CASE REPORT

Severe haemolysis and renal failure precipitated by hepatitis E virus in G6PD Deficient patient: A case report

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Abstract

Hepatitis E virus is the etiological agent for Hepatitis E infection, which is congruent to Hepatitis A infection. The clinical spectrum of the disease range from asymptomatic self-limiting disease which requires no treatment to life threatening fulminant liver disease in pregnancy, G6PD deficient and post-liver transplant patients, which necessitate urgent treatment. Similarly we are reporting a case of a 28 year old male with no previous known comorbids, who presented in emergency department with low grade fever, yellow discolouration of eyes and upper abdominal pain for last 5-6 days. We affirmed the diagnosis of acute viral hepatitis E with G6PD deficiency. This case had a different prospect of HEV infection and its coexistence with G6PD deficiency, which lead to investigations, management and avoidance of complications of the disease.

Keywords: Glucose-6-phosphate dehydrogenase, G6PD, Hepatitis E, Haemolysis.

Introduction

According to World Health Organization (WHO), every year around 20 million people get infected with hepatitis E virus.[1] Of these 3.3 million people have the disease.[1] Hepatitis E infection in 2015 resulted in around 44000 deaths worldwide.[1,2] The highest prevalence of Hepatitis E is in East Asia and South Asia due to inadequate sanitation.[3-5] It is a mild and self-limiting disease, which requires conservative management with no aggressive mode of treatment.[6,7]

Glucose - 6 - phosphate dehydrogenase (G6PD) deficiency is one of the most common type of enzyme deficiencies. It is estimated to affect millions of people worldwide.[6] G6PD deficiency is an X-linked recessive hereditary disorder characterized by abnormally low levels of glucose-6-phosphate dehydrogenase.[6,8]

The coexistence of Hepatitis E infection in G6PD patients can result in severe haemolysis, renal failure, anaemia, jaundice and other complications such as fulminant hepatitis and acute liver failure. It may consequence in morbidity and mortality, if critical attention to the patient is not provided immediately.[4,6,9]

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Case Report

On 21st of May 2016, a 28-year-old male, bank executive by profession with no known comorbids, presented in emergency department of Liaquat National Hospital, Karachi with complaints of low grade fever, dark coloured urine, yellow discoloration of eyes and right sided upper abdominal pain for last 5-6 days. On general physical examination the patient was lethargic, dehydrated, jaundiced and pale with a blood pressure of 130/60mmHg, heart rate 112/min, respiratory rate 17/min and temperature of 100°F. On abdominal examination there was tenderness in right hypochondrium and epigastric region. Haematology revealed haemoglobin 3.5gm/dl, WBC 61000/cmm (neutrophils 83%, lymphocyte 15%, eosinophil 2%). Platelets 252,000ml. Biochemistry panel revealed total serum bilirubin of 51 mg/dl with a direct bilirubin of 38.7 mg/dl and indirect bilirubin was 12.9 mg/dl. The alanine aminotransferase (ALT) was 1939 U/L, serum aspartate aminotransferase (AST) was 1217U/L and alkaline phosphatase was 156 U/L. At the time of admission, serum creatinine was 2.22 mg/dl. On 3rd day of admission it escalated upto 8.9 mg/dl and urea was 152 mg/dl. The pro-thrombin time was 11.8sec, and indirect and direct Coombs test was negative. Lactate dehydrogenase was 1482 U/L. On peripheral blood smear numerous blister cells were seen (Figure). Malaria Parasite Test was negative. Viral serologies were positive for IgM anti-bodies to hepatitis E virus (HEV). With all above examination and extensive workup the diagnosis of acute viral hepatitis E infection with G6PD deficiency was determined.

The patient was managed in High Dependency Unit (HDU). All hepatotoxic, oxidant and nephrotoxic drugs were avoided. Over the course of next two weeks in the hospital the patient improved clinically and on the basis of Lab reports (total serum bilirubin declined from 51 mg/dl to 45.4 mg/dl. AST from 1217U/L to 107U/L and ALT from 1939 U/L to 166 U/L. Haemoglobin increased to 9.7

