Clinics in Surgery

Case Report
Published: 01 May, 2017

Biliary Lithiasis Associated with the Use of Ceftriaxone for Gastroenteritis in Children: Case Report and Literature Review

Carlos Teixeira Brandt, Maria Cecilia Santos Cavalcanti Melo, Monize Naara Lourenço de Morais Soares and Daniella Bandin Cruz*

Department of Pediatric Surgery, Olinda Medical School, Brazil

Abstract

Obejective: Ceftriaxone is used for the treatment of gastroenteritis in children when hospitalized, with the possible complication of cholelithiasis in the first days of administration of this antimicrobial. The handling of this side effect remains discordant among surgeons. The present report aims at showing different views between two pediatric surgeons and questions the weight of evidence among the proposed approaches.

Case Presentation: MSAS, white female, age of 3.5 years admitted to hospital for gastroenteritis and dehydration. In the therapeutic prescription there was inclusion of ceftriaxone. After three days, the child healed the gastroenteritis. However, she began to present abdominal pain that required analgesic and antispasmodic. Abdomen ultrasound revealed the presence of multiple bile stones with an average size of 0.4 cm. In the follow-up, abdominal pain became more frequent and intense. After 10 days of hospital discharge, new ultrasound showed the presence of an echogenic image measuring 1.5 cm, compatible with bile stone. The presumption was that cholelithiasis would be related to the use of ceftriaxone. The opinions of pediatric surgeons differed as to the need for emergency cholecystectomy. Significant and persistent abdominal pain continued. Follow-up ultrasound evidenced a change in the aspect of the bile stone, passing from the multilobulated aspect suggesting compact bile conglomerate. In the latter ultrasound, three small bile stones were observed, the largest one measuring 0.3 cm ("pseudo biliary lithiasis"). The argument of one of the surgeons that this situation was more serious, because it added the possibility of producing jaundice or pancreatitis weighed on the parents' acceptance of cholecystectomy. The child underwent surgery without complications and the evolution was satisfactory.

Discussion: The management of pseudo biliary lithiasis due to ceftriaxone is still controversial and additional evidence is required for gold standard conduct in the resolution of these cases. Post-cholecystectomy syndrome needs to be included in this decision-making process.

Keywords: Ceftriaxone; Biliary lithiasis; Pseudolithiasis; Post-cholecystectomy syndrome; Children

OPEN ACCESS

Correspondence:
Carlos Teixeira Brandt, Department of Pediatric Surgery, Olinda Medical School – Pernambuco, Brazil, E-mail: carlosbrandt@bol.com.br

Received Date: *08 Mar 2016*
Accepted Date: *23 Apr 2017*
Published Date: *01 May 2017*

Citation:
Brandt CT, Melo MCSC, de Morais Soares MNL, Cruz DB. Biliary Lithiasis Associated with the Use of Ceftriaxone for Gastroenteritis in Children: Case Report and Literature Review. Clin Surg. 2017; 2: 1455.

Introduction

Childhood biliary lithiasis, although increasing in incidence, persists as an infrequent problem and is usually associated with hemolytic diseases, congenital anomalies of the bile ducts, prolonged parenteral nutrition, diseases of the terminal ileum, and transplantation of bone marrow or solid organ [1,2]. Its prevalence in children is estimated at 0.13% to 1.9% [3,4].

Ceftriaxone is a parenteral, third-generation cephalosporin commonly used as an antimicrobial agent in pediatric practice because of its broad spectrum, prolonged half-life, and relatively few side effects [5-8]. Among these effects is the association with the formation of bile sludge that can evolve to lithiasis [6-8]. This complication, although reported for more than three decades [9,10], presents no gold standard therapeutic approach, which is still controversial [6-8]. However, the evidence that this condition was reversible had already been and continues to be reported [8,11,12]. On the other hand, the conduct of cholecystectomy in these cases requires the concern of the post-cholecystectomy syndrome that can occur in the late follow-up of these patients [13-16].

The present case report aims to encourage reflection on the therapeutic management of biliary

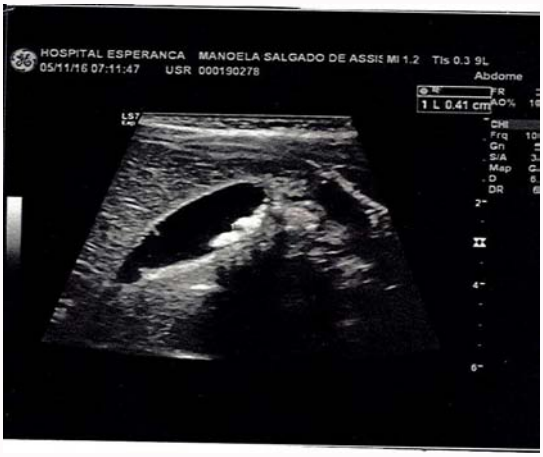

Figure 1: Normal-looking gallbladder with thin wall (presence of multiple stones with a mean size of 0.4 cm).

