76(2):127-128

6. Wrong O. Nephrocalcinosis. In: Oxford Textbook of Clinical Nephrology, Davison AM, Cameron JS, Grünfeld J, et al (Eds), Oxford University Press, Oxford 2005. p.1375 *

7. Grases F, Isern B, Sanchis P et al. Phytate acts as an inhibitor in formation of renal calculi. Front Biosci. 2007 Jan 1;12:2580-7 *

8. Lopez AA, Grases F, Mari B et al. Urinary phytate concentration and risk of fracture determined by the FRAX index in a group of postmenopausal women. Turk J Med Sci. 2019 Apr 18;49(2):458-463