CASE REPORT

Uncommon gastrointestinal complications of enteric fever in a non-endemic country
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ABSTRACT
Enteric fever is a systemic illness with varying presentation. It is an important infectious disease in developing countries and also in industrialized countries where many migrants reside. Enteric fever can result in complications in different organ systems and delay in identification and prompt treatment can be fatal. The important gastrointestinal complications of enteric fever include hepatitis, intestinal ulcers, bleeding and bowel perforation. We report three relatively uncommon complications of enteric fever in Qatar, a non-endemic country, ileal ulcer presenting with hematochezia; duodenal ulcer with polyserositis, cholestatic hepatitis and bone marrow suppression; enteric fever related peritonitis.

Keywords: enteric fever, gastrointestinal bleed, cholestatic hepatitis

INTRODUCTION
Enteric fever generally presents as fever with constitutional symptoms and responds to antibiotics and supportive treatment. The presentation of enteric fever is sometimes very enigmatic. Ten percent of cases develop complications. The complications can involve the gastrointestinal tract, bone marrow, central nervous system, lungs, joints (arthritis), pancreas (pancreatitis) and less commonly can involve other organs. Due to the involvement of different organ systems and varying modes of presentation, enteric fever can pose a significant challenge to clinicians. We report three cases of complicated enteric fever, all identified in expatriates in Qatar with a history of travel to endemic regions or contact with those who had.

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CASE 1

A 32-year-old Nepali gentleman presented to Hamad General Hospital in Qatar with a two day history of hematochezia (three bouts of moderate amount of blood in stools). He was also complaining of low grade fever for the past one week. He had no history of diarrhea, abdominal pain or weight loss. General physical examination revealed mild pallor. His hemogram revealed hemoglobin of 9.0 g/dl, total leucocyte count of 3200/mm³, absolute neutrophil count of 2100/mm³ and platelet count of 42000/mm³. His liver function test (LFT) showed mildly elevated alkaline phosphatase (ALP = 313, normal < 129 I U/L), aspartate transaminase (AST = 132, normal < 40 U/L), alanine transaminase (ALT = 83, normal < 40 U/L) and normal bilirubin and albumin levels. Ultrasound of the abdomen was unremarkable. His tests for dengue serology and viral markers (IgM Anti Hbc, IgM anti HAV, IgM anti HEV) were negative.

During his hospital stay, the patient developed two more bouts of massive hematochezia and his hemoglobin dropped to 5.9 g/dl. He was resuscitated with intravenous fluids and packed red blood cell transfusion and underwent emergency colonoscopy. He was empirically started on ceftriaxone. An ulcer with a spurt of blood was seen in the terminal ileum and a few small ulcers in the ileocecal valve and terminal ileum. The active gastrointestinal bleeding was managed with hemoclips and epinephrine injection. The patient did not have further episodes of hematochezia and subsequently improved over the hospital stay. Later, his computed tomography (CT) of the abdomen revealed only small mesenteric lymphnodes. His widal test was strongly positive and ileal ulcer biopsy grew Salmonella enterica serotype Typhi sensitive to ceftriaxone, trimethoprim-sulfamethoxazole and ampicillin. He completed a seven day course of ceftriaxone and was discharged from hospital with hemoglobin of 12 g/dl. His pancytopenia resolved. A follow up liver function test after two weeks was normal and the patient remained asymptomatic up until the last follow-up.

CASE 2

A 45-year-old Nepali gentleman presented with a 20 day history of high grade fever with chills, melena for one week (5 to 6 bouts of moderate amount) and jaundice for 10 days. He had a dull aching epigastric pain and weight loss of 6 kg in the last two weeks. On general physical examination he was febrile, icteric, had an enlarged palpable liver (3 cm below costal margin) and mild epigastric tenderness. His complete hemogram revealed hemoglobin of 8.2 g/dl, total leucocyte count of 2200/mm³, absolute neutrophil count of 1600/mm³, lymphocyte count of 600/mm³ and platelet count of 12000/mm³. His LFT showed elevated total bilirubin (174, normal < 24 μmol/L, and direct component 154), ALP (258 U/L), AST (200 U/L) and ALT (121 U/L), and albumin 25g/l (normal 35 g/dl) levels. INR was 1.4 and ALT/LDH (lactate dehydrogenase) ratio was < 9. Ultrasound of the abdomen showed ascites and thickened gall bladder wall. Ascitic tap showed protein of 25 g/l, serum ascites albumin gradient of 10 and total count of 1200/mm³ (neutrophils 77% and lymphocytes 20%). CT of the abdomen showed mild hepatosplenomegaly, ascites and thickened gall bladder with sludge. His upper gastrointestinal endoscopy showed an ulcer in the duodenal bulb with visible vessel and ooze (Figure 1). He underwent epinephrine injection followed by hemoclip placement for the ulcer.

