

Hepatitis A Virus-induced Severe Hemolysis Complicated by Severe Glucose-6-Phosphate Dehydrogenase Deficiency

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Abstract

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an x-linked recessive genetic disorder with mutation in the G6PD gene. Defect in the enzyme G6PD causes red blood cells (RBCs) to breakdown prematurely causing hemolytic anemia. Hemolytic anemia is also a known hematological complication associated with viral hepatitis. In such patients, hemolysis may be more severe if there is any secondary injury to RBC in the form of membrane defect, oxidative stress, or enzyme deficiency like in G6PD deficiency. Here, we present a case of an adult, not previously diagnosed with G6PD deficiency, who presented with viral hepatitis, severe hemolysis, and multiorgan failure.

Keywords: Glucose-6-phosphate dehydrogenase deficiency, hemolytic anemia, hemoperfusion, hepatitis A, methemoglobinemia, multiorgan failure

INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an x-linked recessive genetic disorder with mutation in the G6PD gene. Defect in the enzyme G6PD causes red blood cells (RBCs) to breakdown prematurely causing hemolytic anemia. Mostly, patients with G6PD deficiency remain asymptomatic, but following any trigger, symptoms of hemolysis may develop. It is more prevalent in the African, Asian, Mediterranean, and middle-east regions.^[1-5]

Hemolytic anemia is also a known hematological complication associated with viral hepatitis. In such patients, hemolysis may be more severe if there is any secondary injury to RBC in the form of membrane defect, oxidative stress, or enzyme deficiency like in patients with G6PD deficiency.^[6-8] Here, we present a case, not previously diagnosed with G6PD deficiency, who presented with viral hepatitis, severe hemolysis, and multiorgan failure.

CASE REPORT

A 39-year-old male presented with a history of high-grade fever of 15 days and yellowish discoloration of eyes and urine of 10-day duration. Associated features included dull aching pain in the right hypochondrium and epigastric region, dyspnea

at rest, decreased urine output, and vomiting. He also had a history of use of analgesics such as paracetamol (up to 3 g/day), tramadol, and diclofenac for his back pain for the past 15 days.

On examination, the patient was drowsy, and had a heart rate of 100/min, blood pressure of 136/82 mmHg, respiratory rate of 36/min, and was maintaining saturation SpO₂ of 88%–92% on 15 L of oxygen through nonbreathing mask. Icterus was present, but there was no flapping tremor, pedal edema, or lymphadenopathy. The patient was anuria. Basic investigations are shown in Table 1.

Over the next few hours, the patient continued to deteriorate with worsening of sensorium and hypotension with increasing vasopressor requirement and need for noninvasive ventilation. One unit packed RBCs were transfused, and hemodialysis plus hemoperfusion was done using ammonia (Jaffron HA330-II) and bilirubin (Jaffron BS330) filters in view of worsening sensorium, life-threatening multiorgan failure, and high bilirubin and ammonia levels [Figures 1 and 2].

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How to cite this article: Sharma D, Singh O, Juneja D, Goel A, Garg SK, Shekhar S. Hepatitis a virus-induced severe hemolysis complicated by severe Glucose-6-Phosphate Dehydrogenase deficiency. Indian J Crit Care Med 2018;22:670-3.

Access this article online

Quick Response Code:



