

Ceftriaxone associated urolithiasis in a child with hypercalciuria

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Abstract

We present a 5-year-old boy with pneumonia who complained of right lumbar pain on the 7th day of treatment with Ceftriaxone. Ultrasound examination revealed mild to moderate right hydronephrosis. Under spasmolytic therapy and hydration there was spontaneous passage of three small calculi. Infrared spectroscopy showed that the calculi were composed of calcium-ceftriaxonate. Full metabolic investigation was performed and moderate hypercalciuria was detected, suggesting the role of hypercalciuria in ceftriaxone-associated nephrolithiasis. Hippokratia 2011; 15 (2): 181-183

Key words: biliary pseudolithiasis, ceftriaxone, child, infrared spectroscopy, urolithiasis, hypercalciuria

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Metabolic factors, urinary tract infection and obstruction are the most common etiologies of nephrolithiasis in children. Drug induced nephrolithiasis is rarely described in children¹. The incriminated drugs are ceftriaxone (CTX), trimethoprim-sulfamethoxazole, topiramate, antiretroviral drugs (atazanavir, indinavir, sulfadizine). CTX is a third generation cephalosporin antibiotic widely prescribed for respiratory and urinary tract infections. Biliary pseudolithiasis and urolithiasis are rare complication of CTX therapy and both conditions are usually transient²⁻⁷. Cessation of the drug, spasmolytic therapy, good hydration and follow up ultrasound studies are sufficient treatment measures in patients with suspected CTX induced urolithiasis. Finally, infrared (IR) spectrum⁸ of the calculi is critical for establishing the correct diagnosis.

Case report

A 5-year-old boy was admitted to the Hospital for treatment of community acquired pneumonia. CTX was prescribed in intravenous infusion 1.0 g/day (45 mg/kg). His general condition promptly normalized and on the 7th hospital day he was placed on oral cephalosporin. He suddenly complained of intensive right sided lumbar pain. Renal percussion was positive on that side. Microscopic examination of the urinary sediment revealed numerous red blood cells (eumorphic). Ultrasound scan showed grade II hydronephrosis of the right kidney (Figure 1). No calculi were detected in the kidneys. The gallbladder examination did not reveal pseudolithiasis. The child was given intravenous spasmolytics for pain. Full metabolic investigation was performed and normal serum levels of calcium, phosphate, magnesium and uric

acid were observed. Urinary excretion of cystine, uric acid, oxalate and citrate was also within normal limits. There was moderate hypercalciuria (5.4 mg/kg/day). Within the next two hospital days under forced hydration there was spontaneous passage of three calculi. IR spectroscopy was performed and the recorded spectrum identified the calculi as calcium ceftriaxonate (Figure 2). Follow up ultrasound scans revealed prompt resolution of the right hydronephrosis. Hypercalciuria was confirmed several times during the follow up and increased hydration was advised.

Discussion

CTX is a widely used third generation cephalosporin antibiotic and clinicians should be aware of the possible appearance of CTX-induced precipitates within the gall-

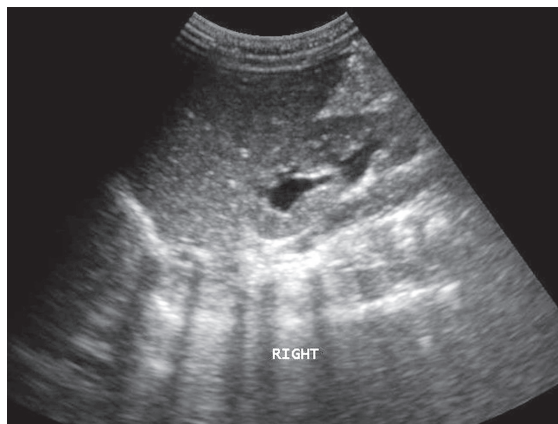


Figure 1: Hydronephrosis of the right kidney.

