ORIGINAL RESEARCH PAPER

Volume-7 | Issue-1 | January-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A CASE OF ACUTE CHOLECYSTITIS IN ADULT REQUIRING SURGERY DURING INTRAVENOUS CEFTRIAXONE TREATMENT.

Surgery

Alberto Schanaider Postgraduate Program In Surgical Science. Department of Surgery, School of Medicine, Federal University of Rio De Janeiro, Brazil. FAPERJ, CNPq.

Ricardo Antônio Correa Lima Department of General And Specialized Surgery, School Of Medicine And Surgery, University of The State of Rio De Janeiro, Brazil

Marcel Vasconcellos* Postgraduate Program In Surgical Science. Department of Surgery, School of Medicine, Federal University of Rio De Janeiro, Brazil *Corresponding Author

ABSTRACT

Background: Intravenous ceftriaxone therapy in adults can cause microlithiasis and acute cholecystitis. Conservative treatment has been the ordinary choice for dealing with such situation, most of the times because of benign evolution observed in children.

Presentation of case: The authors present a case report of acute cholecystitis with microlithiasis in a 56-year-old male following ceftriaxone therapy, that requires a surgical management.

Discussion: Adults receiving ceftriaxone therapy must have a closely follow-up considering, the potential risk of surgical complications, mainly the acute cholecystitis.

Conclusion: Acute abdomen after intravenous ceftriaxone treatment has been usually underestimated and surgeons must be aware about such complication in adult population.

KEYWORDS

Ceftriaxone, Cholecystitis, Surgery, Case report, Adult

Introduction

The authors present a case acute cholecystitis, during intravenous ceftriaxone treatment for Lyme disease that requires surgical management. In the scientific literature and even in the pharmaceutics' leaflets, most of the reports are limited to describe the formation of biliary sludge in the gallbladder[1], which disappears at the end of the treatment, underestimating surgical complications. In adults, the choice of a conservative regimen to deal with an acute cholecystitis developed during an intravenous ceftriaxone treatment is highly risky considering the potential of microlithiasis to cause not only cholecystitis but also choledocholithiasis, cholangitis and pancreatitis[2].

Case report

A 56-year-old Caucasian man, working as high educational teacher, was admitted in the Emergency Department of a private hospital coming from its residence in Rio de Janeiro, Brazil. The major complaining was a right upper quadrant pain beginning six hours earlier, after an abrupt onset during a dinner, associated with both moderate pain in the back relieved when leaning forward and nausea. In his background history, it was mentioned a metabolic syndrome, taking regular medication for diabetes mellitus, hypertension and dyslipidemia control. A gallbladder ultrasonography (for steatosis evaluation) evaluation six months before, was consistent with normality and the patient was asymptomatic until the acute abdominal condition appeared. He had also a diagnostic hypothesis for Lyme disease and had already begun a treatment with ceftriaxone, sixteen days before. Antibiotic prescription covered a dose of 2 g once daily, from day one to 5th and 1g for further 15 days, dissolved in a dextrose 5% solution with a dripping for at least 30 minutes, into a peripherally inserted central catheter. Former gallbladder ultrasonography (for steatosis evaluation), six months before, was consistent with normality. On admission, the patient was slightly febrile without liver function test abnormalities. He had only an amylase level of 149U/L and the white blood cells count was 10.300/µl with 85% neutrophils. A positive Murphy's sign at physical examination and even during ultrasound evaluation were present. Abdominal ultrasound image showed thickness of the gallbladder wall with biliary sludge and multiple and mobile microlithiasis in lateral decubitus position consistent with cholecystitis (Figure 1). One shot of an intravenous second-generation cephalosporin (2g) was administered prophylactically. The staff team with great expertise performed a laparoscopic cholecystectomy under general anaesthesia and patient discharged occurred 24 hours later with an excellent outcome. The main histopathological finding was a marked inflammatory infiltrate in the wall of gallbladder characterizing an acute cholecystitis with microlithiasis.

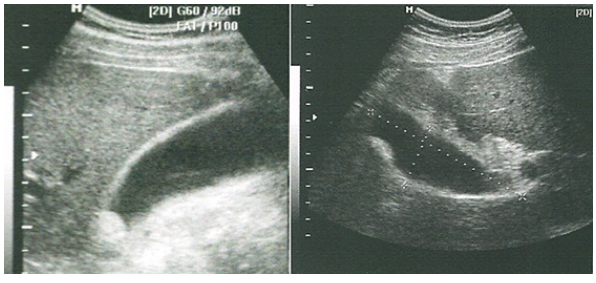

Fig. 1- Ultrasonography showing a distended gallbladder (11 cm on longitudinal axis) with wall thickening, containing sludge and mobile microlithiasis.

