4th Edition of the Clinical Cases Competition related to the non-surgical clinical management of non-surgical clinical management of renal litiasis

Official template

Title: Pharmacological chemolysis of sulphadiazine lithiasis in a patient with cerebral toxoplasmosis.

Keywords (between 3 and 6): toxoplasmosis, sulphadiazine, lithiasis

1. Abstract

The case of a male patient recently diagnosed with cerebral toxoplasmosis is presented. A few weeks after starting medication for the treatment of his disease, he attended the emergency department presenting right renal colic with evidence of significant deterioration of renal function in complementary laboratory tests and the presence of bilateral renal lithiasis and right ureteral lithiasis, not present in previous imaging tests. After adjusting the treatment regimen for toxoplasmosis, urinary alkalinisation and intensive fluid therapy, complete chemolysis was achieved with no side effects throughout the process. Subsequent follow-up of the patient in outpatient clinics was favourable, with no additional urological symptoms.

2. Introduction

Renal lithiasis is a very common pathology, especially in industrialised countries. Those secondary to drugs represent a small percentage of the total (1-2%) and may develop due to oversaturation in the urine of the poorly soluble drug, or due to metabolic alterations related to the drug.

Toxoplasma gondii is an opportunistic protozoan with a worldwide distribution. It is estimated that approximately one third of the world's population is a carrier (1,2). It causes a systemic zoonosis called toxoplasmosis which, in the vast majority of immunocompetent individuals, results in an asymptomatic primary infection (1). However, in a number of generally immunocompromised individuals, it can cross the blood-brain barrier and lead to cerebral toxoplasmosis. Some of the therapeutic regimens proposed for its management include sulphonamides, which have been shown to be associated with the formation of lithiasis and episodes of acute renal failure due to their intratubular crystallisation. The development of more soluble sulphonamides has significantly decreased the incidence of these episodes, with the exception of sulfadiazine.

Factors favouring this effect may include the presence of a low urinary pH, decreased urinary volume or be directly related to the drug doses administered. Knowledge of their existence allows action to be taken on them in the therapeutic management of complications. Chemolysis of sulphadiazine lithiasis is rare in our setting.

We present the case of a male patient recently diagnosed with cerebral toxoplasmosis who, after starting oral treatment with sulphadiazine, abruptly developed acute renal failure secondary to drug lithiasis. Medical treatment led to a complete resolution of the condition.

3. Clinical case description

a. Relevant background

We present the case of a 71-year-old man with no relevant past history. He was seen in the emergency department after presenting with an episode of dysarthria accompanied by mandibular tremor. The cranial computerised axial tomography (CAT) scan showed a right frontal focal lesion that suggested a differential diagnosis of primary tumour or single metastasis. He was admitted to the neurosurgery department and surgery was performed to resect the lesion. The anatomopathological report was compatible with necrotising granulomatous inflammatory granulomatous lesion. Silver, Giemsa, Zheel-Nielsen stains and complementary techniques for HSV, CMV and EBV were negative. The study was completed with a Toxoplasma gondii PCR on the paraffin-embedded biopsy specimen, which was positive. An immunology study was performed without evidence of immunodeficiency. To complete the study, an extended abdominopelvic CT scan was performed, with no pathological findings. Treatment was started with sulphadiazine 1000 mg/6h, pyrimethamine 50 mg/24h and folinic acid 5 mg/24h.

b. Diagnostic support studies and results

- Blood tests: glomerular filtration rate 10 ml/min/1.73m2; creatinine 5.38 mg/dl; leukocytes 10400 cells per microlitre.

- Urinalysis: pH 5.5; density 1.0 g/mL (1.005- 1.03 g/L); urine protein 100 mg/dl. Other values in the normal range.

- Abdominal X-ray: a 1 cm radiopaque image in the theoretical lower calyx of the right kidney and a 9 mm image in the right bony pelvis with doubts between phlebolith and lithiasis in the theoretical right urinary tract (Figure 1).

- Abdominal ultrasound: both kidneys without hydronephrosis, with correct corticomedullary differentiation. Stones occupying calyces of the middle and lower group are observed in both kidneys with a size less than or equal to 4 mm on the right side and a size less than or equal to 9 mm in the left kidney (Figure 2). (Figure 2).

- Abdominal CT scan without contrast: left kidney with at least 5 lithiasis up to 10 mm. Lithiasis of 10 mm at the level of the left ureteral meatus. Right kidney with 2 lithiasis up to 5 mm. No dilatation of the excretory tract (figure 3).