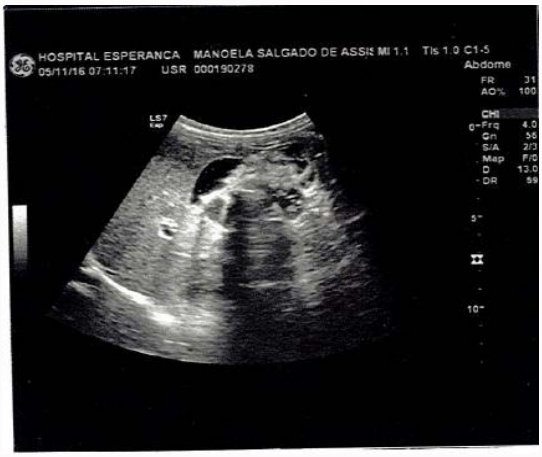

Figure 2: Distended gallbladder of thin wall showing the presence of echogenic image, producing posterior acoustic shadow measuring 1.5 cm, compatible with bile sludge (stone?).

lithiasis due to the use of ceftriaxone and to add to the problem of developing post-cholecystectomy syndrome.

Case Presentation

MSAS, white female, age 3.5 years, eutrophic, was admitted to a tertiary hospital due to diarrhea, vomiting and abdominal pain, having had the initial diagnosis of gastroenteritis and dehydration. The blood cell count showed leukocytes count as 20,800/mm^3, without left shift, lymphocytosis (20%), and high platelet count.

The child received hydroelectrolytic repair and antibiotic therapy (parenteral ceftriaxone). In the sequence she received water and electrolyte maintenance and progressive oral intake; besides the antimicrobial. After three days of admission, the child evolved to cure gastroenteritis, but then presented abdominal pain that required analgesic and antispasmodic. Ultrasonography of the abdomen revealed an abnormal presence of multiple stones with a mean size of 0.4 cm (Figure 1).

In the follow-up the abdominal pain became more intense and frequent, but the child was discharged from hospital. Ten days later new ultrasound showed an abnormal echogenic image, which produced posterior echogenic acoustic shadow measuring 1.5 cm

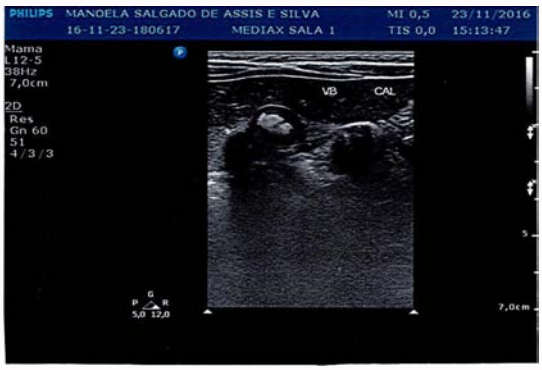

Figure 3: Normal-looking gallbladder with thin wall. Irregular stone (compact bile sludge). Possibility of stone dissolution.

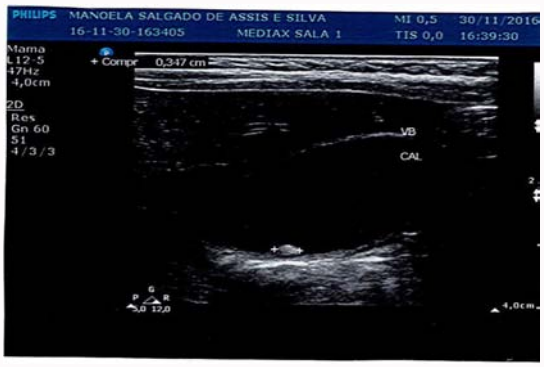

Figure 4: Normal-looking gallbladder (thin normal wall). Three small stones, the largest one with diameter of 0.3 cm (pseudo bile stone in the resolution phase?).

compatible with bile stone (Figure 2).

The diagnosis presumption was that cholelithiasis would be related to the recent use of ceftriaxone. The opinions of two pediatric surgeons differed as to the need for emergency cholecystectomy. The clinical picture of persistent and important abdominal pain continued. Follow-up ultrasonography evidenced a change in the appearance of stone, passing from the multilobulated aspect suggesting compact bile conglomerate (Figure 3).