Discussion

Cholelithiasis affects approximately 10% of the adult population in Western countries[3]. An estimated 30% of adults with asymptomatic cholelithiasis will require surgery during their lifetime[4]. However, cholelithiasis in the pediatric age group has been considered rare and is associated with low rates of complications. Gallstone formation is multifactorial but very little has been reported linking gallstone formation and ceftriaxone in adult population[5]. Biliary lithiasis smaller than 3mm are called microlithiasis[6]. About 20% of cases of microlithiasis can cause pancreatitis, but cholecystitis and cholangitis have also clinical relevance[7]. The syndrome commonly referred as "pseudo-lithiasis" consists of sludge and stones formation after ceftriaxone treatment that has a spontaneous resolution between 3 days up to 3 months when the drug is withdrawal[8]. Symptoms of cholecystitis are usually reported in up to 5% of pediatric patients who develop pseudo-lithiasis but there are some reports showing some severe outcome in children.

Rodriguez Rangel identified the presence of pseudolithiasis in 42.5% patients of a prospective study, with 73 individuals (from 1 month to 18 years-old), after ceftriaxone treatment. Symptoms were present in 22.6% of them and a four year-old child had choledocolithiasis with cholangitis[9]. Kim reported a case of acute necrotizing cholecystitis also in a child[10] and Alemayehu had to perform a laparoscopic cholecystectomy in another one with ceftriaxone-induced pseudolithiasis, former treated for perforated appendicitis[11].

On the other hand, it is remarkable the existence of very few data with accuracy about the incidence of ceftriaxone inducing surgical complications, in adult population. In the present case, the patient had

never presented complaints of biliary colic, fat intolerance, or any evidence of biliary lithiasis and there was no previous biliary calculus or sludge proven by a normal ultrasound performed only a few months before the acute episode.

The authors developed a bibliographic research on Medline database covering the last 30 years, combining the following keywords: [“ceftriaxone" AND (“acute cholecystitis” OR “microlithiaisis” OR “pancreatitis”)] with a filter for “Adult 19+ years”.

Becker et al.[12] assume, in 2009, that they reported the first case in the medical literature with symptomatic acute cholecystitis triggered by ceftriaxone-associated gallbladder sludge and solid ceftriaxone gallstone formation in an adult patient, requiring cholecystectomy. However, among 29 case reports of adult patients receiving parenteral ceftriaxone therapy, 89% had symptoms and 40% developed complications such as acute biliary cholecystitis, acute biliary pancreatitis and choledocolithiasis eventually with cholangitis. Laparoscopic cholecystectomy was performed in 18 cases (28%), 78% of them related to Lyme treatment as seen in the case we have reported. Ettestad analysed two case-control studies in patients with suspected Lyme disease receiving a daily ceftriaxone dose greater than 40 mg/kg. Fourteen of 25 biliary case-patients underwent cholecystectomy with histopathological evidence of cholecystitis and half of them had gallstones[13].

In an adult patient, Famularo et al reported a case of acute cholecystitis and pancreatitis with biliary sludge associated with the use of ceftriaxone treated with open cholecystectomy[2]. Likewise, Lopes et al reported another adult patient with intravenous ceftriaxone therapy for endocarditis, who underwent cholecystectomy because of development of pancreatitis and ceftriaxone stones[14].

It is worrisome that even in patient information in the medicine package leaflet, from almost all pharmaceutical laboratories; an important complication like cholecystitis has been underreported. In general, they highlight the presence of biliary sludge and more rarely pancreatitis, both reversible, disappearing after interrupting therapy. Indeed, children and infants are associated with low rates of adverse effects and isolated evidences in adults are commonly used to reinforce a conservative approach, suggesting that ceftriaxone-induced both cholelithiasis and cholecystitis can be a relatively benign condition[7]. However, we emphasize that this argument cannot be applied to adults because life-threatening risks have different prognosis from those in childhood, including the incidence of surgical intervention, higher in adults.

Ceftriaxone is a third generation of cephalosporin. Approximately 60% of dose are excreted in the urine and the remainder is secreted in the bile as unchanged drug. In serious miscellaneous infections, it is recommended ceftriaxone intravenously with total daily dose of 50 to 100 mg/kg, with a maximum dose of 2 grams daily, except in meningitis treatment (2g iv. q12 hours). For intravenous administration, as seen in the case report, a sterile powder of ceftriaxone has to be dilute in some compatible solutions, such as 5% Dextrose or 0.9% Sodium Chloride and infused for at least 30 minutes of dripping. It seems that greater severity of the effects is directly proportional to the dose of the drug. Bile nucleation with crystals precipitation in a ceftriaxone supersaturated bile is the initial step in the complex process of lithogenic bile and subsequent onset of microlithiasis development. Maranan presented a 13-year-old patient, which developed pancreatitis after combining treatment with ceftriaxone. He was submitted to a cholecystectomy and the analysis of stones composition showed 100% of ceftriaxone[15].