Figure 1. Duodenal bulb ulcer in enteric fever. 1A: Duodenal bulb ulcer with bleeding vessel (black arrow); 1B: Application of hemoclips (yellow arrow) over the ulcer.
His blood culture grew S. Typhi with the same sensitivity pattern as the previous patient. He was started on cefriaxone 1 g (intravenously 12 hourly). He improved during the hospital stay with follow up hemogram and liver function tests showing gradual improvement which completely normalized in two weeks. Follow up ultrasound scan after one month showed resolution of ascites and the patient was asymptomatic till the last follow up. His complete diagnosis thus constituted enteric fever complicated by duodenal ulcer, polyserositis, cholestatic hepatitis and bone marrow suppression, all of which resolved completely.

CASE 3
The third patient we report was a 22-year-old Nepali gentleman presenting with abdominal pain for ten days. Pain was present diffusely all over the abdomen and on examination, the patient had guarding and mild rigidity over the anterior abdominal wall. He had no fever or gastrointestinal bleed. He was provisionally diagnosed to have peritonitis. His laboratory investigations showed leukocytosis with reactive lymphocytes in peripheral smear. His LFT showed increase in ALT (79 U/L) and AST (251 U/L). However, his CT abdomen showed no evidence of bowel perforation or any other acute abdominal condition. He was managed conservatively with nasogastric aspiration, intravenous fluids and supportive care. His blood culture sensitivity showed S. Typhi with similar sensitivity pattern as the previous two patients. He was started on recommended doses of ceftriaxone and showed a dramatic response. His abdominal symptoms resolved, LFT improved and leukocytosis resolved with antibiotics and supportive care. He thereby represented a case of enteric fever related peritonitis (serositis).

DISCUSSION
Enteric fever includes typhoid (caused by S. Typhi) and paratyphoid fever (Salmonella enterica serotype Paratyphi A). Salmonella spreads through poor hygiene habits and public sanitation conditions, and sometimes also by flying insects feeding on feces. Simple measures such as washing hands before and after defecation and food intake and chlorination of drinking water decreases the transmission of enteric fever.

Interestingly, all the patients mentioned in this case series were from Nepal. Kathmandu, the capital of Nepal is sometimes coined as the enteric fever capital of the world. Poor living conditions and sanitation account for the high burden of enteric fever in developing countries.

Complications related to enteric fever can occur in almost all the organ systems. The important gastrointestinal manifestations of enteric fever includes hepatosplenomegaly (35 – 65%), jaundice (35 – 65%), hemorrhage (25%), intestinal perforation (5 – 35%) and acalculous cholecystitis (<5%). Less commonly it causes cholestatic hepatitis, transaminitis, serositis and peritonitis. Gastrointestinal hemorrhage evolves through four classic pathologic stages: (1) hyperplastic changes, (2) necrosis of the intestinal mucosa, (3) sloughing of the mucosa and (4) the development of ulcers. The ulcers may perforate into the peritoneal cavity. Enteric hepatitis is characterised by bradycardia, moderately high ALT (< 10 times) and ALT/LDH ratio of < 9.

Acute viral hepatitis is a close differential diagnosis to enteric hepatitis however, in acute viral hepatitis ALT is elevated > 20 times and ALT/LDH ratio is usually > 9. For diagnosis, culture of S. Typhi is considered most specific from the bone marrow in the first week, blood in the second and stool and urine in third and forth weeks from onset of fever; rarely can it be cultured from ileal ulcers. Widal test alone is no longer considered an acceptable method of diagnosis and only has a supportive value.

We reported in this case series some of the uncommon complications encountered with enteric fever. Although hematochezia, cholestatic hepatitis and bone marrow depression are rather uncommon, the rarity of enteric fever itself in the Middle East made the diagnosis of the cases more challenging. However, enteric fever presenting with the clinical presentation of peritonitis was the most uncommon finding.

Treatment should not be delayed till confirmatory tests are available. Resistance to routine antibiotics is not uncommon and multidrug resistant (MDR) isolates pose significant therapeutic challenges. However, a recent meta-analysis from Nepal indicates an increase in the occurrence of ciprofloxacin and nalidixic acid resistant forms. A decrease in MDR isolates and decrease in resistance to first-line antibiotics such as chloramphenicol and co-trimoxazole and commonly prescribed ceftriaxone was noticed in the study. This reversal of trend in MDR forms provides an opportunity to reconsider.
these first-line antimicrobials as therapeutic options. During treatment, antibiotics may need to be changed as per the culture and sensitivity pattern. However, prompt treatment drastically reduces the risk of complications and fatalities. With the increase in expatriates from developing countries in the Middle East, we highlighted the importance of identification of this condition in expatriates as well as their contacts. Prompt identification of the disease and appropriate medical care can reduce the complications and avoid mortality.

REFERENCES

1. Karkey A, Aryjal A, Basnyat B, Baker S. Kathmandu, Nepal: still an enteric fever capital of the world. J Infect Developing Countries. 2008;2(6):461 – 465.

2. Crump JA, Mintz ED. Global trends in typhoid and paratyphoid fever. Clin Infect Dis. 2010;50(2):241 – 246.

3. Karki S, Shakya P, Cheng AC, Dumre SP, Leder K. Trends of etiology and drug resistance in enteric fever in the last two decades in Nepal: a systematic review and meta-analysis. Clin Infect Dis. 2013;57(10):e167 – e176.