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

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Abstract

Objective: 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

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 lithiasis.
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/mm³, 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 acoustic shadow measuring 1.5 cm, compatible with bile sludge (stone?).

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).

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 mind 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 glucuronosyltransferase (UDPG) [22].

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