In the last one, three small mobile echogenic stones were observed, the largest one measuring 0.3 cm, being considered the possibility of "pseudolithiasis" in the resolution phase (Figure 4).

One of the surgeon's arguments that this situation was more serious, because it added the possibility of producing jaundice or pancreatitis weighed in the parents' acceptance of cholecystectomy by video laparoscopy. The child underwent surgery without complications and the postoperative follow-up was satisfactory. Up to the present she is well, under the care of gastroenterologist who maintains adequate diet for age with slight restriction to lipid intake.

Discussion

The prevalence of pseudolithiasis after the use of ceftriaxone ranges from 12% to 45% [17,18] probably due to the pediatrician's attention and vigilance for this possible complication and good quality ultrasound follow-up, and the image professional with good experience [19].

The etiology of this phenomenon persists as a matter of debate,

with opinions ranging from the presence of calcium salts in the components of the products administered with ceftriaxone, which presents 40% of biliary excretion [20] and that of interaction with the bile salts. Other possibilities include prolonged bruising and bed immobilization [21], to genetic alterations related to the "A (TA) 7TAA-UGT1A1" polymorphism encoding UDP-glucuronosyltransferase (UDPG) [22].

The symptomatology of this complication is translated by intense abdominal pain, colic type, symptoms presented by the child's reason of the present report. However, the child described in this case did not present with fever, nausea and bilious vomiting that may occur in some of these cases [8].

The diagnosis is often made by ultrasound of the abdomen, a diagnostic tool that can be used to monitor the evolution of bile sludge, through calculation and its possible spontaneous resolution [1,2,4,6-8].

The core of the present case report is the two pediatric surgeon's opinions regarding the urgent need for cholecystectomy. One of the surgeons did not accept this approach having in minded that cholecystectomy not only can produce morbidity or even mortality, but also can be associated with post cholecystectomy syndrome.

The occurrence of jaundice and pancreatitis has been reported in rare cases, with no more than 3% of these patients [23,24], however the present child presented with improving clinical signs and particularly the images from the ultrasonography that indicated the direction of spontaneous resolution. The question posed by one of the pediatric surgeons was whether one or two days of clinical follow-up could complete the time of resolution without surgical intervention.

In general, the rate of dissolution of cholelithiasis in children is higher in infants, with biliary mud and particularly that related to the use of ceftriaxone. Thus, it is possible that the clinical follow-up of the child, object of the present report, could benefit from the increasing the clinical follow-up, without surgical intervention. On the other hand, non-removal of the gallbladder could prevent post-cholecystectomy syndrome, reported by several researchers [13-15], especially Russians [25-27].

Studies with more consolidated evidence are necessary for the definition of precision medicine (gold standard approach) in these cases, since the long-term follow-up of these children may be associated not only with digestive symptoms (post cholecystectomy syndrome) that may require the need of enzymes [16], but also because the greater risk factor of adenocarcinoma development of the right colon [13] of these patients.

