

Hepatitis-Induced Hemolysis in Pediatrics: A Rare Case Report

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Abstract: This article presents a case study of a 6-year-old boy diagnosed with acute Hepatitis A virus (HAV) infection compounded by glucose-6-phosphate dehydrogenase (G6PD) deficiency. The patient exhibited a constellation of symptoms, including low-grade fever, upper abdominal pain, fatigue, and anorexia, over an 8 to 10-day period. Notably, jaundice, dark-colored urine, and hepatomegaly were prominent clinical features. Laboratory investigations revealed severe intravascular hemolysis, evidenced by a decline in hemoglobin, elevated reticulocytes, and unconjugated hyperbilirubinemia. The diagnosis of HAV hepatitis was confirmed through positive IgM anti-hepatitis A virus. Over the subsequent two weeks, the patient experienced peak levels of serum bilirubin, AST, and ALT. Conservative management focused on avoiding hepatotoxic drugs, ensuring adequate urine output, and monitoring metabolic parameters. Gradual improvement was observed over the subsequent month, with a significant reduction in bilirubin levels, restoration of hemoglobin, and a decline in liver enzymes. The patient was discharged for outpatient follow-up, and four weeks post-onset, G6PD levels approached normal, emphasizing the importance of comprehensive care in such complex cases. This case underscores the intricate interplay between viral hepatitis and G6PD deficiency, contributing valuable insights into the clinical presentation and management of severe hemolysis in this specific population.

Keywords: Hepatitis; hemolysis; G6PD; Children; Hemoglobin

Introduction

Glucose-6-phosphate dehydrogenase (G6PD) deficiency stands as one of the most prevalent inherited enzyme disorders globally, affecting over 400 million people worldwide (Mehta et al., 2000). The distribution of this deficiency is notably high in regions such as Africa, Southeast Asia, the Mediterranean, the Middle East, and the Indian subcontinent (Smith, 2005). The enzyme G6PD, crucial for various cellular functions, is present in varying concentrations across multiple cell types, including red blood cells.

Concurrently, hepatitis A ranks among the most common causes of foodborne infections, accounting for an estimated 1.5 million cases annually (1). Typical manifestations of hepatitis A infection encompass symptoms such as fever, malaise, anorexia, abdominal discomfort, diarrhea, dark-colored urine, and jaundice. Importantly, acute hepatitis A tends to be a self-limiting illness, rarely progressing to chronic conditions, with acute liver failure occurring in approximately one percent of cases (2).

In the context of viral hepatitis, mild to moderate hemolysis is a recognized complication. However, the occurrence of severe hemolysis is less common and tends to be more frequent in individuals with coexisting G6PD deficiency (2–9). The relationship between viral infections and severe hemolysis in G6PD-deficient patients has been postulated, and certain drugs and dietary factors are known to exacerbate this condition (2). Moreover, G6PD deficiency has been implicated in hindering the repair of damaged hepatocytes, potentially leading to fulminant hepatitis and liver failure in the setting of acute viral hepatitis (10, 11).

In this report, we present a case study involving a previously undiagnosed G6PD-deficient patient who presented with hyperbilirubinemia and severe hemolysis precipitated by acute hepatitis A infection. This case sheds light on the intricate interplay between G6PD deficiency and acute viral hepatitis, emphasizing the need for heightened awareness and comprehensive management strategies in such clinical scenarios.

Case report

The case report describes a 6-year-old boy who presented with symptoms including low-grade fever, upper abdominal pain, fatigue, and loss of appetite over a span of eight to 10 days. The patient also reported yellow discoloration of the eyes for three days and dark-colored urine for five to six days. Upon examination,

profound jaundice was observed, and abdominal examination revealed a soft, tender liver palpable 4 cm below the costal margin. No splenomegaly was noted, and the rest of the physical examination was unremarkable.



Figure 1: A 6-year-old boy presented with yellow discoloration of the eyes

Laboratory investigations revealed a hemoglobin concentration of 8 g/L, a total leukocyte count of $12.2 \times 10^9/L$, corrected reticulocytes at 10%, and a total serum bilirubin of [missing value] with a conjugated fraction of 25.7 mg/dL. Additionally, the serum aspartate aminotransferase (AST) concentration was 1053 U/L, and the alanine aminotransferase (ALT) concentration was 250 U/L. The prothrombin time was 15 s (control: 12 s). Immunoglobulin (Ig) M anti-hepatitis A virus was positive, while hepatitis B surface antigen, IgM anti-hepatitis B core, anti-hepatitis C virus, and Coombs test were negative. A diagnosis of HAV hepatitis was established, and the patient was managed conservatively.