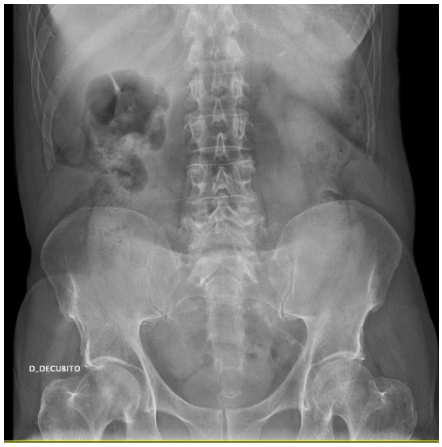

Figure 1

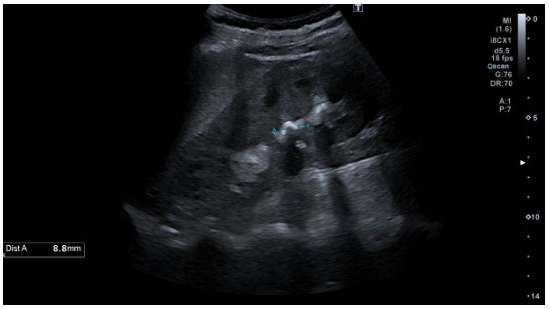

Figure 2

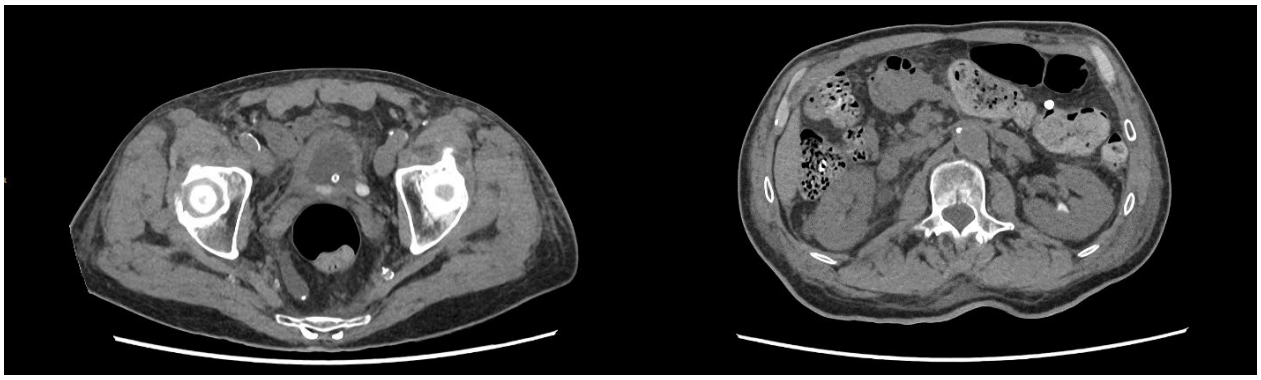

Figure 3

c. Diagnosis

Twelve days after starting the oral medication described above, the patient came to the emergency department with right renal colic pain of four hours' duration, accompanied by nausea and vomiting. He did not present febrile syndrome. A blood test was performed and no alterations in renal function or infectious data were detected. The semi-quantitative urine test showed a pH of 7.5 with the rest of the values in the normal range. The abdominal X-ray showed a possible lithiasis in the lower calyx of the right kidney. A diagnosis of uncomplicated right renal colic was made and the patient was discharged after achieving good control of pain and emetic symptoms.

On the sixth day after this episode, he presented a new episode of colic pain with the same characteristics, for which he returned to the emergency department. The complementary tests described in the previous section were performed with the results shown.
With the diagnosis of acute renal failure secondary to obstructive lithiasic uropathy, bilateral double J ureteral catheterisation was performed urgently and treatment was started as specified in the following section.

d. Treatment

Analgesic treatment with intravenous paracetamol and metamizole is performed. Withdrawal of sulphadiazine was agreed and an alternative therapeutic regimen was started, based on clindamycin 600 mg/6h intravenously, pyrimethamine 25 mg (two tablets daily), and folinic acid 5 mg (2 tablets daily). It is complemented with 500 cc of ⅙ molar sodium bicarbonate in a continuous daily infusion and intensive fluid therapy with 0.9% physiological saline solution, achieving a diuresis of approximately three litres per day.

e. Evolution and follow-up

The patient remained in hospital for five days. After clinical improvement and normalisation of renal function, he was discharged with a treatment regimen of clindamycin 600mg/6h, pyrimethamine 50mg/day and calcium folinate 15mg/day, with the intention of completing two months of treatment. The use of myLit-Control® App was recommended for close monitoring of urinary pH and quantification of the patient's water intake to ensure adequate diuresis volume. In subsequent consultations, complete chemolysis with medical treatment was confirmed by imaging tests (Figure 4).

f. Clinical results

After one month of treatment, the patient presented the following results in complementary tests:

- Blood tests: glomerular filtration rate 82 ml/min/1.73m2, creatinine 0.66 mg/dl, leukocytes 9600 cells per microlitre.
- Urinalysis: urinary pH 7.5. Other values without pathological significance.
- Abdominal TAC scan without contrast: ureteral catheters normally positioned. Ureteral and renal lithiasis resolved (Figure 4).

