CASE REPORT

Fulminant hepatitis in typhoid fever

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Summary

Aim: To report a patient with typhoid fever who presented with fulminant hepatitis and was found to have a co-infection with hepatitis A.

Case: An 11-year-old girl presented with fever and jaundice after arrival from India. Her blood culture was positive for Salmonella typhi. While on treatment with ceftriaxone, she had worsening of her jaundice with abrupt elevation of liver transaminases associated with coagulopathy. She was found to have an associated hepatitis A infection. Liver enzymes all reverted back to normal upon follow up.

Conclusion: The association of typhoid fever with hepatitis A can result in fulminant hepatitis but in this case, is associated with complete recovery.

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Introduction

Hepatic involvement has been reported in 23—60% of patients with typhoid fever [1]. However, severe hepatic derangement simulating acute viral hepatitis is uncommon and might indicate an association with viral hepatitis. In this case a patient is reported with typhoid fever who had developed fulminant hepatitis and was found to have simultaneous infection with hepatitis A. This is followed by a review of hepatic manifestations of typhoid fever and consequences of association with hepatitis viruses.

Case

An 11-year-old girl presented to the Infectious Diseases Hospital with three-day history of fever and diarrhea and one day history of jaundice. The girl had been previously healthy and had arrived from India six days prior to presentation. Examination revealed a well looking child with a temperature of 39.2°C, the other vital signs were stable. She was mildly jaundiced and had hepatomegaly of 2 cm. The rest of the physical exam was within normal. Initial investigations revealed: WBC 11.4 × 10⁹/L with 64% polymorphonuclear cells, platelets 90 × 10⁹/L, ESR 28, ALT 737 U/L, AST 731 U/L, total bilirubin 91.9 mmol/L with direct bilirubin 63.4 mmol/L, PT 19.8 s, PTT 41 s, FDP > 2000 ng/ml. Malaria thin and thick smears were negative. The patient was started on

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intravenous ceftriaxone. Within 12 h of admission the blood culture obtained grew Gram-negative bacilli which was later identified as *Salmonella typhi* sensitive to ceftriaxone. The next day following admission, she was noted to be deeply jaundiced and had developed epistaxis. Repeated liver function profile and coagulation profile showed marked elevation of liver transaminases and prolongation of PT (Table 1). Ammonia level was 89 mmol/L, acetaminophen level was <0.1 mmol/L. The patient was alert, awake and had a normal neurological assessment. Based on prolongation of PT and acute worsening of her liver she was transferred to the Intensive Care Unit for further monitoring. Blood was drawn for hepatitis serology. Hepatitis A IgM was positive and all other hepatitis viruses (B, C, and E) were negative. Ultrasound of the abdomen showed moderate hepatomegaly but no other masses. The management was mainly supportive with vitamin K for prolonged PT. The patient was monitored in the ICU until her PT was less than 20 s and liver enzymes were improving. She had received treatment for typhoid fever with parenteral ceftriaxone for two weeks. She had a complete resolution of hepatitis with normalization of hepatic transaminases at the six-week follow up (Table 1).

### Discussion

Hepatomegaly has been reported in 55% of patients with typhoid fever [2]. Hepatitis has been described as a constant feature of the disease rather than a complication occurring during the second and the third week of onset of symptoms in up to 60—100% of the cases [1,3]. The pathogenesis of hepatic involvement in salmonella infection may be multifactorial and include bacterial endotoxin [4] or a host reaction with hyperplasia of the liver reticuloendothelial system and infiltration of portal spaces with reduction of the microcirculation causing necrosis [2,3]. Patients with typhoid hepatitis can fall into two categories: (a) those with evidence of hepatic enlargement or abnormal liver function tests; (b) those with hepatic manifestations as the dominant feature of the disease [5]. Deep jaundice is a rare presentation of typhoid fever occurring in 5—8% of children [2,6]. Therefore in patients with typhoid fever who are deeply jaundiced, other diagnoses like viral hepatitis should be considered especially that both are enterically transmitted and can occur simultaneously.

Association of typhoid with enteric hepatitis viruses and subsequent development of fulminant hepatitis has been reported previously. Hepatitis A IgM was positive in a nine-year-old girl who was diagnosed with typhoid fever with high conjugated hyperbilirubinemia [7]. Pandey et al. reported a co-infection of hepatitis E and typhoid with fulminant hepatic failure in a 15-year-old [5].

It remains difficult to distinguish clinically viral hepatitis from salmonella hepatitis. This is more attainable biochemically as the levels of aminotransferases are markedly elevated in hepatitis compared with typhoid hepatitis. Admission ALT/LDH ratio has been reported to be the best discriminator between both diagnoses (<4 for typhoid hepatitis, and >4 for viral hepatitis) [8]. In this case, the admission ALT/LDH ratio was 4.9, suggestive of viral hepatitis which was confirmed by the presence of hepatitis A IgM.

The prognosis is usually good as salmonella hepatitis responds well to specific antibiotic therapy and jaundice resolves with clinical improvement.

The etiological agents of hepatitis A and typhoid fever share similar mode of transmis-

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ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; Tbil, total bilirubin; Dbil, direct bilirubin.
sion (fecal–oral route) and global distribution. Travelers from non-endemic countries are often advised to receive both typhoid fever and hepatitis A virus vaccines when traveling to areas where the two diseases are endemic. Lately, combined typhoid fever/hepatitis A vaccines have proven to be immunogenic and safe in adults [9].

In conclusion, fulminant hepatitis in patients with typhoid fever should be differentiated as typhoid hepatitis or associated with other enteric viral hepatitis.

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**Competing interests**

None declared.

**Ethical approval**

Not required.

**References**