Over the next two weeks, serum bilirubin peaked at 30 mg/dL (conjugated fraction: 27 mg/dL), AST at 1500 U/L, and ALT at 2000 U/L. Hemoglobin decreased to 7.5 g/L. Peripheral blood smear revealed polychromasia, anisopoikilocytosis, and reticulocytosis (reticulocyte count: 14.6%). Bile pigments were detected in urine. Direct and indirect Coombs tests were negative, and eye examination ruled out Keyser-Fleischer rings, excluding Wilson's disease.

Conservative management involved avoiding hepatotoxic, nephrotoxic, and oxidant drugs while maintaining adequate urine output. Metabolic parameters gradually improved over the subsequent month, with hemoglobin reaching 11.5 g/L, bilirubin falling to 5 mg/dL (conjugated fraction: 3 mg/dL), AST decreasing to 121 U/L, ALT dropping to 200 U/L, and the reticulocyte count decreasing to 4.4%. The patient was discharged for outpatient follow-up. Four weeks post-onset, the G6PD level was 5 U/gHb, and serum bilirubin and aminotransferase levels were nearly normal.

Discussion

In individuals with viral hepatitis, concurrent mild hemolysis is not uncommon but is typically of minimal clinical significance (6,7). However, when viral hepatitis occurs in individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency, the hemolytic response may escalate to a severe level (7,8). The case presented here exemplifies intravascular hemolysis, as indicated by a decline in hemoglobin levels, reticulocytosis, and unconjugated hyperbilirubinemia. Severe hyperbilirubinemia in the context of viral hepatitis and G6PD deficiency has been previously documented (9-11).

Gotsman and Muszkat conducted a case-control study evaluating the impact of G6PD deficiency on patients with Hepatitis A virus infection, revealing that while patients with G6PD deficiency exhibited a more severe initial clinical presentation, the overall clinical outcome was not significantly affected (12). Similarly, Abid and Khan reported on a cohort of G6PD-deficient patients with Hepatitis E viral infection, noting severe and protracted illness in all cases, with four individuals developing acute renal failure (5).

While profound hemolysis in G6PD-deficient individuals is typically associated with exposure to specific drugs, this case underscores that viral hepatitis alone can precipitate massive hemolysis, even in the absence of such drug intake (5,7,10). The proposed mechanism involves a decrease in reduced glutathione levels in red blood cells, potentially resulting from the accumulation of oxidants due to hepatic dysfunction. This scenario could amplify hemolysis in the presence of G6PD deficiency. Despite the elevated bilirubin levels in

these patients, the prognosis appears primarily linked to the severity of hepatic injury (9). Acute renal insufficiency, an uncommon complication in uncomplicated acute viral hepatitis, may arise as a fatal consequence of severe intravascular hemolysis (3). Excess hematin and bilirubin can obstruct renal tubules, leading to acute renal insufficiency with increased morbidity. Regular monitoring of blood chemistry, urinary sodium, and osmolarity is crucial, and preventive measures include maintaining good hydration, ensuring adequate urine output, and avoiding nephrotoxic drugs. Hepatitis A virus (HAV) infection, transmitted via the feco-oral route, differs from other enteric agents in its limited transmission from infected persons to close contacts (13). In cases of acute viral hepatitis with unexplained anemia and significantly elevated serum bilirubin levels, consideration and investigation of intravascular hemolysis are warranted. Wilson's disease, which can manifest with jaundice and hemolysis, must be ruled out. Testing for G6PD deficiency may yield false-negative results during and immediately after a hemolytic episode, as the old G6PD-deficient red blood cells are hemolyzed, and the new red blood cells may exhibit falsely normal G6PD levels. Repeat testing should be performed 8 to 10 weeks after the resolution of the disease (14).

Recommendations arising from this case include the avoidance of vitamin K treatment in suspected G6PD deficiency cases, as it may exacerbate hemolysis. Furthermore, universal vaccination against Hepatitis A and B is advised for all G6PD-deficient individuals, especially in communities with high prevalences of G6PD deficiencies.

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