Open Journal of
Clinical & Medical
Case Reports

Volume 4 (2018)
Issue 17

ISSN 2379-1039

Acute cholangitis after ceftriaxone administration: A case report

Kuniyasu Harimoto*; Tatsuya Kawasaki; Tadaaki Kamitani; Satoru Sekoguchi; Hirokazu Oyamada

***Kuniyasu Harimoto, MD**

Department of Cardiology, Matsushita Memorial Hospital, Sotojima 5-55, Moriguchi, Osaka 570-8540, Japan
Phone: +81-66992-1231, Fax: +81-66992-4845; E-mail: harimoto.kuniyasu@jp.panasonic.com

Abstract

Ceftriaxone is a third-generation cephalosporin with a long half-life and no dose adjustment is required in most cases. Attention should, however, be paid to biliary sludge, since ceftriaxone is excreted mainly in the bile. Here, we report a 70-year-old man in whom acute cholangitis developed 10 days after administration of intravenous ceftriaxone at a dose of 2.0 g daily for pneumonia. A large amount of biliary sludge was detected on abdominal ultra sonography, accompanied by enlarged bile ducts on computed tomography, although the patient had had three meals a day after admission. No gallstone was shown on endoscopic retrograde cholangiopancreatography. Endoscopic nasobiliary drainage was placed and ceftriaxone was withdrawn, followed by other antibiotics. The drainage fluid was sterile. The patient died 4 days after the onset of acute cholangitis because of the rapid deterioration of respiratory status.

Keywords

biliary sludge; ceftriaxone; cholangitis; side effect

Introduction

Ceftriaxone is an antibiotic to be widely used in clinical practice because of its long half-life and broad spectrum activity [1]. This third-generation cephalosporin is excreted mainly in the bile, and no dose adjustment is required in most situations, even in cases with renal impairment [1]. This unique feature, however, may provoke uncommon side effects, as compared with other antibiotics, such as biliary sludge, gallstones, cholecystitis, cholangitis, and pancreatitis [2-4]. Here, we report a case with pneumonia in whom acute cholangitis with a large amount of biliary sludge developed after administration of ceftriaxone.

Case Report

A 70-year-old man was admitted to our hospital because of dyspnea. The patient had been doing well a week before admission, when shortness of breath on exertion developed. Medical treatment including antibiotics was prescribed at another hospital, without improvement. He reported that the symptom gradually deteriorated and that dyspnea started to occur even on rest. He had a medical history of diabetes, cholelithiasis, chronic renal impairment, chronic heart failure, previous myocardial infarction, and atrial fibrillation. Medications included aspirin, amlodipine, nifedipine, olmesartan,

warfarin, torasemide, and rabeprazole.

On physical examination, he was alert but lethargic. The height was 170 cm, the weight was 97 kg, and the body mass index was 33.6 kg/m^2. The body temperature was 38.2°C, the blood pressure was 132/68 mmHg, the pulse was irregular and 133 beats per minute, and the oxygen saturation was 82% while he was breathing ambient air. No dilation of the jugular veins was detected. Auscultation of the chest showed bilateral inspiratory crackles. The heart sound revealed systolic ejection murmurs best heard at the fourth left sternal border, with no extra heart sound. Abdominal examination was normal and there was severe edema in the both legs. An electrocardiogram showed atrial fibrillation with a heart rate of 90-110 beats per minute and left ventricular hypertrophy. A chest radiograph showed bilateral opacities with a cardiothoracic ratio of 58% (Figure 1A). Computed Tomography (CT) without the administration of contrast material showed infiltration in both lungs (Figure 1B). Although gallstones were seen (Figure 1C), neither biliary sludge nor abnormal findings of the hepatobiliary tract was recognized.

