Co-infections in tropics. Rare or Underreported?

Sir,

Concurrent infection with two infectious agents can result in an illness having overlapping symptoms, resulting in a situation where both diagnosis and treatment of a patient may become difficult for a physician and misdiagnosis in a treatable systemic disease with liver involvement such as typhoid can have fatal consequences.

A 15years old male child was admitted with the complaints of fever and loose stools for five days, yellowish discoloration of eyes and urine for four days. There was no history of vomiting, melena, rashes, oliguria, previous blood transfusions or bleeding from any site. The temperature of the child was 38.50 C, pulse rate 124/min, respiratory rate 28/min, blood pressure 88/48 mm Hg. General examination revealed icterus and bilateral pitting pedal edema. Liver was palpable 3 cm below the right costal margin, spleen was palpable 2 cm below the left costal margin and shifting dullness was present in the abdomen along with decreased breath sounds over lower zones of both lungs.

Investigation revealed a hematocrit of 42%, total leukocyte count of 11,100 /µL (neutrophils 78%, lymphocytes 20%, monocytes 2%) and platelet count of 20,000/µL. Serum sodium 138meq/l, serum bilirubin 8.5mg/dl (direct 7.5mg/dl), alanine transaminase (ALT) 129 IU/L, aspartate transaminase (AST) 385 IU/L, alkaline phosphatase 680 IU/L, total serum protein was 4.6 g/dl (albumin 2.2g/dl and globulin 2.4g/dl). Renal function tests were slightly deranged; PT and aPTT were normal. Viral markers for hepatitis (A, B, C and E) as well as peripheral blood smear for malarial parasite were negative. Blood culture and urine culture were sterile. Ultrasonography of the abdomen and chest revealed distended gall bladder with thickened wall, hepatomegaly, splenomegaly and moderate ascites along with minimal bilateral pleural effusion. The diagnosis of dengue infection was confirmed by positive IgM ELISA for dengue virus

During hospitalization the child developed one episode of hematuria. According to WHO, the diagnosis of severe dengue is made when one or more of the following is present: evidence of plasma leakage, severe bleeding, and severe organ dysfunction. As this child had evidence of plasma leakage (ascites, pleural effusion, shock), bleeding (hematuria) and evidence of organ dysfunction (icterus and deranged liver functions), diagnosis of severe dengue was made and was treated in intensive care unit with intravenous fluids and vasopressors under strict central venous pressure and hematocrit monitoring. By 3rd day of admission, the child's hematocrit started declining and platelet count started increasing which became normal by 6th day of admission. As fever persisted, on 8th day of admission, work up for the cause of fever was done. Widal test was sent which was strongly positive (>1/480). Typhidot test was sent and was positive. Patient was started on intravenous ceftriaxone in the recommended dose for typhoid fever and fever subsided by 14th day of admission. Repeat investigations on day 11 are shown in [Table 1], which shows that the liver enzymes peaked in 1st week, reaches maximum value around 9th day and then gradually tapered off towards normality within two weeks. Patient was discharged on 18th day and is well on follow up.

Table 1: Liver function tests

Investigations	Day 6th of illness	Day 11th of illness
AST	385 IU/L	198 IU/L
ALT	189 IU/L	97 IU/L
ALP	680 IU/L	318 IU/L
Serum bilirubin	8.5mg/dl	4.6mg/dl

The index case with fever, icterus, hepatomegaly, thrombocytopenia and shock was confirmed as a case of severe dengue by positive IgM ELISA and had co-infection with Salmonella. A similar co-infection has been reported in an adult.[1] Fever and jaundice can occur in a number of infections including typhoid, viral, malarial and amoebic infections.

There are certain distinguishing features in each of these infections which help us to narrow down the cause. In case of dengue fever, the elevation of AST enzyme is more than ALT during first week of illness. This feature helps to differentiate it from hepatitis A, B or C.[2,3] The release of AST from damaged myocytes may be responsible for this.[3] In Dengue, the levels of these enzymes start to increase around the third day after the onset of the disease; they reach a peak on the seventh or eighth day and gradually taper off towards normality within two weeks.[4,5] In our patient, the peak of the liver enzymes was observed on 7th day of illness which started decreasing by 11th day suggesting dengue as the cause of hepatitis. In viral hepatitis, a prodromal illness precedes the jaundice; fever subsides with the appearance of jaundice and elevation of bilirubin is associated with corresponding elevation of liver enzymes.[6-8] Typhoid hepatitis occurs during the second and third week of the illness and varies from mild hepatic dysfunction to severe hepatic dysfunction (0.5%-7.6%).[8] Fever persists despite the appearance of jaundice and there is a rise in serum bilirubin with modest increase in serum alanine transaminase and aspartate transaminase.[8-10] Hepatomegaly which usually appears in the second and third week of illness often takes several weeks to disappear.[11]

Hepatic manifestations of typhoid fever and dengue infection have varying patterns of presentation and lab parameters.[4,9,12] Knowledge of these parameters are important in the diagnosis of a case with fever and jaundice especially in presence of co-infection such as in this case, which is not an uncommon event in a tropical country though may be underreported. It is important to delineate the cause in every case as treatment varies in each of these conditions. Misdiagnosis in a treatable systemic disease with liver involvement such as typhoid can have fatal consequences.

REFERENCES

1. Sudjane P, Jusuf H. Concurrent infection of Dengue Hemorrhagic fever and Typhoid in adult patient. Southeast Asian J Trop Med Public Health.1998;29(2):370-2.
2. EI-Newihi HM, Alamy ME, Reynolds TB. Salmonella hepatitis: analysis of 27 cases and comparision with acute viral hepatitis. Hepatology. 1996; 24:516-519.

3. Kno CH, Toi DI, Chang-Chien CS, Lan CK, Chiou SS, Liaw YF. Liver biochemical tests in dengue fever. Am J Trop Med Hyg. 1992;47(3):265-70

4. Mohan B, Patwari AK, Anand V.K. Hepatic dysfunction in Childhood dengue infection. J Trop Pediatr. 2000 ;46(1):40-3.

5. Rigato I, Ostrow JD, Tiribelli C. Biochemical investigations in the management of liver disease. In: Rodés J, Benhamou JP, Blei A, Reichen J, Rizzetto M (Eds): Textbook of Hepatology: From Basic Science to Clinical Practice (Boston. MA: Blackwell Publishing). 3rd edition. 2007:451-467.

6. Khosla SN. Typhoid hepatitis. Postgrad Med J 1990; 66:923-5.

7. Macher D, Harries A. Pitfalls in the diagnosis and management of the jaundiced patient in the tropics. Trop Doc.1994;24:128-30.

8. Nazmul-Ahsan HA, Jalil-Chowdhury MA, Azharr MA, Rafiqeuddin AK. Pitfalls in the diagnosis of jaundiced patient in the tropics. Trop Doc. 1995; 25:191.

9. Morgenstern R, Hayes PC. The liver in typhoid fever: always affected, not just a complication. Am J Gastroenterol 1991; 86:1235-1239.

10. Kamath PS, Jalihal A, Chakraborthy A. Differentiation of typhoid fever from fulminant hepatic failure in patients presenting with jaundice and encephalopathy. Mayo Clin Proc 2000;75:462-6.

11. Ahmed A, Ahmed B. Jaundice in typhoid patients: Differentiation from other common causes of fever and jaundice in the tropics. Ann Afr Med. 2010;9:135-40

12. Ahasan HA, Chowdhury MA, Azhar MA, Rafiqeuddin AK. Pitfalls in the diagnosis of jaundiced patient in the tropics. Trop Doc. 1995;25:191.

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