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Short Communication

A patient with typhoid fever, *Giardia lamblia* gastroenteritis and hepatitis E

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Qing Zhang[1], Jonathan Guo Xiang Teh[1] and Webber Pak Wo Chan[2]

Abstract

Marked elevation of transaminases is rare in typhoid enteric fever. Co-infections with hepatitis A or E, dengue, or other pathogens should be suspected and investigated. Here we report a case of a 29-year-old Bangladesh man who presented with typhoid, hepatitis E and *Giardia lamblia* complicated by severely deranged liver enzymes. With early institution of antibiotics and active supportive treatment, the patient clinically recovered. The underlying mechanism of co-infection is still not clear. As clinicians, comprehensive workup for potential pathogens helps expedite diagnosis, especially in patients from endemic areas or patients who deteriorate rapidly. Current diagnostic methods, treatment modalities and preventive measures still need to be improved in the future.

Keywords

Co-infection, typhoid hepatitis, enteric fever

Introduction

Typhoid fever caused by *Salmonella typhi* is common in tropical areas, presenting with hepatomegaly and mildly elevated transaminases in 21%–60% of cases.[1–3] It has the potential for asymptomatic long-term colonization in the gallbladder, which acts as a reservoir for re-infections. In rare cases of acute hepatitis, certain clinical features were suggested to differentiate typhoid hepatitis from viral hepatitis.[4] If presenting with high fever, relative bradycardia, jaundice within the first two weeks, alanine aminotransferase/lactate dehydrogenase (ALT/LDH) ratio below 9 or neutrophil predominance, the diagnosis is suggestive of typhoid hepatitis.[5] Hepatitis E virus is an RNA virus that infects humans via the fecal-oral route from contaminated water, predominantly seen in Southeast and Central Asia, the Middle East, Africa, or in travelers returning from endemic areas. Acute hepatitis E has an incubation period of three to eight weeks.[6] Giardiasis is most frequently associated with the consumption of contaminated water or food.

Here we report a young patient diagnosed with typhoid, hepatitis E and *Giardia lamblia* who recently came back from Bangladesh. With intensive antibiotics and supportive treatment, his acute hepatitis finally resolved.

Case report

A 29-year-old Bangladesh man presented to the emergency department with a history of high-grade fever for five days complicated with two episodes of non-bloody vomiting and watery diarrhea. Diarrhea was five to six times per day for the past three days, without blood or mucus. He also noticed a pustule developing on his left anterior lower leg. There was mild loss of appetite but no weight loss or night sweats. He denied any chest pain, shortness of breath, cough, dysuria or other localizing symptoms. There was no history of significant medical illness, sexual contact, intravenous (IV) drug abuse, blood transfusions, alcohol consumption, or herbal medication use. He stayed in the city area of Bangladesh for the past six months and returned to Singapore to work for a local chemical company 22 days prior to admission. He is a non-smoker and non-drinker with no known drug allergies.

On examination, he was ill-looking, febrile with stable vital signs. Abdominal examination revealed a non-tender hepatomegaly palpable 1 cm below the right costal margin. Murphy's sign was negative. The pustule was 1 × 1 cm, erythematous, warm and painful with yellowish discharge. Laboratory investigations showed a normal full blood count, negative

[1]Department of Internal Medicine, Singapore General Hospital, Singapore
[2]Department of Gastroenterology and Hepatology, Singapore General Hospital, Singapore

Corresponding author:
Qing Zhang, Department of Internal Medicine, Singapore General Hospital, Academia Level 4, 20 College Road, 169856, Singapore.
Email: qing.zhang@mohh.com.sg

