Hepatitis E: A rare cause of immune thrombocytopenic purpura

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ABSTRACT

Acute viral hepatitis in children usually is a self-limiting mild disease which does not require any specific treatment. It is most commonly caused by hepatotropic viruses, hepatitis A and hepatitis E virus spread by the feco-oral route. Hepatitis E infection mostly follows an asymptomatic and anicteric course in the younger age group than icteric hepatitis. Rarely, they cause cholestatic hepatitis and fulminant hepatitis. It may rarely be associated with various extra-hepatic autoimmune manifestations. We herein report an extremely rare case of immune thrombocytopenia in a young girl associated with acute hepatitis E infection, who had an uneventful course on conservative management. She presented to us with nausea, vomiting, lethargy, jaundice, and petechial spots. On examination and investigating further, the patient had features of immune thrombocytopenic purpura and positive serology for IgM hepatitis E, whereas, a workup for other causes was normal.

Key words: *Extra-hepatic manifestations, Hepatitis E, Immune thrombocytopenia*

Hepatitis E virus (HEV), a single-stranded RNA virus, is a major cause of sporadic as well as epidemic hepatitis transmitted by the feco-oral route [1]. Usually, it is a self-limiting illness, but sometimes liver failure can also occur. Rarely, extra-hepatic manifestations such as neurological, hematological, renal disorders, myocarditis, arthritis, acute pancreatitis, and autoimmune thyroiditis can also occur [2]. HEV infection can present as asymptomatic, icteric, or with fulminant hepatitis [3]. It may rarely be associated with various extra-hepatic autoimmune manifestations [2]. Hepatitis B and C are very well known to cause thrombocytopenia. A comprehensive review of extra-hepatic manifestations associated with HEV infection by Bazerbachi *et al*. documented five case reports of severe thrombocytopenia in adults [4]. In another case series comprising nine cases of thrombocytopenia, two were reactive for antiplatelet antibody out of four who were tested [5], but acute hepatitis E causing immune thrombocytopenia is extremely rare in the pediatric population and only once been reported previously by Thapa *et al*. [6].

We herein report an extremely rare case of immune thrombocytopenic purpura (ITP) in a child with acute viral hepatitis E.

CASE REPORT

A 14-year-old female was admitted with complaints of nausea, vomiting, and lethargy for 14 days, jaundice for 10 days, and skin petechiae for 2 days. There was no history of fever, bleeding from other sites, and altered sensorium. Past, family, birth, and developmental histories were normal.

On examination, the patient was conscious and had stable vitals. Abdominal examination revealed mildly tender hepatomegaly without any splenomegaly. Respiratory, cardiovascular, and nervous system examinations were normal.

Laboratory investigations at admission were as follows: Total leukocyte count – 4300/mm^3 (polymorphs – 40%, lymphocytes – 50%, and eosinophils – 5%), hemoglobin – 12.7 g%, and platelet 80,000/mm^3. Peripheral smear showed reduced platelets with no platelet clumps. Total bilirubin – 2.42 (direct – 1.71/indirect – 0.71), SGOT – 110 IU/dl, SGPT – 339 IU/dl, alkaline phosphatase was 195 IU/dl. Total protein- 7.66 g/dl, serum Albumin- 4.54 g/dl and serum Globulin- 3.12 g/dl, and serum lactate dehydrogenase level was- 183 IU/L. A routine urine examination was normal. Blood and urine cultures were sterile. Typhidot IgM and Widal were non-reactive. Dengue NS1 IgM, IgG and chikungunya IgM, IgG were negative.

