

Post Treatment Complication of Enteric Fever: A Rare Presentation

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Abstract

Background: Enteric fever is one of the common infectious diseases worldwide. Ceftriaxone is the most commonly used sensitive antibiotic for enteric fever. Biliary sludge is an important complication of ceftriaxone. Biliary sludge refers to a viscous mixture of small particles derived from bile. These sediments consist of cholesterol crystals, calcium salts, calcium bilirubinate, mucin, and other materials. For patients without symptoms, no treatment is recommended. If patients become symptomatic and/or develop complications, cholecystectomy is indicated. This is case report of a 9 year old boy diagnosed as a case of enteric fever and treated with appropriate dose of ceftriaxone for 8 days. On the day of discharge, at night the boy developed severe abdominal pain. They took surgical consultation; ultrasonography of whole abdomen was done which revealed multiple calculi in gall bladder. Symptomatic treatment was planned followed by surgical removal of biliary calculi. After 20 days they took surgical consultation again. Surgeon was ready to perform surgery. The worried mother requested for repeat USG of whole abdomen and this time finding was normal. We must be aware about side effects of ceftriaxone. Patients should be followed up after completion of treatment and as biliary sludge is often self-limiting and surgery is not required for all cases.

Keywords: Enteric fever; abdominal pain; ceftriaxone; biliary sludge.

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Introduction

Enteric fever is a common bacterial disease worldwide, caused by a Gram-negative organism *Salmonella enterica* - either serovar Typhi (*S. typhi*) or serovar Paratyphi (*S. paratyphi*).¹ The term enteric fever is a collective term that refers to severe typhoid and paratyphoid.² Classically, the course of untreated typhoid fever is divided into

four individual stages, each lasting approximately one week. Over the course of these stages, the patient becomes exhausted and emaciated.³

Diagnosis is made by blood, bone marrow or stool cultures and with the Widal test.⁴ The treatment of choice is a fluoroquinolone such as ciprofloxacin.^{5,6} Otherwise, a third-generation

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cephalosporin such as ceftriaxone or cefotaxime is the first choice.⁷ Cefixime is a suitable oral alternative.^{8,9} Sanitation and hygienic measures are the critical steps that can be taken to prevent typhoid fever. There are two vaccines licensed for the prevention of typhoid.¹⁰ The live, attenuated oral vaccine Ty21a (sold as Vivotif by Crucell Switzerland AG) and the injectable capsular polysaccharide vaccine (sold as Typhim Vi by Sanofi Pasteur and Typherix by Glaxo Smith Kline). Each of them provides 50% to 80% protection.¹¹

Ceftriaxone may cause reversible gallbladder pseudolithiasis, detected by abdominal ultrasonography. This is usually asymptomatic but may be associated with emesis and upper quadrant abdominal pain.¹¹

Case Report

Shimanto, a 9 year old boy from a middle class family, second issue of a nonconsanguineous parents hailing from Paikpara, Dhaka was admitted in Delta Medical College & Hospital with the complaints of high grade continued fever for 6 days, anorexia for same duration and mild abdominal pain for 2 days. Before admission the boy received 4 days antimicrobial therapy with ciprofloxacin. The mother also gave history of anorexia and insufficient weight gain for a long time. The boy off and on used to take street food.

On examination, he was found ill looking with high fever (105°F), chest finding was normal, tongue was coated, mild tenderness was found in right hypochondriac region, liver was just palpable and weight was 26 kg.

Following investigations were done –

CBC: Total count of WBC was 7,500/cu mm with neutrophil 67%. ESR was 27. Blood for C/S showed no growth, urine for R/M/E & C/S revealed normal study. Widal test was also normal (TO 1:160, TH 1:160, AH 1:160 and BH 1:80). CXR also revealed findings.

The boy was diagnosed as a case of enteric fever. He received symptomatic treatment and antibiotic therapy with ceftriaxone 2.5 g/day for 8 days. The boy was afebrile after 5 days of starting antibiotic therapy and felt better.

He was discharged on the 8th day of hospital stay at morning but at night on that day the boy developed severe abdominal pain. Surgical consultation was taken immediately, ultrasonography of whole abdomen was done which revealed multiple calculi in gall bladder and suspected mesenteric lymph nodes. Symptomatic treatment was started and it was planned to do surgery after wards. On the next morning the boy was symptom free. The patient was advised to continue conservative treatment and to repeat ultrasound after 3 weeks. After 20 days surgeon was ready to perform cholecystectomy according to previous treatment plan and advised some preoperative investigations. All investigation reports were normal. The worried mother requested for repeat USG of whole abdomen and this time USG report came normal. There was no gall bladder calculus. On follow up after one month, the boy was still symptom free.

