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CEFTRIAZONE-ASSOCIATED ACUTE GALLBLADDER ENLARGEMENT – AN UNEXPECTED DIAGNOSIS IN THE CHILD WITH URINARY TRACT INFECTION

OSTRE POWIĘKSZENIE PĘCHERZYKA ŻÓŁCIOWEGO ZWIĄZANE Z LECZENIEM CEFTRIAKSONEM – NIESPODZIEWANE ROZPOZNANIE U DZIECKA Z ZAKAŻENIEM UKŁADU MOCZOWEGO

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Abstract

Biliary sludge and/or biliary pseudolithiasis occur in patients treated with ceftriaxone with prevalence of 3-57%. Biliary obstruction can be the cause of the acute gallbladder enlargement. It is a minor complication, that usually does not give clinical symptoms and resolves once the drug is discontinued. The authors present a case of a 5-month old boy treated for the acute pyelonephritis. Routine ultrasound, performed on the 5th day of treatment with ceftriaxone, showed gallbladder enlargement. In the consecutive studies small gallbladder sludge was visible. Patient had no symptoms related to the gallbladder enlargement. Ultrasound performed 6 weeks from the drug discontinuation was completely normal.

Conclusions: *Patients treated with ceftriaxone should be monitored for biliary sludge and pseudolithiasis.*

Key words: biliary sludge, biliary pseudolithiasis, ceftriaxone, children, gallbladder

Streszczenie

Zagęszczenie żółci i/lub rzekoma kamica pęcherzyka żółciowego rozpoznawana jest u pacjentów leczonych ceftriaksonem z częstością od 3 do 57%. Utrudnienie odpływu żółci może być przyczyną ostrego powiększenia pęcherzyka żółciowego. Jest to łagodne powikłanie, które na ogół nie daje objawów klinicznych i ustępuje po odstawieniu antybiotyku.

Opisano 5-miesięcznego chłopca przyjętego do szpitala z powodu ostrego odmiedniczkowego zapalenia nerek. Rutynowe badanie USG jamy brzusznej wykonane w 5 dobie leczenia ceftriaksonem wykazało powiększenie pęcherzyka żółciowego. W kolejnym badaniu uwidoczniono niewielką ilość zagęszczonej żółci w postaci poziomego osadu w świetle pęcherzyka. Dziecko nie demonstrowało żadnych objawów klinicznych związanych z powiększeniem pęcherzyka żółciowego. Kontrolne badanie USG wykonane po 6 tygodniach od odstawienia antybiotyku było prawidłowe.

Wnioski: *Pacjenci leczeni ceftriaksonem powinni być monitorowani w kierunku zagęszczenia żółci i rzekomej kamicy pęcherzyka żółciowego.*

Słowa kluczowe: zagęszczenie żółci, rzekoma kamica żółciowa, ceftriakson, dzieci, pęcherzyk żółciowy

INTRODUCTION

Ceftriaxone – the 3rd generation cephalosporin antibiotic for its broad spectrum, long halftime period and convenient once-a-day dosing is widely used for treating infections in pediatric patients [1, 2]. In circulation the drug combines with albumins in about 85-95%, in 60% it is eliminated unchanged by kidneys and in 40% by biliary route [3, 4, 5]. Concentration of ceftriaxone in bile can be 100-200 times greater than in the blood serum [4, 6, 7, 8]. Liver eliminates high proportion of the drug in the form of water soluble salts. When there is a high concentration of ceftriaxone in the bile, it can react with calcium ions and form insoluble substances, which precipitate and lead to biliary sludge and/or cholelithiasis [1, 2, 5, 7]. Obstruction of the bile outflow can be the cause of acute gallbladder enlargement. Biliary sludge and/or pseudolithiasis (name underlines its reversible character) is a known side effect of ceftriaxone, and was reported for the first time in 1986 (9). Biliary sludge and pseudolithiasis occurs shortly after the introduction of the treatment with ceftriaxone and resolves soon after its discontinuation (3, 10). Insoluble compounds of ceftriaxone and calcium can precipitate also in urine and lead to urinary lithiasis. (3, 7)