Website:
www.ijccm.org

DOI:
10.4103/ijccm.IJCCM_260_18

Table 1: Basic laboratory investigations during the Intensive Care Unit stay

	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
HB (g/dl)	6.9	8.5	7	7.6	7.4	6.8	8.8	8.5
TLC (10 ⁹ /L)	65.3	74.7	69.2	58.1	36.1	18.9	12.4	8.5
CPK (U/L)	1422	1041	874	882	639			
LDH/(U/L)	7465	6867	4503	3975	2489			
Uric acid (mmol/L)	11.9	7.1		6.4	10.1	9.5		
Ammonia (µmol/L)	1806.9	1641.4	478.6	252	169	122		
PT (s)	13.8	18.5	18.2	16.7	17.8	17.4	17.1	16.5
INR	1.21	1.6	1.6	1.47	1.56	1.53	1.48	1.44
Bilirubin (total) (µmol/L)	35.3	28.2	37.8	48.9	44.3	40.2	37.7	
Bilirubin (direct) (µmol/L)	20.7	18	26.2	33.3	26	24.1	20.2	
Bilirubin (indirect) (µmol/L)	14.6	10.2	11.6	15.6	18.3	16.1	17.5	
SGOT (U/L)	2422	1863	925.6	627	389	246	181	137
SGPT (U/L)	1963	1353	715.6	561	373	238	169	119
Ferritin (ng/ml)	>7500					>7500		
Urea (mmol/L)	121.1	148.7	124.6	139.2	135.1	141.2	140.3	99.7
Creatinine (mg/dl)	7.2	8.3	7.2	5.7	5.6	6.0	6.6	5.4

Hb: Hemoglobin, TLC: Total leukocyte count; CPK: Creatinine phosphokinase; LDH: Lactate dehydrogenase; PT: Prothrombin, INR: International normalized ratio; SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase

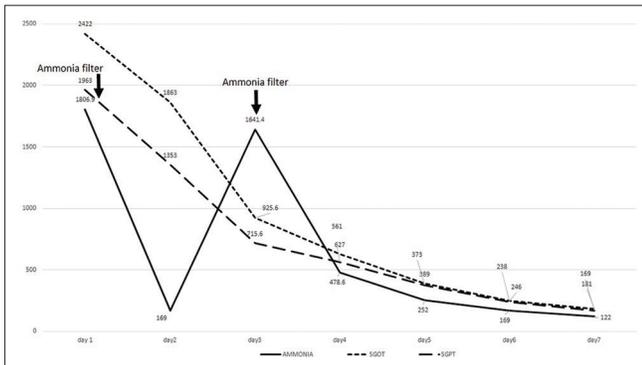


Figure 1: Serial ammonia, serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase levels, and effect of ammonia filters

Arterial blood gases showed disparity between SpO₂ (86%) and SaO₂ (99.9%), and hence, Co-oximetry was done which showed raised levels of methemoglobin (9.8%) [Table 2]. High-performance liquid chromatography G6PD levels were sent which came out to be very low 2.5 u/ghb (normal range: 7–20 u/ghb).

Workup for fever was done, including for tropical fevers, which was negative, but hepatitis A virus antigen was positive. Peripheral blood smear showed microspherocytes and fragmented RBCs. Hence, the diagnosis of acute liver failure, secondary to hepatitis A infection, with G6PD deficiency, acute severe hemolysis, and multiorgan dysfunction was made. The possibility of need for liver transplantation was also assessed. However, after 48 h of aggressive management, the patient started to show clinical recovery with the improvement in sensorium, normalization of blood pressure, and reduced oxygen requirement. Liver and kidney function tests continued to remain deranged, and hemodialysis was continued. Multiple blood transfusions were given, as and when indicated. He

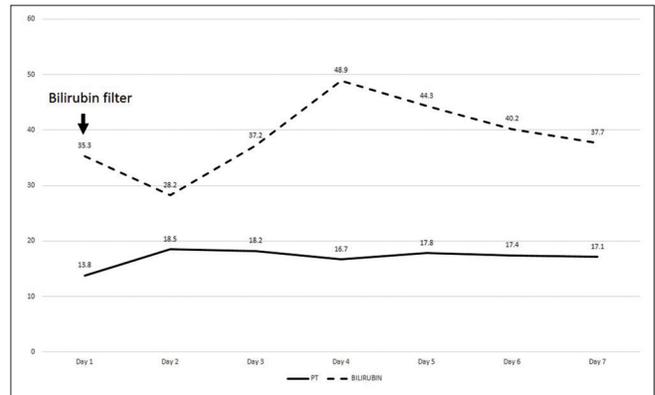


Figure 2: Serial bilirubin and prothrombin levels and effect of bilirubin filter

was shifted out of the intensive care unit after day 6 and was discharged from the hospital after 11 days of hospitalization. However, he remained anuria and required intermittent hemodialysis.