The white-cell count was 11,600 per cubic millimeter, with 84.9% neutrophils, 7.1% lymphocytes, 6.0% monocytes, and 1.2% eosinophils. The C-reactive protein level was increased to 9.95 mg per deciliter. The serum creatinine level and blood urea nitrogen level were 2.24 mg per deciliter and 44 mg per deciliter, respectively, which were not different from previous data. The brain natriuretic peptide level was 144.7 pg per millimeter. Level of serum electrolytes and glucose, and liver functions were normal. Cultures of blood, sputum, and urine were drawn, which were later found to be sterile. A diagnosis of pneumonia was made and intravenous ceftriaxone at a dose of 2.0 g per hour daily as well as oral azithromycin of 2.0 g once were administered.

His symptoms, inflammatory markers, and imaging findings had gradually improved. However, 10 days after the administration of ceftriaxone, epigastric pain, along with cold sweats, suddenly developed after midnight. There was no evidence of electrocardiographic and echocardiographic findings to support acute coronary syndrome. Blood examination showed an aspartate aminotransferase of 176 U per liter, alanine aminotransferase of 52 U per liter, alkaline phosphatase of 753 U per liter, and gamma-glutamyl transpeptidase of 331 U per liter although these 4 markers had been within normal ranges before this attack. The C-reactive protein level was still elevated to 2.10 mg per deciliter, but the white-cell count was normal, as were the total bilirubin, creatine kinase, amylase, and electrolyte balance.

Abdominal ultrasonography showed a large amount of debris in the gall bladder (Figure 2), although the patient had had three meals a day since admission. No evidence of stones in the gallbladder or bile duct was detected. CT of the abdomen without the administration of contrast material showed high density areas in the gallbladder neck as well as enlarged bile ducts, with no evidence of cholecystitis, findings suggestive of a diagnosis of acute cholangitis. The presume diagnosis was supported by elevated hepatobiliary enzymes on blood tests. Intravenous ceftriaxone was discontinued and sulbactam-cefoperazone was intravenously administered at a dose of 1.0 g twice a day. Two days after the onset of abdominal pain (i.e., 12 days after admission), meropenem at a dose of 1.5 g daily was added because of poor response to treatment. No gallstone was detected on endoscopic retrograde cholangio pancreatography and endoscopic nasobiliary drainage was placed. The drainage bile was viscous and sterile. Although liver enzyme levels improved, the patient died because of the rapid deterioration of

respiratory status 14 days after admission. Autopsy was not obtained.

Discussion

Intravenous ceftriaxone as well as oral azithromycin were administered in our patient who was diagnosed with pneumonia. Although his clinical course regarding pneumonia was good, epigastric pain developed 10 days later and a large amount of gallbladder sludge was observed on ultrasonography. The diagnosis of acute cholangitis was made and intensive treatment including endoscopic nasobiliary drainage was added, without success.

Biliary sludge is particulate solids that have precipitated from bile and composed of cholesterol crystals, calcium bilirubinate pigment, and calcium salts, etc [4,5]. Causes of biliary sludge vary, including pregnancy, rapid weight loss, obesity, critical illness, bone marrow or solid organ transplantation, the use of total parenteral nutrition, gastric surgery, and drug-induced conditions [4-6]. Although direct histological examination was not obtained in our case, we may safely consider that ceftriaxone-associated biliary sludge and cholangitis was the most likely cause. Given the presence of gallstones on CT at the time of admission, the possibility of gallstone-related cholangitis may not be completely ruled out in the current case, although endoscopic retrograde cholangiopancreatography showed no evidence of stones.

