Hepatitis E with Intravascular Hemolysis in Beta Thalassemia Trait: A Rare Association or Coincidence

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Abstract

Hepatitis E virus is one of the leading causes of acute viral hepatitis in India but usually manifests as a mild self-limiting illness. It is known that severe intravascular hemolysis can occur in the course of acute Viral Hepatitis E in association with a G6PD deficiency state. Thalassemias are known to cause extravascular hemolysis. The role of β thalassemia trait in hemolysis during acute hepatitis E infection is not known. In this report we describe a rare coexistence of severe intravascular hemolysis in a patient with hepatitis E infection and β Thalassemia trait with bilirubin going upto 85 mg/dl without any renal dysfunction or complication. It may point towards an etiological basis of hemolysis in Hepatitis E due to Thalassemia.

Introduction

Hepatitis E is an enterically transmitted virus and is one of the most common causes of acute

viral hepatitis in India.[1] The coexistence of viral hepatitis and G6PD deficiency has been reported to be associated with severe jaundice, intravascular hemolysis and other complications.[2,3] But hepatitis E presenting with intravascular hemolysis in Thalassemia trait is yet to be reported. Thalassemia syndromes are inherited disorders of α or β globin synthesis. It causes Extravascular Hemolysis and ineffective erythropoiesis.[7] We report a case of Acute hepatitis E with intravascular hemolysis in a patient of Beta Thalassemia trait.

Case Report

A 25-year-old man with no history of alcoholism or liver disease presented with Yellowish discoloration of the eyes since 10 days. On further asking he complained about dark coloured urine in last 5 days. His mother was a known case of beta thalassemia trait. On examination, he was pale and deeply icteric. Abdominal examination was grossly normal with no organomegaly.

On admission, laboratory investigations showed hemoglobin of 9.8 g/dL, a total leucocyte count of 6790, and a total serum bilirubin of 39 mg/dl with a conjugated fraction of 21.11 mg/dl. The serum aspartate aminotransferase (AST) concentration was 1769 mU/mL(normal-15-37mu/ml) and the alanine aminotransferase(ALT) concentration was 988 mU/mL(normal-15-63mu/ml). The prothrombin time was 13 s (control: 11 s).USG showed mild hepatomegaly and rest was normal. Immunoglobulin (Ig) M anti-hepatitis A virus, hepatitis B surface antigen, IgM anti-hepatitis B core and anti-hepatitis C virus were negative, while IgM antihepatitis E virus (HEV) was positive. A diagnosis of HEV

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hepatitis was made and the patient was managed conservatively.

Over the next 4 weeks, the serum bilirubin peaked at 85.8 (conjugated fraction: 35.22 mg/dl), AST peaked at 3260 mU/mL, and ALT peaked at 2170 mU/mL. The hemoglobin decreased to 6.8 g/dL. The peripheral blood smear showed hypochromasia, anisopoikilocytosis, occasional target cells, few punctate basophilia and reticulocytosis (the reticulocyte count was 14%). INR increased to 3.05 Urine was positive for hemoglobinuria. The serum lactate dehydrogenase concentration was 1225 mU/L (normal: 81-234 mu/ml) and serum haptoglobin was 7 mg/100 ml(normal-90-200). Direct and indirect Coomb's tests were negative. Both the peripheral blood smear and the antigen-test were negative for malaria. Serum Ceruloplasmin levels were normal. The G6PD level was normal. Hb electrophoresis showed picture of β thalassemia trait with HbA-94.2% and Hb A2 - 5.8% (1-4%) . Serum lead, arsenic and mercury levels were normal. Slit-Lamp Examination was normal.

The patient was managed conservatively, including good hydration and maintaining an adequate urine output and avoiding all hepatotoxic, nephrotoxic and oxidant drugs. The metabolic parameters of the patient gradually improved over the subsequent 3 weeks. The hemoglobin mass concentration increased to 9.8 g/dL, bilirubin fell to 32mg/dl (conjugated fraction: 27mg/dl), AST was still 245 mU/mL, ALT was 114 mU/mL and reticulocyte count fell to 3.5%.The patient was discharged to be followed in the outpatient department. About 4 months after the discharge his bilirubin and aminotransferase levels were nearly normal.

Discussion

Bilirubin levels more than 20 mg/dl is very uncommon in uncomplicated viral hepatitis.[4] It is a known fact that hepatitis E causes mild hemolysis due to decreased RBC survival but is of less significance. The presence of very high bilirubin in hepatitis E and severe intravascular hemolysis due to G-6-PD Deficiency has been seen earlier.[5] Wilson's Disease also can rarely present with acute liver disease and intravascular hemolysis. It is therefore important to look for Wilson's disease since it requires prompt institution of specific therapy.

There has been one case report of acute hemolysis in hepatitis B infection in a child with thalassemia trait.[6] Thalassemia trait as such rarely causes severe hemolysis and the anaemia is minimal. Thalassemia is known to cause ineffective erythropoiesis and Extravascular hemolysis.[7] Hematological manifestations reported in Hepatitis E are hemolytic anemia in G6PD deficiency, Aplastic anemia, Pure red-cell aplasia, Severe thrombocytopenia, Hemophagocytic syndrome, MGUS and Auto-immune.[8]

Our patient had reticulocytosis, indirect hyperbilirubinemia, very high LDH, hemoglobinuria and very low haptoglobin levels indicative of severe intravascular hemolysis. Excess hematin and bilirubin may result in the obstruction of renal tubules, leading to acute renal insufficiency. Therefore renal function should be monitored regularly. Interestingly, Our patient in spite of severe intravascular hemolysis and such high bilirubin did not have any complications and his renal functions were normal too. Hemoglobin electrophoresis revealed that he was heterozygous for β thalassemia. Bilirubin besides being unusually high, took around 5 months to normalize in our patient. No specific etiology could be found out for severe intravascular hemolysis. It remained unclear whether β thalassemia trait was a coincidental finding or whether it had played a role in causing intravascular hemolysis in Hepatitis E.

Thus in a patient with Viral hepatitis E, with low hemoglobin and unusually high bilirubin levels, intravascular hemolysis should be suspected and further investigations including thalessemia work up should be done. Such patients might have prolonged jaundice without complications as seen in this case report. Measures such as correction of anaemia, hypotension, avoidance of nephrotoxic drugs and maintenance of a high urine output, should be instituted in patients with viral hepatitis and haemolytic anaemia.

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