CASE REPORT

The patient was a boy, born from the 3rd pregnancy, 41 weeks of gestation, body weight at birth 3880 g, Apgar score 10. Postnatal period was uneventful and abdomen ultrasound was normal. At the age of 5 months he was admitted to our hospital because of high fever 39°C, malaise and lack of appetite. Laboratory blood tests showed: elevated inflammation markers: WBC 20,1 G/l, CRP 18,6 mg/dl (norm <1.0 mg/dl), procalcitonin 2.68 ng/ml (norm <0.05 ng/ml), urinalysis showed leukocyturia 15-20 (HPF), urine culture was positive for *Escherichia coli* >10⁵. Other blood tests including: aminotransferases, gamma-glutamyl transferase, ALP, BUN and serum creatinine

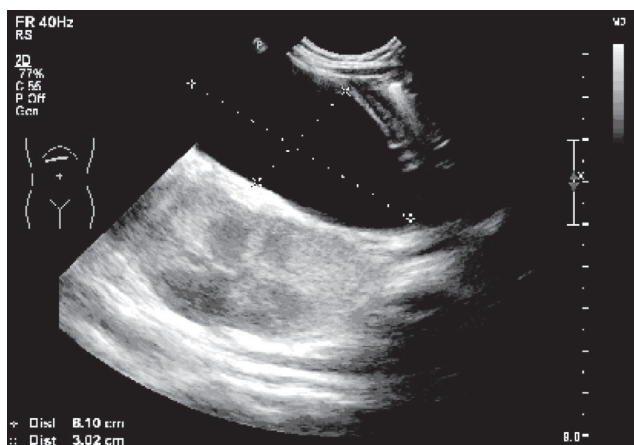


Fig. 1. Gallbladder enlargement 61 x 30 mm.

Ryc. 1. Powiększenie pęcherzyka żółciowego do wymiarów 61 x 30 mm.

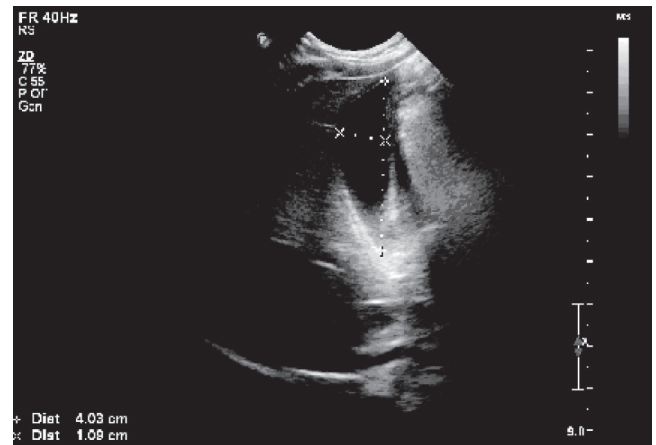


Fig. 2. Gallbladder enlargement 40 x 10 mm, some biliary sludge.

Ryc. 2. Powiększenie pęcherzyka żółciowego do wymiarów 40 x 10 mm, niewielka ilość zagęszczanej żółci w postaci poziomego osadu w świetle pęcherzyka.



Fig. 3. Normal gallbladder.

Ryc. 3. Prawidłowy pęcherzyk żółciowy.

were normal. Treatment with IV ceftriaxone 100 mg/kg/24 h was introduced. Ultrasound performed in the 5th day of treatment revealed gallbladder enlargement (61 x 30mm), with no signs of biliary sludge nor gallbladder wall thickening. (Figure 1). Follow up examination was done after 6 days and showed similar result, in the consecutive study performed after 22 days some biliary sludge was found (Figure 2). Antibiotic therapy was continued for 10 days with clinical status improvement and normalization of the laboratory tests. Ultrasound examination performed after 6 weeks from drug discontinuation showed normal size gallbladder (Figure 3).

