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Severe Hemolysis as the First Manifestation of Acute Hepatitis A in an Adult with G6PD Deficiency and Positive ANA

Dhrubajyoti Bandyopadhyay[1,*], Adrija Hajra[2], Sabyasachi Mukhopadhyay[3], Vijayan Ganesan[4], Manas layek[5], Debarati Bhar[4], Diptak Bhowmick[4], Cankatika choudhury[4], Partha Sarathi Karmakar[4]

[1]Department of accident and emergency, Lady Hardinge Medical College, New Delhi
[2]Department of Internal Medicine, IPGMER, Kolkata
[3]RG Kar medical college, Kolkata
[4]Department of Internal Medicine, RG Kar Medical College, Kolkata
[5]Lady hardinge medical college, New delhi
*Corresponding author: drdhrubajyoti87@gmail.com

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Abstract We report a case of hemolytic anemia as an initial manifestation of hepatitis A virus infection. On admission, the patient had anemia, reticulocytosis, and direct and indirect hyperbilirubinemia. On subsequent examination, he had both glucose-6-phosphate dehydrogenase deficiency (G6PD) and autoimmune antibodies.

Keywords: *Glucose-6-phosphate dehydrogenase deficiency (G6PD), Hepatitis A, Antinuclear antibody (ANA)*

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1. Introduction

Here we present a case of hepatitis A induced hemolytic anemia which can be due to both G6PD deficiency and autoimmune hemolytic anemia.

2. Case Report

A 20yr- old male patient was admitted with fever for 3wks associated with yellowish discoloration of sclera and brownish discoloration of urine for last 15 days. Fever was associated with occasional vomiting and anorexia. He had past history of occasional alcohol intake**.** On examination he had severe pallor, jaundice and soft, tender hepatomegaly.

Laboratory investigations revealed following –

Hemoglobin	3.9gm/dl
red cell count(RBC)	1.17 million/cmm, (macrocytic)
white blood cell count(WBC)	5800/cmm(N_{68} L_{25} M_7)
mean corpuscular volume(MCV)	106.8fl
red cell distribution width(RDW)	17%
reticulocyte percentage	12%,
erythrocyte sedimentation rate(ESR)	10mm/hr
urea	22mg/dl
normoblast	6/100 WBC
creatinine	0.6mg/dl
bilirubin(total)	15.2mg/dl (conjugated-8.8,unconjugated-6.4)
total protein	4.1 gm/dl
serum albumin	2.1gm/dl
aspartate aminotransferase	81U/L
alanine aminotransferase	249U/L
alkaline phosphatase	56U/L
Lactate dehydrogenase(LDH)	466 U/L
Prothombin time	16.7sec(control-14.5sec)

USG whole abdomen showed hepatomegaly, thick edematous gall bladder wall. Anticipating the possibility of intravascular hemolysis we further investigated and found haptoglobulin level -8 mg/dl (normal range, 30–300 mg/dl), direct and indirect Coombs' tests-negative, urine for hemosiderin-positive, and the results of hemoglobin

electrophoresis was within the normal range. Hepatitis B, C, D, and Eviruses, Cytomegalovirus, Epstein-Barr virus, human immunodeficiencyvirus, parvovirus B 19, herpes simplex virus types 1 and 2, toxoplasmosis, and rubella infection were ruledout by the results of serologic assays. The results of testing for serum hepatitis A virus immunoglobulin G and immunoglobulinM antibodies were positive. Malaria parasite dual antigen (MPDA) and leptospiralIgM antibody were negative.At this point we confirmed that it was a case of hepatitis A virus induced intravascular hemolysis. To search for other causes which had precipitated hemolysis, we found that G6PD was 1.5 U/g Hb (normal range, 4.6–13.5 U/g Hb) and ANA titre was positive in 1:160 dilution. Patient was put on supportive treatment with adequate hydration and vitamin K injection. Within one week he was discharged from hospital. On subsequent follow up after 6 weeks repeat G6PD was 2.5 U/Hg and ANA titre was 1:40.

3. Discussion

Infection with hepatitis A generally is believed to be self-limited; however, it can produce effects that range from alack of symptoms to death from fulminant hepatitis. [1] Hemolyticanemia is a less commonextra- hepatic manifestation of viralhepatitis, including hepatitis A. Hepatitis A infection is known to induce autoimmune hepatitis and autoimmune hemolytic anemia. Although in our case the results of direct and indirect Coombs' tests were negative, there was presence of autoimmune antibody such as ANA which disappeared during follow-up. Berlin and associates reported that in non-autoimmune individuals with various infections, elevated titers of autoanti bodies could be detected by molecular mimicry of microbial peptides similar to self-tissues. The transient nature of the autoantibodies in our patients could be explained by this [2].

This patient also had low level of G6PD. G6PD is the only way to generate a reducedform of nicotinamide-adenine dinucleotide phosphate, asubstance that maintains the reduced form of glutathione(which protects against oxidative damage) in cells. Hemolysis may develop in G6PD-deficient patients with viralhepatitis A. Abnormally low levels of glutathione, which revert to normal levels after a patient's recovery, have been identified during hepatitis infection [3]. The level of glutathione, which is already low in patients with G6PD deficiency, decreases further in people with infections, including hepatitis [4]. There is evidence of hemolysis in 23% of patients with viral hepatitis who were not G6PD deficient. However, mild, moderate,or severe hemolysis occurs in 87% of G6PD-deficient persons. Also acute viral hepatitis with G6PD deficiency with or without hemolysis hadhigher bilirubin values than did patients with viral hepatitis without G6PD deficiency. [5] The high bilirubin level in patient with G6PD deficiency and hepatitis A could not be entirely explained by hemolysis, because both total and direct bilirubin levels were significantly higher. In patients with a G6PD deficiency, the prothrombin time was statistically significantly longer than that it was in control. Increased morbidity and initial clinical severity was reported in acute viral hepatitis with glucose-6-phosphate dehydrogenase deficiency [6].

In this patient we found both G6PD deficiency and positive ANA titre which is extremely rare. Moreover this patient was detected as G6PD deficient after the onset of viral hepatitis. After the resolution of viral hepatitis the G6PD increased a little as the acute stress in the form of viral hepatitis is over.

From the above discussion we can conclude that all patients with acuteviral hepatitis A and marked hyperbilirubinemia should be carefully observed for hemolysis. If hemolysis is found then search for the causes like G6PD deficiency or ANA titre. Whenever abnormality is detected, follow-up should be done. Persistence of ANA in high titre will make us aware of concomitant or future occurrence of autoimmune hepatitis. To prevent such excessive hemolytic episodes our suggestion is to consider hepatitis A vaccination for all G6PD deficient individuals. Universal vaccination against the hepatitis A virus should be considered in the ethnic population where G6PD deficiency is very common.

Conflict of Interest and Funding Source

None.

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