Serology for hepatitis was non-reactive for anti-HAV, anti-Hep-C, and HBsAg. Vitamin B12 and folic acid levels were normal (Vit. B12 – 345 pg/mL, serum folate – 3.18 ng/mL). Tests for Epstein-Barr virus, parvovirus, cytomegalovirus, and HIV were negative. On the slit-lamp examination, Kayser–Fleischer ring was absent. Serum ceruloplasmin (40 mg/dL) and 24 h urine copper (10 μg) were within normal limits. The antinuclear antibodies and Coombs tests were negative. Immunoglobulin levels were within normal limits (IgA – 134 IU/mL, IgG – 764 IU/mL, IgM – 275 IU/mL, and IgE – 70 IU/mL). The chest radiograph was normal. Ultrasound of the abdomen revealed mild hepatomegaly with normal echotexture. Gallbladder, portal vein, spleen, and kidneys were normal. Serology for anti-HEV IgM antibodies was reactive.

The patient was managed conservatively with IV fluids, antiemetics, and supportive treatment for hepatitis. The liver function test (LFT) and platelets were monitored serially over 4 weeks of the hospital stay. The lowest platelet count of 20,000/cu.mm was documented on the 17th day of illness. Bone marrow aspiration and biopsy done on day 18 of illness were suggestive of megakaryocytic hyperplasia. The antiplatelet antibody assay was negative. The platelet count began to increase from day 22 of illness and platelet count was more than 100,000/mm^3 by day 24 of illness and remained normal thereafter. The patient did not develop other extra-hepatic manifestations of HEV. The liver enzymes and bilirubin started to fall from the 24th day of illness.

As the patient had isolated thrombocytopenia with megakaryocytic hyperplasia in the marrow and in the absence of other apparent causes of thrombocytopenia, it fitted in the accepted diagnostic criteria of ITP. A simultaneous association of active hepatitis E infection, in this case, pointed toward a causal relation. At follow-up, the patient was asymptomatic and complete blood counts and LFTs were within normal limits.

DISCUSSION

HEV is a non-enveloped single-stranded RNA virus causing 3.4 million symptomatic cases of acute hepatitis and 70,000 deaths due to acute liver failure annually [7].

Detection of anti-HEV IgM, anti-HEV IgG, and HEV RNA detection is helpful in the diagnosis of HEV infection. IgM anti-HEV is positive for the 1st month after HEV infection, whereas IgG anti-HEV suggests current or previous infection. HEV RNA detectable for more than 3 months is labeled as chronic hepatitis E. However, chronicity is rare in HEV infection and may occur in immunocompromised patients [8].

Studies mainly from the adult population suggest that neurological manifestations (Guillain-Barre syndrome, encephalitis, meningitis, myositis, Bell's palsy, and mononeuritis multiplex), acute pancreatitis, glomerulonephritis, cryoglobulinemia, Henoch–Schonlein purpura, ITP, etc., are rare extra-hepatic manifestations of HEV infection [9]. Hematological manifestations are quite rare and rarely reported in the pediatric population. Hepatitis E causing immune thrombocytopenia is extremely rare and has been reported only once in the pediatric population [6]. In this previously reported case, an 8-year-old female child presented with gum bleeding and painless hematuria in the 2nd week of illness with platelet counts of 21,000/mm^3. This patient required platelet transfusions, intravenous immunoglobulin infusion, and improved gradually over 1 week (i.e., during the 3rd week of illness) with platelets rising to 94,000/mm^3 by the end of the 3rd week of illness [6]. No other pediatric data were available in the literature.

The pathophysiologic mechanism of extra-hepatic manifestations still remains unclear. HEV infection triggers a variety of host defense mechanisms, which may not be limited to the primary location of infection, and therefore, multisystem manifestations are mostly attributed to cross-reactions between viral epitope and self-antigens [4]. Although the association with hepatitis E is uncertain, temporal occurrence and additionally exclusion of other etiologies suggest that HEV infection could be a cause of ITP in the current case.

CONCLUSION

HEV infection causing immune thrombocytopenia is extremely rare in children. It may be useful to do HEV testing in patients of severe thrombocytopenia associated with elevated liver enzymes as the next level of etiological evaluation of patients with ITP. Furthermore, we must be aware of extra-hepatic manifestations while treating patients of HEV infection.

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