

Anemia-induced liver injury: A rare case revealing glucose-6-phosphate dehydrogenase deficiency

Yosra Zaimi^{1,2} | Myriam Ayari^{1,2}  | Asma Mensi^{1,2} | Emna Chelbi² | Shema Ayadi^{1,2} | Yosra Said^{1,2} | Leila Mouelhi^{1,2} | Radhouane Debbeche^{1,2}

¹Department of Hepato-Gastroenterology, Charles Nicolle Hospital, Tunis, Tunisia

²Faculty of Medicine of Tunis, University of Tunis El Manar, Tunis, Tunisia

Correspondence

Myriam Ayari, Department of Hepato-Gastroenterology, Charles Nicolle Hospital, Tunis, Tunisia.

Email: ayari.myriam@hotmail.fr

Abstract

Hypoxic hepatitis may occur due to hemodynamic mechanisms of hypoxia secondary to anemia without any context of reduced blood flow, respiratory failure, or shock state. Etiology of anemia should be investigated in order to avoid recurrence.

KEYWORDS

acute liver injury, anemia, G6PD deficiency, hypoxic hepatitis

1 | INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common inherited enzyme deficiency in red blood cells worldwide.¹ It is an X-linked recessive congenital hemolytic anemia, as the G6PD gene is located on the distal long arm of the X-chromosome (Xq28) and is therefore classically encountered in male patients. Although most carriers remain asymptomatic, clinical manifestations of G6PD are polymorphic and may range from erythroblastosis fetalis, chronic hemolysis, acute hemolysis, and hyperbilirubinemia. Acute hemolytic crises are usually caused by medications, systemic infections, or fava bean consumption and may induce severe anemia. Hypoxic hepatitis due to anemia is an extremely rare condition that can lead to acute life-threatening liver failure. Herein, we report the case of an adult female patient presenting acute liver injury due to severe anemia revealing G6PD deficiency.

2 | CASE PRESENTATION

A 47-year-old Caucasian woman presented with acute jaundice, extreme weakness, abdominal pain, palpitations, and acute breathlessness. She had no other significant

personal or family past medical history. Physical examination showed intense icterus, high heart rate (124 beats per minute), and respiratory rate (28 breaths per minute). The investigations blood tests indicated elevated liver enzymes alanine aminotransferase (ALAT) of 1540 IU/L, aspartate aminotransferase (ASAT) of 952 IU/L, decreased prothrombin time 37%, elevated international normalized ratio (INR) of 2.05, normochromic anemia of 2.5 g/dL, and hyperbilirubinemia of 482 µmol/L (normal range = 1.71 - 20.5 µmol/L). Hemolysis markers were positive with lactate dehydrogenase level of 4701 U/L (normal <250 U/L), unconjugated bilirubin of 250 µmol/L, haptoglobin <0.024 mg/dL (normal range = 44 - 215 mg/dL), and test coombs was negative. Acute liver injury was diagnosed. There was no encephalopathy. The patient did not take any medications, did not consume alcohol, herbs, or toxics. There were no risk factors for viral hepatitis or chronic liver disease. Serological markers of hepatitis A/B/C/E, cytomegalovirus, Epstein-Barr, and Herpes simplex virus were negative. Autoimmune hepatitis profile including anti-smooth muscle antibody, antimitochondrial, and anti-liver kidney microsomal came out to be negative. Cupric tests were also normal as well as alpha1-antitrypsin level. Abdominal computed tomography scan showed no abnormal findings except homogenous hepatosplenomegaly.

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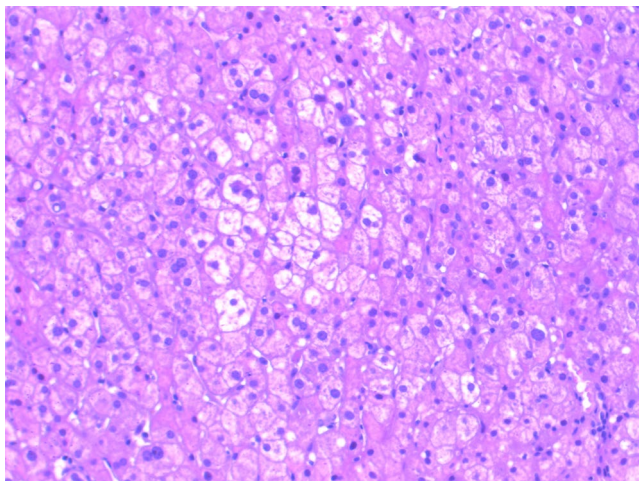


FIGURE 1 Histologic examination of hepatic biopsy (hematoxylin and eosin stain) showing moderate ballooning degeneration of hepatocytes