Growing up evidences have been showing that cholecystitis, although rare in youngsters, has become increasingly recognized in adults. However, the underreporting of surgical complication, especially in the adult group can give a false sense of security with a conservative treatment based on antibiotic withdrawal. We should be aware of the fact that sometimes administration of ceftriaxone results in the formation of biliary sludge and can cause severe adverse events such as acute cholecystitis and pancreatitis mostly in adult patients. Clinical evidences suggest that an ultrasonographic surveillance should be performed closely in adults treated with intravenous ceftriaxone, in order to allow an early detection of complications.

Once a patient develops symptoms or complications related to gallstones (biliary colic, acute cholecystitis, cholangitis, and/or pancreatitis) a wise judgment has to be done. In several circumstances, it is recommended an interventional or surgical therapy (for instance a cholecystectomy or an endoscopic sphincterotomy with stone extraction or biliary drainage). The likelihood of subsequent symptoms or complications with conservative treatment is high in adults and include the development of gallbladder gangrene or perforation, acute pancreatitis with abscess, necrosis, and even acute cholangitis that can be life threatening.

Further prospective studies are needed to evaluate the real incidence of both acute cholecystitis and pancreatitis in adult's patients treated with intravenous ceftriaxone in order to evaluate the risks and to prevent serious injury.

Conclusion

In conclusion, several life-threatening complications after intravenous ceftriaxone administration in adult patients are usually underestimated. When microlithiasis are associated with cholecystitis, it must be considered the surgical intervention as a first-choice treatment.

References

1. Stinton LM, Shaffer EA. Epidemiology of gallbladder disease: cholelithiasis and cancer. Gut Liver 2012;6(2):172-87.
2. 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.
3. Brazzelli M, Cruikshank M, Kilonzo M, Ahmed I, Stewart F, McNamee P, et al. Systematic review of the clinical and cost effectiveness of cholecystectomy versus observation/conservative management for uncomplicated symptomatic gallstones or cholecystitis. Surg Endosc 2015;29(3):637-47.
4. Schirmer BD, Winters KL, Edlich RF. Cholelithiasis and cholecystitis. J Long Term Eff Med Implants 2005;15(3):329-38.
5. Jüngst C, Kullak-Ublick GA, Jüngst D. Gallstone disease: Microlithiasis and sludge. Best Pract Res Clin Gastroenterol 2006;20(6):1053-62.
6. Ruggiero S, DI Nardo R, Polimeno T, Rossi F, Capuano A. Ceftriaxone-induced pancreatitis in a pediatric patient: case report. J Chemother 2010;22(1):63-5.
7. Tomoda T, Ueki T, Saito S, Tatsukawa M, Nawa T, Hamamoto H, Endo H, et al. A case of ceftriaxone-associated pseudolithiasis in an adult patient that disappeared after the discontinuation of ceftriaxone. Nihon Shokakibyo Gakkai Zasshi 2013;110(8):1481-6.
8. 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.
9. Rodríguez Rangel DA, Pinilla Orejarena AP, Bustacara Diaz M, Garcia H, 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.
10. Kim S, Gura KM, Puder M. Acute necrotizing cholecystitis: a rare complication of ceftriaxone-associated pseudolithiasis. Pediatr Surg Int 2006;22(6):562-4.
11. Alemayehu H, Desai AA, Thomas P, Sharp SW, St Peter SD. Ceftriaxone-induced pseudolithiasis in children treated for perforated appendicitis. Pediatr Surg Int 2014;30(3):323-6.
12. Becker CD, Fisher RA. Acute cholecystitis caused by ceftriaxone stones in an adult. Case Rep Med 2009; 2009:132452.
13. Ettestad PJ, Campbell GL, Welbel SF, Genese CA, Spitalny KC, Marchetti CM, et al. Biliary complications in the treatment of unsubstantiated Lyme disease. J Infect Dis 1995;171(2):356-61.
14. Lopez AJ, O'Keefe P, Morrissey M, Pickleman J. Ceftriaxone-induced cholelithiasis. Ann Intern Med 1991;115(9):712-4.
15. Maranan MC, Gerber SI, Miller GG. Gallstone pancreatitis caused by ceftriaxone. Pediatr Infect Dis J 1998;17(7):662-3.