Discussion

In many developing countries including Bangladesh, typhoid fever is endemic and constitutes a major public health problem.¹² Typhoid fever is caused by *Salmonella enterica* seroenteritidis. A similar but less severe disease is caused by *S. paratyphi* A and rarely by *S. paratyphi* B and *S. paratyphi* C.¹³ Disease transmission occurs through faeco-oral route. Infecting dose is 10⁵-10⁹ organisms. Incubation period ranges from 4-14 days. After ingestion, gut invasion occurs in the terminal ileum, where they enter into the mesenteric lymph nodes, then via lymphatics enter into the blood stream. Primary bacteremia occurs. Organism colonizes in the RE system, where they replicate and thereafter secondary bacteremia occurs. At that time clinical features develop.

Classically, the course of untreated typhoid fever is divided into four stages, each lasting approximately one week. Over the course of these stages, the patient becomes exhausted and emaciated. In the first week, the temperature rises slowly with relative bradycardia (Faget sign), malaise, headache, and cough. In the second week of the infection, the patient becomes prostrated with high fever, classically with a dicrotic pulse wave. Delirium is frequent, often calm, but sometimes agitated. Rose spots appear on the lower chest and abdomen is distended and painful in the right lower quadrant in about a third of the patients. There are rhonchi and crepitation in lung bases. In the third week of typhoid fever, a number of complications can occur: intestinal haemorrhage, intestinal perforation, septicaemia, encephalitis, neuropsychiatric symptoms, metastatic abscess, cholecystitis, endocarditis and osteitis. By the end of third week, the fever starts subsiding (defervescence). This carries on into the fourth and final week.

Investigations

In first week complete blood count shows leukopenia with eosinopenia and relatively lymphocytosis, blood cultures are positive for *Salmonella typhi* or *paratyphi*. Culture of marrow is more often positive than blood. In the second week the Widal test is strongly positive with anti O and anti H antibodies. Blood cultures are sometimes still positive at this stage. Stool and urine culture become positive after 1st week.¹³ Platelet count goes down slowly in the third week. Newer diagnostic test is detection of *S. Typhi* antigen in serum and in urine.

Treatment

Where resistance is uncommon, the treatment of choice is a fluoroquinolone such as ciprofloxacin.⁶ Otherwise, a third-generation cephalosporin such as ceftriaxone or cefotaxime is the first choice.⁷ Cefixime is a suitable oral alternative.⁹

In addition to antibiotic therapy supportive treatment and fluid electrolyte balance should not be underscored. Additional treatment with dexamethasone has been recommended for severely ill patients.¹³

Prevention

Sanitation and personal hygiene are the critical measures that can be taken to prevent typhoid. There are two vaccines licensed for use for the prevention of typhoid.¹¹

Ceftriaxone is a sterile, semi-synthetic, broadspectrum third generation antibiotic of cephalosporin group for intravenous and intramuscular administration. Thirty three to 67% of a ceftriaxone dose is excreted in the urine and the remainder in the bile. Ceftriaxone is effective against a wide range of micro-organisms and rationally or irrationally it is being used in various clinical situations. Though safety and efficacy of ceftriaxone in paediatric practice is well established, sometimes it is associated with few side effects; biliary sludge formation is one of them (5-15%).¹⁴ Biliary sludge was first discovered in 1970s with the advent of ultrasonography (USG). Biliary sludge is defined as a mixture of particulate matter and bile that occurs when various solutes in bile precipitate. It differs from small biliary stone which is a particle with a diameter of more than 2 mm and which cannot be crushed by digital compression.^{15,16} Apart from ceftriaxone therapy, biliary sludge may be associated with pregnancy, rapid weight loss, prolonged fasting, critical illness, and prolonged Total Parenteral Nutrition (TPN) therapy.¹⁷

The clinical course of biliary sludge varies. It often vanishes, particularly if the causative event disappears; other cases wax and wane, and some go on to gallstones.¹⁸

Conclusion

Ceftriaxone is a relatively safe antimicrobial agent for the treatment of serious bacterial infections in

children but one of its unpleasant side effects is the formation of biliary sludge. Biliary sludge or pseudocholelithiasis appears by USG to be a surgical problem. So the patients should be followed up after completion of treatment and if develops cholelithiasis like symptoms, they should be re-evaluated before performing surgical intervention.

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