Liver biopsy revealed moderate ballooning of hepatocytes without any specific findings (Figure 1). Bone marrow biopsy was performed while investigating anemia and showed erythroid hyperplasia without specific findings. Hemoglobin electrophoresis showed normal results. Supportive care was initiated and the patient was transfused with six units of red blood cells. Hemoglobin gradually improved over the subsequent following days, closely followed with normalization of prothrombin time and transaminases. After improvement of clinical and biochemical features, the patient was discharged from hospital with a bilirubin level of 5.7 mg/dL and hemoglobin of 10 g/dL. Acute hemolytic anemia was found to be linked to G6PD deficiency, leading to hypoxic hepatitis and acute liver injury. The diagnosis was made one month after the patient was discharged, away from the hemolytic episode, and based on reduced enzyme activity. Recommendations to follow in order to avoid other acute hemolysis crises were clearly explained to the patient.

3 | DISCUSSION

Hypoxic hepatitis is secondary to a mismatch between hepatic oxygen requirements and blood supply. It is characterized by a massive but transient increase in both serum transaminases level, often predominant over aspartate aminotransferase followed by a normal return of levels over few days to a week. The work of Henrion's team had classified acute hypoxic liver into four etiological groups: decompensated congestive heart failure, acute cardiac failure, exacerbated chronic respiratory failure, and toxic/septic shock,² which account for more than 90% of hypoxic hepatitis cases. However, specific conditions such as profound

acute anemia can also lead to hypoxic liver injury. It's an extremely rare cause of hypoxic hepatitis and to our knowledge, only four cases have been reported in the literature³⁻⁶ in which hemoglobin level ranged between 1.7 and 3.2 g/dL. In one report etiology of anemia was specified and was linked to pernicious anemia.⁴

Such impairment is caused by a sudden and highly reduced oxygen delivery to the liver, as hemoglobin's first function is an oxygen carrier, resulting in hepatocellular suffering and necrosis.

The diagnosis of hypoxic hepatitis is primarily clinical, but can still be a diagnosis of exclusion. Typically it does not require liver biopsy. However, in such rare cause of hepatitis, biopsy may be needed to exclude others causes of liver injury as well as exhaustive etiological workup of acute hepatitis. Ischemic hepatitis prognosis is known to be poor as it is usually associated with life-threatening underlying conditions. Nevertheless, when it's due to anemia, prognosis may be better if timely oxygen-carrying capacity is restored with red blood cells transfusion and will essentially depend on the etiology of anemia.

In our case, severe anemia was found to be related to G6PD deficiency. It is an X-linked recessive genetic disorder characterized by enzymatic defect causing prematurely red blood cell breakdown induced by certain exogenous hemolytic trigger such as medications, chemicals, bacterial and viral infections, or favism. The spectrum of the disease includes hyperbilirubinemia, acute hemolysis, and chronic hemolysis,⁷ depending upon the specific form of the disorder that is present. Acute hemolytic anemia is one of the most frequent clinical manifestations. The degree of hemolysis associated with G6PD deficiency may vary greatly among affected individuals. Another particularity of our case is that G6PD deficiency was diagnosed in a female patient since it is mainly affecting males as it is X-linked inheritance. Usually, women are affected only if they are homozygous for G6PD mutation which is a very rare situation. Nevertheless, G6PD deficiency had been observed in symptomatic heterozygous women.⁸ This phenomenon is explained by the inactivation of one of the X chromosomes (lyonization).⁸

To the best of our knowledge, this is the first reported case of G6PD deficiency revealed by acute liver injury by hypoxic hepatitis due to severe hemolytic anemia in a female patient. Diagnosis might be challenging; however, it is important to promptly recognize this rare situation.

In conclusion, this case highlights many points. First, hypoxic hepatitis may occur due to hemodynamic mechanisms of hypoxia secondary to anemia without reduced blood flow, respiratory failure, or shock state. Second, symptomatically treatment should be based on rapid restoration of oxygen-carrying capacity. Finally, etiology of anemia should be

investigated to allow specific treatment of the underlying disease and avoid recurrence.

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CONFLICT OF INTEREST

Nothing to declare.

AUTHOR CONTRIBUTIONS

MA and YZ: Gathered the information, involved in intellectual content, wrote the manuscript. AM: assisted in the preparation of manuscript. EC: extracted and interpreted histologic data. SA, LM, and YS: contributed to the critical review of the manuscript. RD: revised the manuscript and acted as guarantor for the research.

ETHICS STATEMENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

DATA AVAILABILITY STATEMENT

All data are available as part of the article and no additional source data are required.

ORCID

Myriam Ayari  <https://orcid.org/0000-0001-7361-8248>

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