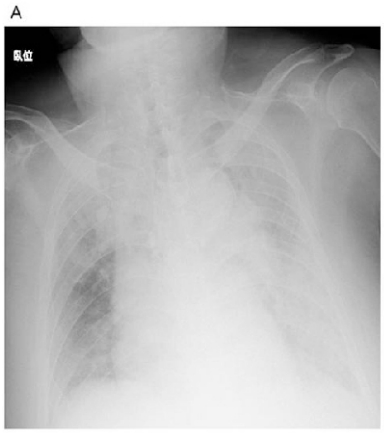
In human subjects, one-third to two-thirds of ceftriaxone is secreted in the urine as unchanged drug, and the remaining one-third is excreted into the bile and ultimately is found in the feces as microbiologically inactive compounds [1,7]. This pharmacological profile is one of the advantages associated with ceftriaxone because dose adjustment is not always required in the elderly or patients with renal or hepatic dysfunction with a ceftriaxone dosage up to 2 g per day [1,7]. However, attention should be paid to patients on hemodialysis because ceftriaxone could be significantly reduced regarding the elimination rate and because ceftriaxone is not removed to any significant extent from plasma by hemodialysis [1,7]. Under these conditions, plasma concentrations of ceftriaxone are required to be monitored if ceftriaxone administration is unavoidable.

A calcium-binding property of ceftriaxone has been proposed as the pathogenesis of ceftriaxone-associated biliary sludge formation because analysis of the biliary concretions showed calcium-ceftriaxone salts [8]. Furthermore, it is also noted that metastability of the calcium salt of ceftriaxone was observed in human gallbladder bile in vitro [8]. It is reasonable to consider that high-dose treatment (i.e., greater than or equal to 2 g per day) is a risk factor of developing ceftriaxone-related biliary sludge, given that calculated saturation indices for calcium-ceftriaxone in human bile generally increased with increasing ceftriaxone dose [8].

Other risk factors associated with ceftriaxone-induced biliary sludge formation include gram-negative sepsis, hypercalcemia (increased calcium secretion into bile), post surgery, fasting or total parenteral nutrition (i.e., impaired gallbladder emptying), renal failure, and long-term treatment with ceftriaxone [9-11], the last two factors of which were present in our case. Although ceftriaxone-associated biliary sludge is usually benign and asymptomatic and the resolution of sludge occurs after interruption of ceftriaxone in most cases [6,12], it is noted that a critical condition could be raised with the use of ceftriaxone [13], as observed in our case.

In conclusion, although similar cases previously had been reported [14,15], it should still be kept in mind that ceftriaxone can provoke a lethal condition associated with ceftriaxone-induced biliary sludge in particular situations, as shown in our case.

Figures



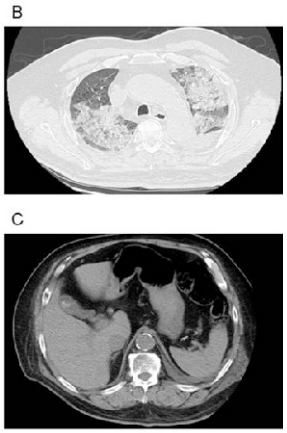


Figure 1: Chest radiography and CT. A portable, anterior-posterior chest radiograph, obtained on admission, shows a cardiomegaly and opacities in both lung fields (A). CT images without the administration of contrast material show bilateral infiltration (B) and gallstones in the absence of evidence of cholecystitis or cholangitis (C).

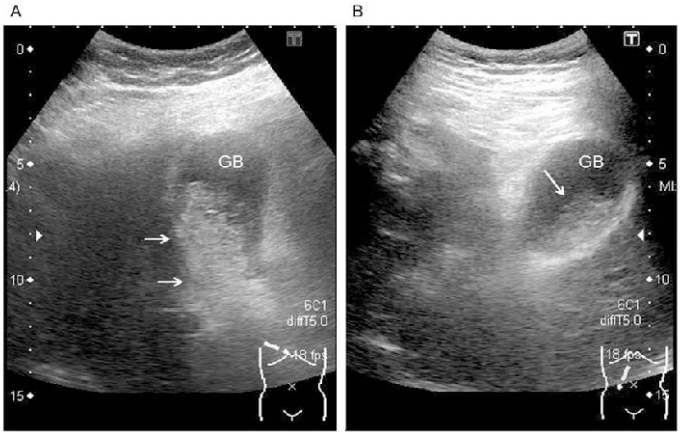


Figure 2: Ultrasonography of the gallbladder. A long axis view (A) and short axis view (B) show a large amount of movingechoes(arrows) without acoustic shadowing in the gallbladder (GB), findings consistent with biliary sludge.