References

1. Campbell S, Richardson B, Mishra P, Wong M, Samarakkody U, Beasley S, et al. Childhood cholecystectomy in New Zealand: A multicenter national 10 year perspective. J Pediatr Surg. 2016;51(2):264-7.
2. Walker SK, Maki AC, Cannon RM, Foley DS, Wilson KM, Galganski LA, et al. Etiology and incidence of pediatric gallbladder disease. Surgery. 2013;154(4):927-31.
3. Wesdorp I, Bosman D, de Graaff A, Aronson D, van der Blij F, Taminiau J. Clinical presentations and predisposing factors of cholelithiasis and sludge in children. J Pediatr Gastroenterol Nutr. 2000;31(4):411-7.
4. Ganesh R, Muralinath S, Sankaranarayanan VS, Sathiyasekaran M. Prevalence of cholelithiasis in children--a hospital-based observation. Indian J Gastroenterol. 2005;24(2):85.
5. Araz N, Okan V, Demirci M, Araz M. Pseudolithiasis due to ceftriaxone treatment for meningitis in children: report of 8 cases. Tohoku J Exp Med. 2007;211(3):285-90.
6. Khotchava M, Lashkhi E, Jokhtaberidze T, Shalamberidze I. Ceftriaxone-induced gallbladder lithiasis in case of intestinal bacterial infections (Case reports). Georgian Med News. 2016;250:72-5.
7. Rodríguez Rangel DA, Pinilla Orejarena AP, Bustacara Diaz M, Henao García L, López Cadena A, Montoya Camargo R, et al. Gallstones in association with the use of ceftriaxone in children. An Pediatr (Barc). 2014;80(2):77-80.
8. Costa DL, Barbosa MD, Barbosa MT. Cholelithiasis associated with the use of ceftriaxone. Rev Soc Bras Med Trop. 2005;38(6):521-3.
9. Schaad UB, Tschäppeler H, Lentze MJ. Transient formation of precipitations in the gallbladder associated with ceftriaxone therapy. Pediatr Infect Dis. 1986;5(6):708-10.
10. Lopez AJ, O'Keefe P, Morrissey M, Pickleman J. Ceftriaxone-induced cholelithiasis. Ann Intern Med. 1991;115(9):712-4.
11. Schaad UB, Suter S, Gianella-Borradori A, Pfenninger J, Auckenthaler R, Bernath O, et al. A comparison of ceftriaxone and cefuroxime for the treatment of bacterial meningitis in children. N Engl J Med. 1990;322(3):141-7.
12. Niwa M, Tochii K. Four cases of ceftriaxone-associated biliary pseudolithiasis. Nihon Shokakibyo Gakkai Zasshi. 2016;113(2):281-8.
13. Ure BM, Jesch NK, Nustede R. Postcholecystectomy syndrome with special regard to children--a review. Eur J Pediatr Surg. 2004;14(4):221-5.
14. Jaunoo SS, Mohandas S, Almond LM. Postcholecystectomy syndrome (PCS). Int J Surg. 2010;8(1):15-7.
15. Lamberts MP, Lugtenberg M, Rovers MM, Roukema AJ, Drenth JP, Westert GP, et al. Persistent and de novo symptoms after cholecystectomy: a systematic review of cholecystectomy effectiveness. Surg Endosc. 2013;27(3):709-18.
16. Kharitonova LA, Kuramshin RR. Enzyme Therapy of Postcholecystectomy Syndrome In Children. Eksp Klin Gastroenterol. 2015;(1):55-61.
17. Ustyol L, Bulut MD, Agengin K, Bala KA, Yavuz A, Bora A, et al. Comparative evaluation of ceftriaxone- and cefotaxime-induced biliary pseudolithiasis or nephrolithiasis: A prospective study in 154 children. Hum Exp Toxicol. 2016.
18. Famularo G, Polchi S, De Simone C. Acute cholecystitis and pancreatitis in a patient with biliary sludge associated with the use of ceftriaxone: a rare but potentially severe complication. Ann Ital Med Int. 1999;14(3):202-4.
19. Nayak A, Slivka A. Ceftriaxone-Induced Gallstones: Case Report and Literature Review. ACG Case Rep J. 2014;1(3):170-2.
20. Shaffer EA. Gallbladder sludge: what is its clinical significance? Curr Gastroenterol Rep. 2001;3(2):166-73.
21. Murata S, Aomatsu T, Yoden A, Tamai H. Fastingand bedrest, even for arelatively short period, are riskfactors for ceftriaxone-associated pseudolitiasis. Pediatr Int. 2015; 57(5):942-6.
22. Fretzayas A, Liapi O, Papadopoulou A, Nicolaidou P, Stamoulakatou A. Is Ceftriaxone-Induced Biliary Pseudolithiasis Influenced by UDP-Glucuronosyltransferase 1A1 Gene Polymorphisms? Case Rep Med. 2011;2011:730250.
23. Famularo G, Polchi S, De Simone C. Acute cholecystitis and pancreatitis in a patient with biliary sludge associated with the use of ceftriaxone: a rare but potentially severe complication. Ann Ital Med Int. 1999;14(3):202-4.
24. Tuna Kirsacliogluc, Çuhacı Çakır B, Bayram G, Akbıyık F, Işık P, Tunç B. Risk factors, complications and outcome of cholelithiasis in children: A retrospective, single-centre review. J Paediatr Child Health. 2016;52(10):944-9.

25. Iakimova LV, Kharitonova LA, Kuramshin RR. Risk factors and mechanisms of the postcholecystectomy syndrome development in children. Eksp Klin Gastroenterol. 2013;(1):48-54.

26. Bystrovskaia EV, Il'chenko AA. Pathogenetic and diagnostic aspects of postcholecystectomy syndrome. Eksp Klin Gastroenterol. 2009;(3):69-80.

27. Tsimmerman IS, Kunstman TG. Post-cholecystectomy syndrome: the modern view of the problem. Klin Med (Mosk). 2006;84(8):4-11.