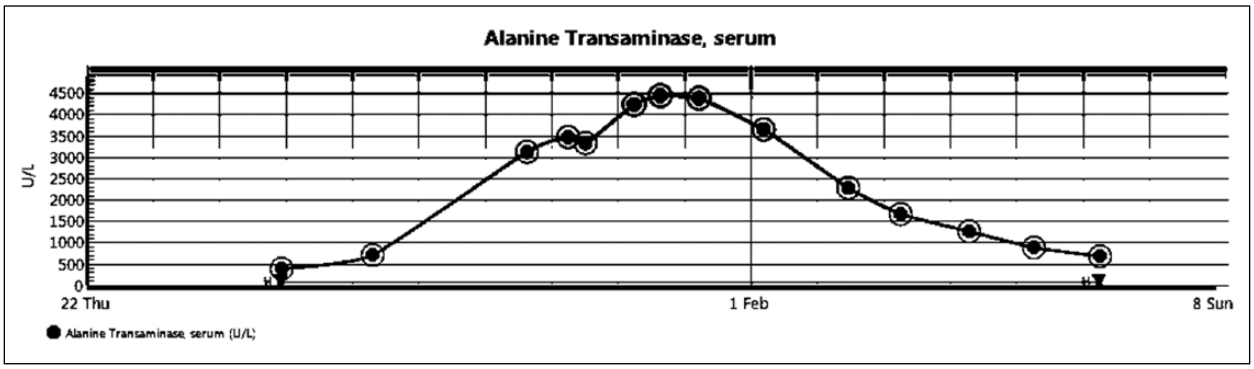

Figure 1. Alanine aminotransferase trend.

peripheral smear for malarial parasite and a normal chest radiograph. Elevated transaminases were noted with elevated aspartate aminotransferase (AST) 408 U/l, ALT 392 U/l, and alkaline phosphatase (ALP) 136 U/l. Total serum bilirubin was 12 µmol/l. *Giardia lamblia* cysts were found in his stools on Day 2. His diarrhea resolved after being treated with a course of metronidazole.

Further inquiry into the patient's past medical history revealed an episode of typhoid fever at age 16 with little details of treatment. On Day 4 blood cultures reported *Salmonella typhi*, sensitive to ceftriaxone. Two grams daily IV ceftriaxone was empirically initiated on Day 2, and further increased to 1.5 g twice per day on Day 4 based on culture results. The pustule on the lower leg was also resolving clinically with antibiotics. On Day 8 Widal study was positive in 1:160 dilutions for "O" antigens yet negative for "H."

However, despite treatment of ceftriaxone and metronidazole, his elevation of transaminases worsened with a peak on Day 7 with AST 4450 U/l, AST 5817 U/l, ALP 329 U/l, gamma-glutamyl transferase 314 U/l, total bilirubin 154 µmol/l, activated partial thromboplastin time 34.9 s and prothrombin time 18.2 s. The trend started to come down only on Day 9, one week post-IV ceftriaxone at the therapeutic dose for typhoid fever. We proceeded to perform an extensive workup for the cause of his elevated transaminases. The serology for hepatitis A/B/C, Epstein-Barr virus, dengue, herpes simplex virus, cytomegalovirus, leptospira, melioidosis and human immunodeficiency virus were all negative. Paracetamol level was below 2.5 and screen for autoimmune diseases was negative. Abdominal ultrasound showed unspecific gallbladder wall thickening. Computed tomographic scan revealed focal fatty infiltration of the liver and no hepatic abscess. Three doses of IV vitamin K were given to correct his coagulopathy and daily laxatives were given. On Day 11 hepatitis E immunoglobulin M (IgM) antibody reported positive. ALT and AST started downtrending on Day 8 with overall clinical improvement (Figure 1), back to within normal range in one month.

Discussion

Possible mechanisms of liver injury by *Salmonella typhi* are either direct invasion or immune-mediated endotoxemia.[2] Re-infection of typhoid fever might be due to an inadequate dose or duration of antimicrobial treatment and a decreased susceptibility to antibiotics. In this case, it might also be attributed to preceding *Giardia lamblia* and hepatitis E infection. The insult to the liver is therefore more severe, mimicking acute liver failure.

Surprisingly, there are several case reports of co-infections in tropical areas involving *salmonella paratyphi* with *Giardia lamblia*[7] or hepatitis A with underlying chronic hepatitis B.[8] In fact, co-infection is common in endemic areas. Suspicion should be raised when clinical presentation is atypical for any single pathogen. In cases of simple typhoid hepatitis, usually the elevation of transaminases is mild, below 500 U/l, as per data from Taiwan[9] and the United Kingdom.[10] Extensive investigations in a timely fashion for potential pathogens like malaria, dengue, typhoid and viral hepatitis are justifiable with deteriorating symptoms.[11] As presented in this case, we think all three infections are acute, despite the relevant past medical history of typhoid at 16 years old. Hepatitis E might play a major role for elevated transaminases while his acute gastrointestinal symptoms were more likely caused by salmonella and giardia infections. To minimize morbidity and mortality in acute patients, clinicians should be highly alert of possible concurrent infections and start early institution of antibiotics for sufficient doses and duration based on sensitivity studies.