References

1. Patel IH, Kaplan SA. Pharmacokinetic profile of ceftriaxone in man. Am J Med. 1984 19; 77: 17-25.

2. Hagiya H, Hasegawa K, Asano K, Otsuka F. Ceftriaxone-induced biliary sludge in a patient with uncontrolled diabetes. Intern Med. 2014; 53: 2549-50.

3. Nayak A, Slivka A. Ceftriaxone-Induced Gallstones: Case Report and Literature Review. ACG Case Rep J. 2014; 1: 170-2.

4. Shaffer EA. Gallbladder sludge: what is its clinical significance? Curr Gastroenterol Rep. 2001; 3: 166-73.

5. Pazzi P, Gamberini S, Buldrini P, Gullini S. Biliary sludge: The sluggish gallbladder. Dig Liver Dis. 2003; 3: S39-45.

6. Kim YS, Kestell MF, Lee SP. Gall-bladder sludge: lessons from ceftriaxone. J Gastroenterol Hepatol. 1992; 7: 618-21.

7. Stoeckel K, Koup JR. Pharmacokinetics of ceftriaxone in patients with renal and liver insufficiency and correlations with a physiologic nonlinear protein binding model. Am J Med. 1984; 77: 26-32.

8. Shiffman ML, Keith FB, Moore EW. Pathogenesis of ceftriaxone-associated biliary sludge. In vitro studies of calcium-ceftriaxone binding and solubility. Gastroenterology. 1990; 99: 1772-8.

9. Zaki SA, Shanbag P. Biliary pseudolithiasis secondary to ceftriaxone therapy. Indian J Pharmacol. 2010; 42: 193-4.

10. Lemberg D, Day AS, Wyeth B. Biliary colic: Is it gallstones? J Paediatr Child Health. 2005; 41: 291-3.

11: Acun C, Erdem LO, Sogut A, Erdem CZ, Tomac N, Gundogdu S. Ceftriaxone-induced biliary pseudolithiasis and urinary bladder sludge. Pediatr Int. 2004 ;46: 368-70.

12. Palanduz A, Yalçin I, Tonguç E, Güler N, Oneş U, Salman N, et al. Sonographic assessment of ceftriaxone-associated biliary pseudolithiasis in children. J Clin Ultrasound. 2000; 28: 166-168.

13. 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: 202-204.

14. Tanaka M, Yabuki T, Chishima S, Chishima I, Kitaoka Y, Nakayama S, et al. A case of ceftriaxone-associated gallbladder stone and cholangitis after the long-term dis continuation of ceftriaxone. Progress of Digestive Endoscopy. 2015; 87: 136-137.

15. Nakajima H, Ota S, Hirose T, Hosokawa T, Ishida S, Kimura F. Ceftriaxone-Associated Cholelithiasis in Adult Patients with Bacterial Meningitis. J Infect Dis Ther. 2014; 2: 161.

Manuscript Information: Received: May 04, 2018; Accepted: September 03, 2018; Published: September 17, 2018

Authors Information: Kuniyasu Harimoto[1*]; Tatsuya Kawasaki[1]; Tadaaki Kamitani[1]; Satoru Sekoguchi[2]; Hirokazu Oyamada[2]

[1]Department of Cardiology, Matsushita Memorial Hospital, Osaka Japan.
[2]Department of Gastroenterology, Matsushita Memorial Hospital, Osaka Japan.

Citation: Harimoto K, Kawasaki T, Kamitani T, Sekoguchi S, Oyamada H. Acute cholangitis after ceftriaxone administration: A case report. Open J Clin Med Case Rep. 2018; 1456.

Journal: Open Journal of Clinical and Medical Case Reports is an international, open access, peer reviewed Journal focusing exclusively on case reports covering all areas of clinical & medical sciences.

Visit the journal website at **www.jclinmedcasereports.com**
For reprints and other information, contact editorial office at **info@jclinmedcasereports.com**