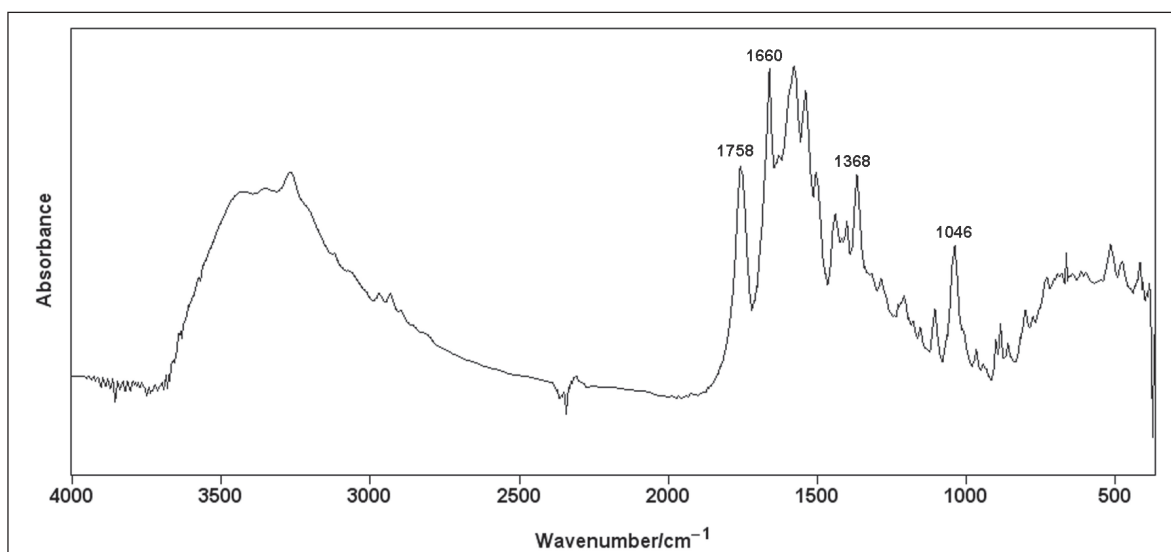


Figure 2: Infrared spectrum of the calculi revealing characteristic peaks for the calcium-ceftioxonate.

bladder and urinary tract²⁻⁷. This complication is termed “biliary pseudolithiasis” or “reversible cholelithiasis”. The majority of patients are asymptomatic but in few of them right upper abdominal quadrant pain, nausea, vomiting, and cholecystitis may develop. Cessation of CTX, symptomatic treatment and follow up ultrasound scan are usually sufficient interventions. Risk factors for CTX induced gallbladder precipitations are well established and include high doses of the drug, hypercalcemia, renal failure, total parenteral nutrition, bile stasis etc. CTX is filtered by the kidneys unchanged and forms insoluble salts with calcium in a 1:1 molar ratio. Risk factors for urolithiasis are not well established but certainly poor urine output, high doses of CTX and hypercalciuria may favor CTX induced nephrolithiasis. Stojanovic and Djuric Vijatovl recently reported a pediatric patient who developed nephrolithiasis in a kidney with congenital ureteropelvic junction obstruction⁹.

CTX induced urinary precipitates may be asymptomatic and detected on routine ultrasound scanning but in some patients may manifest hematuria or renal colic^{2, 10-17}. Bilateral obstruction with calculi may lead to acute renal failure as in the patient reported by Prince and Senac¹⁰. Often there is coexistence with biliary pseudolithiasis and confusion may arise in a child with pain in the right upper abdominal quadrant during CTX treatment¹¹. Thus, besides examination of the gallbladder, careful ultrasound scanning of the kidney and urinalysis should be performed.

The true prevalence of CTX induced nephrolithiasis is not known. The first case of CTX induced nephrolithiasis was reported by Shaad et al in 1988². In their series of 37 children treated with CTX, 16 developed biliary pseudolithiasis and one child had concurrent biliary and urinary calculi, manifesting renal colic and obstruction of the kidney. In the recent prospective study by Biner et

al 156 children with various infections treated with CTX at the doses of 50mg/kg, 75mg/kg and 100mg/kg have been followed by ultrasound scan¹⁷. Twenty seven children (17%) developed biliary pseudolithiasis or sludge, while only one child (0.6%) had urolithiasis. Mohham et al prospectively followed 284 children with pyelonephritis (185 girls and 99 boys)¹⁵. Nephrolithiasis was identified in 4 children (1.4%). None of the children had a metabolic risk factor.

Although our patient received CTX at moderate therapeutic dosage for 7 days, hypercalciuria was the most likely factor favoring development of urinary CTX precipitates. Therefore, in all patients who receive CTX and manifest hematuria, renal colic or lithiasis one should examine the possibility of urinary CTX precipitates. Finally we would like to emphasize the role of IR spectroscopy for the confirmation of ceftriaxone-associated nephrolithiasis⁸.

Conflict of interests: None declared

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