Conclusions

As clinicians, accurately and rapidly diagnosing multiple infections in a single host is understandably difficult. Despite a series of serologic tests that have been developed for antigen/antibody detection, including the classic Widal test or DNA probes, none of these tests is sufficiently sensitive, specific, or rapid enough in clinical use. A high index of suspicion must be held against the possibility of co-infections especially in patients from endemic areas. Secondly, there is a lack of effective treatment available for acute hepatitis E infection apart from supportive care as was performed in this case. It is promising to see combination vaccines against typhoid fever and hepatitis A are already available for susceptible people.[12,13] Last but not least, prevention is the pillar. Tighter control of transmission vectors, clean water provision and sanitation, and raising public awareness can help decrease the incidence of multiple co-infections.[14]

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Authors' contributions are as follows: QZ was involved in the literature review, manuscript preparation, conception of the report and submission. JT was involved in manuscript critique and review. CW

was involved in the manuscript critique and review. All authors read and approved the final manuscript.

Conflict of interest

None declared.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal.

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References

1. Khosla SN, Singh R, Singh GP, et al. The spectrum of hepatic injury in enteric fever. *Am J Gastroenterol* 1988; 83: 413–416.
2. Pandey CK, Singh N, Kumar V, et al. Typhoid, hepatitis E, or typhoid and hepatitis E: The cause of fulminant hepatic failure—a diagnostic dilemma. *Crit Care Med* 2002; 30: 376–378.
3. Morgenstern R and Hayes PC. The liver in typhoid fever: Always affected, not just a complication. *Am J Gastroenterol* 1991; 86: 1235–1239.
4. El-Newihi HM, Alamy ME and Reynolds TB. Salmonella hepatitis: Analysis of 27 cases and comparison with acute viral hepatitis. *Hepatology* 1996; 24: 516–519.
5. Balasubramanian S, Kaarthigeyan K, Srinivas S, et al. Serum ALT: LDH ratio in typhoid fever and acute viral hepatitis. *Indian Pediatr* 2010; 47: 339–341.
6. Mushahwar IK. Hepatitis E virus: Molecular virology, clinical features, diagnosis, transmission, epidemiology, and prevention. *J Med Virol* 2008; 80: 646–658.
7. Nakaya Y, Shiota S, Sakamoto K, et al. Double infection with *Giardia lamblia* and *Salmonella paratyphi A* associated with acute renal failure. *Intern Med* 1998; 37: 489–492.
8. Liu Y, Xiong Y, Huang W, et al. Recurrent paratyphoid fever A co-infected with hepatitis A reactivated chronic hepatitis B. *Ann Clin Microbiol Antimicrob* 2014; 13: 17.
9. Wang JL, Kao JH, Tseng SP, et al. Typhoid fever and typhoid hepatitis in Taiwan. *Epidemiol Infect* 2005; 133: 1073–1079.
10. Patel TA, Armstrong M, Morris-Jones SD, et al. Imported enteric fever: Case series from the hospital for tropical diseases, London, United Kingdom. *Am J Trop Med Hyg* 2010; 82: 1121–1126.
11. Deepak NA and Patel ND. Differential diagnosis of acute liver failure in India. *Ann Hepatol* 2006; 5: 150–156.
12. Beran J, Beutels M, Levie K, et al. A single dose, combined vaccine against typhoid fever and hepatitis A: Consistency, immunogenicity and reactogenicity. *J Travel Med* 2000; 7: 246–252.
13. Van Hoecke C, Lebacq E, Beran J, et al. Concomitant vaccination against hepatitis A and typhoid fever. *J Travel Med* 1998; 5: 116–120.
14. Kappagoda S and Ioannidis JP. Prevention and control of neglected tropical diseases: Overview of randomized trials, systematic reviews and meta-analyses. *Bull World Health Organ* 2014; 92: 356–366C.