Renal Failure Due to Sulfadiazine Induced Calculi: Case Report and Literature Review

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Abstract

Introduction: Renal calculi is a prevalent disease and has some causes described. The drug calculi origin are rare, accounting for around 1% to 2% of cases. The crystals of sulfadiazine are formed in 20% to 45% of cases, but between 0.4% and 4.5% are associated with renal failure. We present a case report and a review of the literature on diagnosis and treatment of this entity, given its rarity and specificity.

Case Report: A 48-year-old male, diabetic, during treatment for acute toxoplasmosis with sulfadiazine initiated renal colic associated with renal failure. The hypothesis of drug calculation was considered, because during the diagnostic investigation of toxoplasmosis, imaging studies were performed and presented without renal calculi. Initially he was treated conservatively with hyperhydration and alpha-blocker, but since he did not present improvement in the exams, he underwent ureterolithotripsy and double j stent.

Conclusion: We present a report of urinary lithiasis of pharmacological origin associated with renal insufficiency and a review of the literature.

Keywords: Kidney Calculi/chemically induced; Renal Insufficiency/chemically induced; Sulfadiazine/adverse effects

Introduction

Urolithiasis is a prevalent disease that affects approximately 10% of the population,¹ characterized by a recurrence rate of approximately 50% within 10 years.² The formation of calculi with pharmacologic etiology is rare, and occurs in about 1% - 2% of stone cases.² These calculi may form by the action of the drug or its metabolites, which crystallize due to their low solubility or because of metabolic changes caused by these drugs.

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We present the case of a patient with acute renal failure due to a sulfadiazineinduced calculus and a literature review of the topic.³

Case Report

A 48-year-old, male, diabetic patient with no prior history of urolithiasis was admitted to hospital because of fever of unknown origin and cervical lymph node enlargement. The pathological examination of the cervical lymph node biopsy revealed the diagnosis of acute toxoplasmosis, and treatment was initiated with sulfadiazine and pyrimethamine.

Six days after hospital discharge, the patient returned to the Emergency Department presenting with malaise, prostration, nausea and vomiting associated with lumbar pain that was more intense on the right. Upon physical examination, the cervical lymph nodes persisted, along with tenderness on fist
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percussion over the right lumbar region. Laboratory test results showed anemia, increased CRP, and elevated urea and creatinine levels (82 and 5.4 mg/dL, respectively). Computed tomography revealed slight dilation of the right collecting system up to distal ureter, where dense material was observed moving along the ureteral orifice with 170-210 Hounsfield Unit. (Fig.s 1 and 2)

During the investigation of the febrile condition of the previous week, an imaging test was performed and did not show any renal or ureteral calculi. Analyzing this information, the presumptive diagnosis was acute renal failure due to sulfadiazine, since urinary calcium stone does not form in a week and the medication was immediately withdrawn to avoid its crystallization in the renal tubules.

Besides withdrawal of the drug, conservative treatment was initially chosen with hyperhydration and an alpha-blocker. After starting treatment, pain relief and better general clinical condition were observed; however, 48 hours later, new laboratory tests showed worsening of creatinine levels.

A new computed tomography diagnosed persistence of the hypodense material in the distal ureter, maintaining the same dilation of the ipsilateral excretory system. Therefore, it was decided to perform ureterolithotripsy with a semirigid ureteroscope and place a double-J stent. The intraoperative aspect was that of apparently non-obstructive multiple small crystals, which were removed with a basket, and no need for lithotripsy.

During the first 24 postoperative hours creatinine levels dropped by 50% (3.0 mg/dL), and four days later returned to normal levels (0.98 mg/dL). The double J stent was removed after seven days.

Figure 1: Dense material in the distal ureter.

Figure 2: Dense material in the uretero-vesical junction.

Discussion

Despite their low incidence, drug-induced calculi have been reported throughout the years. At the beginning of the 1970’s, triamterene was responsible for most of the cases. In the 1990’s, with the treatments for HIV, sulfadiazine and indinavir became the main drugs involved in the genesis of drug-related lithiasis.

The mechanisms of drug-induced calculus formation derive from the medication itself, which crystallizes due to its low solubility or because of metabolic actions. In the first group, there are inotropic agents (ephedrine), diuretics (triateren), antacids, antiretroviral agents (indinavir and atazanavir), and antibiotics (sulfonamides, cephalosporins, and quinolones). In the second group, there are loop diuretics (furosemide), carbonic anhydrase inhibitors (acetazolamide), calcium supplements, vitamin D, anticonvulsants (topiramate), glucocorticoids, and laxatives. Not all patients who are on lithogenic medications will form stones, since calculi are related to high doses of these drugs, prolonged use, deficient hydration, great renal excretion, and characteristics and solubility of the crystals.

The formation of drug-induced stones is also influenced by family or past medical history of lithiasis, urinary stasis, prior lithogenic metabolic changes, variations in pH, environmental factors and low intake of fluids.

The symptoms of patients with drug-induced calculi are similar to that of habitual renal colic, and it is impossible to determine the etiology.

The diagnosis is generally made by imaging tests (ultrasound, computed tomography or magnetic resonance) and not all drug-induced stones are radio-opaque. Indinavir, triamterene, ephedrine, ciprofloxacin and sulfadiazine-related calculi are radiolucent. Those originating from thiazone diuretics, acetazolamide and topiramate are radio-opaque.
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Treatment of these stones consists in withdrawing medication, increasing hydration and urine alkalization for some drugs, such as sulfadiazine. In patients with significant ureteral obstructions, double-J stent or nephrostomy can be used.

Allinson et al., and Kabha et al., reported cases of patients in whom bilateral nephrostomy and double J stent were used, respectively, for treating ureteral obstructions secondary to sulfadiazine-induced stones.5,6

The present report demonstrates the case of a patient who under sulfadiazine, treatment for toxoplasmosis developed ureteral calculi and renal insufficiency, due to deposits of sulfap crystals in the renal tubules probably causing an acute interstitial nephritis (NIA). That is a cause of acute renal failure which can be initiated by medications, infections, neoplasms among others. The NIA in the case of medications is not dose dependent and anti-inflammatory drugs are their main cause these days, but antibiotics such as sulfa, quinolones, penicillin among others are also related. The treatment consists of suspension of the drug, hydration and correction of hydro-electrolytic disorders. The role of corticoid and renal biopsy will depend on the evolution after removal of the aggressor factor.7Although there is no analysis of the calculi, some characteristics make us believe in the sulfa induced etiology:

1 - Patient developed ureteral calculus certainly after the introduction of sulfa, since in the week before the introduction of the medication the tomography did not show renal or ureteral calculi.
2 - The Hounsfield Unit coefficient between 170-210 is not expected for calcium stone.
3 - Light unilateral ureteral obstruction with normal contralateral unit reduces the possibility of renal failure. Previous reports have demonstrated renal tubule crystallization and development of renal insufficiency in patients under sulfa treatment.5
4 - The endoscopic aspect showed fragments of small and non-obstructive crystals.

Conclusion
Sulfadiazine is a sulfonamide used to treat some diseases such as toxoplasmosis and its association with obstructive uropathy is known either by deposit of crystals in the renal tubules or by ureteral obstruction. The objective of this report is to call to mind this etiology of urolithiasis, demonstrate its severe effect on renal function, and give guidance on its management.

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