

# Ceftriaxone-associated biliary pseudolithiasis

M. Rienstra<sup>1\*</sup>, M.J.M. Bonten<sup>2</sup>, C.A.J.M. Gaillard<sup>1</sup>

<sup>1</sup>Department of Internal Medicine, Meander Medical Centre, Amersfoort, the Netherlands,

<sup>2</sup>Department of Medical Microbiology, University Medical Centre, Utrecht, the Netherlands,

\*corresponding author: tel.: +31 (0)33-850 50 50, fax: +31 (0)33-850 26 95, e-mail: M.Rienstra@meandermc.nl

## INTRODUCTION

Ceftriaxone is a commonly used third-generation cephalosporin that has antimicrobial activity against many Gram-positive and Gram-negative organisms. Generally, ceftriaxone is a safe antibiotic. We describe a case of biliary pseudolithiasis due to intravenous ceftriaxone therapy.

## CASE REPORT

A 64-year-old man was admitted with relapsing fever after six weeks of antibiotic treatment for enterococcal aortitis. Eight months before, he underwent aortic root repair surgery for thoracic aorta aneurysm type A, i.e. aortic valve replacement with a bioprosthesis and supra-coronary aorta ascendens replacement.

Because of 1) failure of previous therapy, 2) high-level of aminoglycoside resistance, together with 3) high risk for nephrotoxicity with long-term aminoglycoside use, long-term (three months) therapy with amoxicillin, 2 g every 4 hours, plus ceftriaxone, 2 g every 12 hours was given through a peripherally inserted central catheter. After initiation, antibiotic therapy was continued on an outpatient basis. Every two weeks, the patient was seen at the outpatient clinic.

After three weeks, he developed acute abdominal pain, with elevated bilirubin and liver enzyme levels. Abdominal ultrasound showed multiple, low-echo concretions, but no signs of cholecystitis or choledocholithiasis (*figure 1A*). Previous imaging had been normal. After reduction of the dose and infusion rate of ceftriaxone (to 1 g every 24 hours) the abdominal complaints disappeared and subsequent abdominal ultrasound monitoring failed to demonstrate gall sludge or stones (*figure 1B*).

**Figure 1.** Abdominal ultrasound imaging of the gallbladder, showing biliary pseudolithiasis during ceftriaxone treatment (A) and normal gallbladder after discontinuation of ceftriaxone treatment (B)



## WHAT IS YOUR DIAGNOSIS?

See page 114 for the answer to this photo quiz.

---

ANSWER TO PHOTO QUIZ (ON PAGE 113)  
CEFTRIAXONE-ASSOCIATED BILIARY PSEUDOLITHIASIS

---

## DIAGNOSIS

Recently, Gavalda *et al.* reported on the effective and safe combination of ampicillin plus ceftriaxone as treatment of enterococcal endocarditis.<sup>1</sup> In our patient, unfortunately, a side effect of ceftriaxone occurred, i.e. biliary pseudolithiasis, which diminished after reducing the dose. Ceftriaxone is mainly eliminated by the kidney, although 10 to 20% of the drug is eliminated in the bile. Ceftriaxone salt precipitates occur in 0.1 to 1% of all cases. *In vitro* analysis of the biliary precipitates induced by this agent showed the calcium salt of ceftriaxone. At doses  $\geq 2$  g, precipitation of ceftriaxone could occur.<sup>2</sup> Furthermore, a high infusion rate of ceftriaxone and impaired gallbladder emptying may also lead to high concentrations of ceftriaxone in the human bile and predispose to biliary pseudolithiasis. In rare cases, most of which have involved children, biliary pseudolithiasis led to abdominal pain, and resolved when ceftriaxone was discontinued.<sup>3,4</sup>

Although biliary pseudolithiasis is a relatively rare complication of ceftriaxone therapy, clinicians need to be aware of this complication, since adequate monitoring of biliary pseudolithiasis and hyperbilirubinaemia is necessary.

## REFERENCES

1. Gavalda J, Len O, Miró J, et al. Brief communication: treatment of *Enterococcus faecalis* endocarditis with ampicillin plus ceftriaxone. *Ann Intern Med.* 2007;146:574-9.
2. Shiffman M, Keith F, Moore E. Pathogenesis of ceftriaxone-associated biliary sludge. *In vitro* studies of calcium-ceftriaxone binding and solubility. *Gastroenterology.* 1990;99:1772-8.
3. Cometta A, Gallot-Lavallée-Villars S, Iten A, et al. Incidence of gallbladder lithiasis after ceftriaxone treatment. *J Antimicrob Chemother.* 1990;25(4):689-95.
4. Schaad U, Wedgwood-Krucko J, Tschaeppler H. Reversible ceftriaxone-associated biliary pseudolithiasis in children. *Lancet.* 1988;2:1411-3.