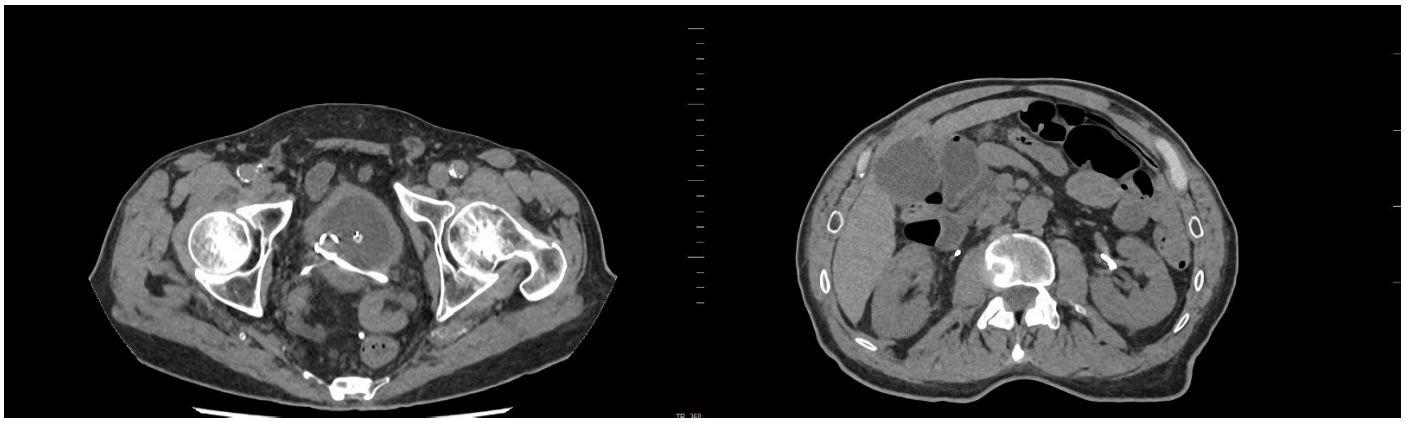

Figure 4

4. Discussion

Treatment of diseases secondary to Nocardia and toxoplasmosis has led to an increase in reported cases of lithiasis secondary to sulphonamides over the last forty years, with an incidence between 0.4 and 20% (1). It is usually within a week of starting treatment that this complication arises (3).

Abdominal pain is the most common form of presentation, with its debut as asymptomatic crystalluria being rare. Abdominal ultrasound shows the presence of lithiasis in the urinary tract in 75% of patients; however, two out of ten individuals will have no findings on ultrasound imaging. (3)

Inhibition of folic acid which prevents bacterial growth is the main mechanism of action of sulphadiazine. Normal pH, its high degree of urinary excretion and the low solubility of its metabolites (especially N-acetyl derivatives) are the main determinants of its precipitation. In addition, prolonged treatment regimens, low urinary pH and low urinary volume are factors favouring the formation of lithiasis (4).

Treatment for resolution of the condition relies on the high solubility of the drug and its metabolites at alkaline pH. If necessary, urinary diversion as a bridging therapy is the treatment of choice.

When the source is identified, the key is to achieve a urinary pH greater than 7.5, for which the use of sodium bicarbonate or potassium citrate is the most effective measure. Definitive withdrawal of sulphadiazine is not necessarily necessary, and dose reduction or temporary discontinuation of sulphadiazine is possible. (5) Resolution time is variable, usually less than a week. (3)

Subsequent follow-up includes maintenance of urinary pH greater than 7.15 with sodium bicarbonate and diuresis of more than two litres daily (6), with weekly checks recommended. (7)

5. Conclusions and recommendations

The use of medicines in our daily practice is not without risk. From a urological point of view, metabolic alterations in urinary formation and excretion can lead to the formation of lithiasis and even complicated renal colic. It is therefore important to know their mechanism of action and excretion.

In particular, in lithiasis secondary to the use of high-dose sulphonamides, medical treatment and prophylaxis is a first-line option and invasive measures can be avoided. It is very likely that *my*Lit-Control® App has played an important role in the adherence to treatment and subsequent outpatient monitoring, which is key to the resolution of the initial picture and the absence of subsequent events.

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

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