Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency in a Patient with Acute Hepatitis A Infection Leading to Massive Hemolysis

*Saqeb KM

Abstract
Hepatitis A is one of the common causes of acute viral hepatitis. Usually the disease is mild in clinical course and resolves spontaneously with conservative care. But when there is co-existing G6PD deficiency the disease may take an adverse course with production of complications like hemolysis, severe anemia, acute kidney injury, hepatic encephalopathy, acute hepatic failure and even death. The incidence of G6PD deficiency in general population is 2.2% to 14%. So, the co-existence of hepatitis A infected and G6PD deficiency is not very rare. But such cases are not reported frequently. We report a case of acute hepatitis A infection with co-existing G6PD deficiency presenting with severe hemolysis and acute kidney injury.

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Keywords: Glucose-6-phosphate dehydrogenase (G6PD) deficiency, Hepatitis A virus (HAV) infection, Viral hepatitis, Hemolysis

Introduction

Mild hemolysis associated with decreased red blood cell survival may be commonly seen with viral hepatitis, but is seldom of clinical significance.[1,2] However, when viral hepatitis occurs in G6PD-deficient patients, hemolysis may be severe.[2,3] In our case report, we describe a man with Glucose-6-phosphate dehydrogenase (G6PD) deficiency who experienced severe intravascular hemolysis following an attack of acute Hepatitis A infection and failed to recover even after all possible interventions & ultimately he died on 13th day of ICU admission .

Case

A 37 years old non-alcoholic man with no history of pre-existing liver disease got admitted to our hospital with the complaints of upper abdominal pain, nausea, loss of appetite, lethargy, low grade fever and altered level of consciousness for last 7 days. He also noticed yellow coloration of eyes for last 3 days. On examination he was deeply icteric, temperature was 101^0 Fahrenheit, GCS was 11. Flapping tremor was present along with a bilateral plantar extensor response. Abdominal examination revealed tender hepatomegaly. There was neither ascites nor splenomegaly. Rest of the physical examination was normal.

**Dr. Khan Md. Nazmus Saqeb, Assistant Professor, Department of Gastrointestinal, Hepatobiliary & Pancreatic Diseases, Jahurul Islam Medical College & Hospital, Bhagalpur, Bajitpur, Kishoreganj, Bangladesh. drsaqebk59@gmail.com*

Investigations

Laboratory investigations revealed a Hb concentration of 6.6 gm/dl, a total count of WBC of 18700 cells/mm^3, a total serum bilirubin of 38.5 mg/dl with a conjugation fraction of 23.1 mg/dl. The SGPT and SGOT was 2074 unit/L and 1527 unit/L, respectively. Serum creatinine was 5.1mg/dl, serum electrolytes were within normal limit. Prothrombin time was 22.3 seconds (control 11.4 seconds) with an INR of 2.05. Serum ammonia was 139 microgram/dl. Anti HEV IgM and anti HBc IgM were negative. But Anti HAV IgM was positive. And a working diagnosis of HAV induced Acute hepatitis with hepatic encephalopathy and AKI was made.

As the condition of the patient deteriorated, he was shifted to ICU. Where the Hb level further dropped to 5.1 and serum bilirubin peaked up to 67.3 mg/dl with a conjugation fraction of 46.1 mg/dl. SGPT and SGOT were 3171 u/l and 2076 u/l, respectively. Serum creatinine became 7.4 mg/dl. Urine output was very scanty. He underwent 3 sessions of hemodialysis. The PBF showed presence of anisocytosis, poikilocytosis with polychromasia and reticulocytosis. Reticulocyte count was 14% (normal range: 0.5-2%). Serum LDH was 3869 U/L, serum haptoglobin was undetectable. Direct and indirect Coombs tests were negative. Peripheral blood smear for Malaria and ICT for Malaria were negative. Serum copper and ceruloplasmin level were normal and there was no Keyser- Fleischer ring on slit lamp examination, excluding Wilson's disease. In order to find out the cause of hemolysis, G6PD level was done. G6PD level was 2.7 U/g Hb, which was far below normal range (5.5-20.5 units/gm of Hb). The patient was managed accordingly in the ICU. All hepatotoxic, nephrotoxic and oxidant drugs were stopped. Blood transfusion was arranged. Even after all possible efforts urine output gradually decreased. Serum creatinine raised up to 9.1 mg/dl and the patient underwent several sessions of hemodialysis. The metabolic and vital parameters gradually deteriorated and the patient died on 13th day of ICU admission.

Discussion

Mild hemolysis associated with decreased red blood cell survival may be commonly seen with viral hepatitis, but is seldom of clinical significance.[1,2] However, when viral hepatitis occurs in G6PD-deficient patients, hemolysis may be severe.[2,3]In our case the patient experienced severe intravascular hemolysis as evidenced by a fall in hemoglobin, reticulocytosis, unconjugated hyperbilirubinemia, hemoglobinuria and undetectable serum haptoglobin levels. In a case control study, Gotsman and Muszkat[4] evaluated the impact of G6PD deficiency on patients with Hepatitis A virus infection. They found that although patients with G6PD deficiency had a more severe initial clinical presentation, the clinical outcome was not affected. But in our case the patient's condition gradually deteriorated and he ultimately died on 13th day of ICU admission despite all possible efforts. The presence of severe hyperbilirubinemia in patients with viral hepatitis and G6PD deficiency has been previously reported.[5-7]Abid and Khan[8] recently reported a cohort of five patients from Pakistan with G6PD deficiency and Hepatitis E viral infection. All five patients had severe and protracted illness, and four developed acute renal failure. But here we present a case of Hepatitis A virus infection with G6PD deficiency with a grave outcome. Profound hemolysis in G6PD-deficient individuals is usually precipitated by exposure to selected drugs. However, as in this case, viral hepatitis may precipitate massive hemolysis even without the intake of such drugs.[2,6,8] The mechanism of hemolysis is thought to occur through decreased levels of

reduced glutathione in red blood cells.[1] Reduced glutathione levels could result from the accumulation of oxidants due to hepatic dysfunction and lead to increased hemolysis in the presence of G6PD deficiency. Despite the high levels of bilirubin in these patients, the prognosis is mainly related to the severity of hepatic injury.[5]

Acute renal insufficiency, though uncommon in uncomplicated acute viral hepatitis, can occur as a fatal complication of severe intravascular hemolysis in these patients.[9] Excess hematin and bilirubin may result in the obstruction of renal tubules, leading to acute renal insufficiency with increased morbidity. Renal failure may be nonoliguric, therefore, kidney function should be assessed by regularly monitoring blood chemistry, and urinary sodium and osmolarity. Measures to prevent renal failure include maintaining good hydration and adequate urine output, and avoiding nephrotoxic drugs.

In patients with acute viral hepatitis and unexplained anemia with very high serum bilirubin levels, intravascular hemolysis should be considered and investigated. Wilson's disease may present with jaundice and hemolysis and must be excluded. Tests for G6PD deficiency may be negative during and immediately after a hemolytic episode because the old red blood cells deficient in G6PD have been hemolyzed and the higher content of G6DP in the new red blood cells may lead to false normal levels. A repeat test should be done eight to 10 weeks after the disease resolves. Finally, all G6PD-deficient individuals should be vaccinated against Hepatitis A and B. Universal immunization against HAV and HBV for communities with high prevalence of G6PD deficiency should also be considered.

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