DISCUSSION

Prevalence of biliary sludge and/or pseudolithiasis in patients treated with ceftriaxone is reported in 3-57% of cases [1, 3, 4, 10, 11]. Low prevalence of

these complications in part of the reports is probably due to the fact that ultrasound was performed late in the course of treatment, and some cases might be missed [8]. Ultrasound changes occur in 2-7 days after the introduction of ceftriaxone [1, 3]. In about 90% of cases in the first 5 days of treatment [10]. Biliary sludge or stones within the gallbladder are the most common findings in ultrasound examination. In most cases the size of the gallstones is below 3 mm [2, 10]. Ultrasound changes resolve in 2-150 days, but usually in the first days, after discontinuation of the treatment [1, 2, 3, 4, 8, 10].

There are many factors predisposing to biliary sludge and gallstones formation in children. The most common are: hemolysis in sickle cell anemia, congenital defects of the biliary tracts, bone marrow disorders, diseases of the bowels, as well as the biliary tract and liver, mucoviscidosis, malabsorption, abdominal surgeries, solid organs transplant, prolonged total parenteral nutrition, obesity and drugs [1, 4, 5, 12]. Ceftriaxone and octreotide are most commonly responsible for biliary sludge and pseudolithiasis [4, 12]. Meng compared the prevalence of pseudolithiasis in children treated with ceftriaxone and ceftazidime. It was present in 43.1% of patients treated with ceftriaxone and only in 2% in ceftazidime group. Ceftriaxone is widely used in patients treated for hepatitis and biliary tract infections. However, pseudolithiasis occurs in this group of patients significantly more often than in those who receive it for other reasons (68.6% vs 11.5%). Because of that, Meng postulates that ceftriaxone should be avoided in patients treated for hepatitis and biliary tract infections [1].

There are many reports of studies considering ceftriaxone side effects. No statistically significant differences have been found in prevalence of ultrasound changes in patients treated with ceftriaxone depending on: age, sex, body weight, time of year, dose, time of treatment, use of calcium supplements, parenteral nutrition nor fasting for surgeries [8, 10, 11]. However, ceftriaxone related biliary sludge and pseudolithiasis occurs slightly more often in children. Possible causes are: 1) non effective bile secretion due to long and narrow biliary tracts in children; 2) weaker contraction of gall bladder due to relatively lower concentration of cholecystokinin; 3) common febrile illnesses and dehydration which may contribute to bile congestion [1].

Biliary sludge and pseudolithiasis are minor complications, and usually do not give clinical symptoms. Nausea, vomiting, abdominal pain, jaundice, cholecystitis, biochemical signs of cholestasis occur in 2.6-43% of cases. [1, 3, 4, 8, 10]. Ultrasound examination should be performed in all children presenting with symptoms of cholelithiasis. In case of ceftriaxone related pseudolithiasis, discontinuation of the drug is the only recommended intervention. All the symptoms resolve once the drug is withdrawn [1, 2, 3, 5]. Need for the surgical intervention is very rare [8]. Precipitation of the compounds of ceftriaxone and calcium in urine can lead to urinary lithiasis in 6.3% of children [3, 7]. Asymptomatic urinary lithiasis

most commonly occurs in 2-7 days of treatment with ceftriaxone [7].

In the presented case the gall bladder enlargement was found in the 5th day of the treatment with ceftriaxone. It was a routine abdominal ultrasound, performed in a child with acute pyelonephritis. The patient had no symptoms related to the gall bladder enlargement. In the consecutive ultrasound examination done after 22 days of treatment some biliary sludge was detected. Ceftriaxone is a broad spectrum antibiotic used for treating the most severe bacterial infections in children [2, 4, 5, 12], and it is rarely required for uncomplicated urinary tract infections. When deciding on the use of ceftriaxone, one has to keep in mind possible side effects.

CONCLUSION

Patients treated with ceftriaxone should be monitored for possible biliary sludge, biliary pseudolithiasis and urinary lithiasis.

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Authors' contributions/Wkład Autorów

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