DISCUSSION

According to the World Health Organization report,^[9] the prevalence of G6PD deficiency in India ranges between 0% and 10% which is population specific and is found to be higher among tribals.^[10] In the present case, severe hemolysis was induced by hepatitis A infection, with a background G6PD deficiency. This might have been further complicated by prolonged and chronic use of paracetamol leading to severe liver dysfunction. Early aggressive care, including the use of hemodialysis and hemoperfusion filters, might have improved the outcome in our case.

Infection or exposure to certain drugs and chemicals may precipitate severe hemolytic anemia in G6PD deficiency patients. Infections such as viral hepatitis, typhoid fever, and

Table 2: Arterial blood gases parameters over the first 4 days

	Day 0 (NRBM)	Day 1 (NIV)	Day 2 (NRBM)	Day 3 (room air)	Day 4 (room air)
pH	7.340	7.263	7.474	7.417	7.417
Methemoglobin levels	9.8	8.0	4.3	3.5	0.9
Lactate	2.5	2.1	2.1	1.7	1.8
Bicarbonate	22.4	17.7	27.4	30.0	23.5
pO ₂	167	111	48.2	53.8	27.1
pCO ₂	42.9	40.3	37.0	48.7	36.1
Oxygen saturation	99.4	97.6	95.8	96.1	96.0

NRBM: Nonrebreathing mask; NIV: Noninvasive ventilation, pO₂: Partial pressure of oxygen, pCO₂: Partial pressure of carbon dioxide

pneumonia, as well as upper respiratory and gastrointestinal infections are well-known triggers of hemolytic episodes in these patients.^[11] As hepatitis A is generally a self-limiting disease, it may get complicated only if there is a secondary stress on RBCs. Severe hemolysis may be precipitated in patients with acute hepatitis A, especially in the background of G6PD deficiency. The initial clinical severity of hepatitis may also be worse in patients with underlying G6PD deficiency.^[12] However, only a few such cases have been described in India.^[13,14]

Our patient presented with multiorgan failure and hepatic encephalopathy with very high ammonia levels. Previous reports have suggested that patients with hepatic coma have worse clinical outcomes.^[14,15] Hence, it may seem prudent to treat these patients aggressively. Extracorporeal therapy, other than hemodialysis, has been tried in such cases, with good results.^[16]

Plasmapheresis has also been used previously in patients with hepatitis A infection with G6PD deficiency in the background of autoimmune hemolysis, with good results.^[17] However, ours is the first report of using hemodialysis with hemoperfusion in such patients.

Liver support system using hemoperfusion cartridge was applied in our case in view of severe hyperbilirubinemia, multiorgan failure, and worsening sensorium. Nonbioartificial liver support may be indicated in patients with acute liver failure as these may have good short-term efficacy and reduce the level of hepatic encephalopathy, reduce serum bilirubin levels, improve prothrombin activity or international normalized ratio, and may also improve other laboratory parameters, including blood ammonia and endotoxins.^[18,19] In our case too, it helped in reducing bilirubin and ammonia levels and tide over the acute crisis.

Our case is unique in several aspects. First, our patient was an adult without any previous history of hemolysis secondary to G6PD deficiency. Then, our patient presented with severe hemolysis and multiorgan failure. His clinical course was further complicated by the development of methemoglobinemia. In the end, early aggressive care, with the use of hemoperfusion filters, might have helped in achieving favorable outcome in our patient.

CONCLUSION

Sometimes, even generally mild diseases such as hepatitis A may get complicated in the presence of underlying occult diseases such as G6PD deficiency, and patients may present with multiorgan failure and may be associated with high mortality rates. Hence, it may seem prudent to look for any such previously undiagnosed medical conditions if the patient presents with any unexpectedly severe clinical symptoms.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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