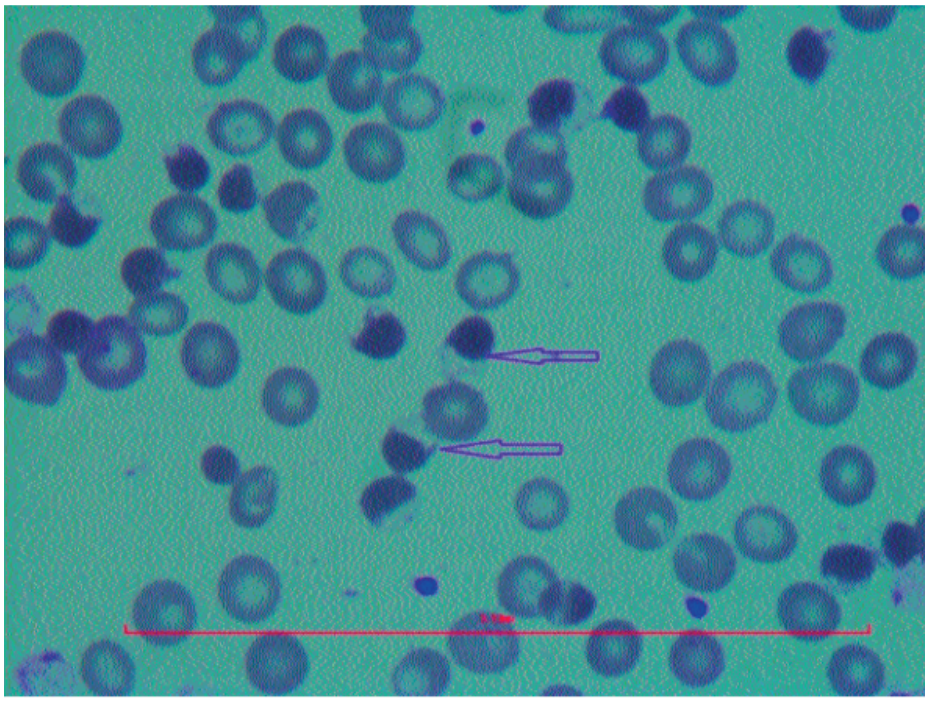

Figure: Numerous blister cells seen in peripheral smear.

gm/dl from 3.5gm/dl, after the transfusion of Packed Red Blood Cells. The patient underwent five sessions of haemo-dialysis during hospital stay and then was discharged.

On follow up the patient's metabolic parameters gradually improved over five weeks. The haemoglobin increased to 10.7 gm/dl, bilirubin count declined to 8.1 mg/dl, AST was 36 U/L, ALT was 65 U/L and reticulocyte count fell to 1.2%. Creatinine level reduced to 5.37 mg/dl without haemodialysis.

Discussion

In Acute Viral Hepatitis, haemolysis is usually mild, rarely there is a drop in haemoglobin level more then 1-2g/dl.[7] It is treatable without any complications. However, the presence of hepatitis E or any other viral hepatitis in G6PD patient can lead to severe haemolytic anaemia. The underlying reason for severe haemolysis in G6PD deficient patient is reduced level of glutathione, which protects against free radicals that cause oxidative damage to the erythrocyte.[6,7] Hence any infection to already damaged erythrocytes due to free radicals can lead to severe haemolysis, severe drop in haemoglobin and renal failure.[7-9] Whereas excess haematin and bilirubin may lead to obstruction of renal tubules, precipitating non-oliguric acute renal failure. Therefore, renal function tests should be performed regularly to prevent further complications.[6-8] Drugs which are oxidative in nature such as sulfonamides, primimaquine and nitrofurantoin should also be avoided along with nephrotoxic drugs.[9] Vitamin K is also prohibited as it also aggravates haemolysis.[7]

Acute viral hepatitis E is a self-limiting disease, which requires no or little hospital admission.[3,5] Hepatitis E has four genotypes, out of which only genotype 1 and 2 affect the human population. Hepatitis E infection in neonate, pregnancy and blood borne disease such as G6PD can present as acute liver failure, which is a life threatening condition,[4,5] with a high morbidity and mortality. It requires immediate hospitalization.[4,5]

In patients suspected with viral hepatitis along with unexplained anaemia, intravascular haemolysis, high direct and indirect bilirubin levels require prompt medical attention. In these patients one should suspect either acute viral hepatitis or Wilson disease, as latter can also emulate haemolytic anaemia and jaundice. Diagnosis of G6PD deficiency can be a challenge because G6PD levels can be normal throughout the course of illness and immediately after an event of haemolysis. The explanations for these false normal values of G6PD are due to the fact that, old RBCs which are deficient in G6PD are haemolyzed earlier while the new RBCS have normal G6PD content. The only way to diagnose during an acute episode is to analyze peripheral blood smears for blister cells. Blister cells are the precursors of bite cells, which appear as red blood cells containing a peripherally located vacuole. It is advisable to repeat G6PD levels 8-10 weeks after the haemolytic event.[6,9] In G6PD deficiency, Coomb's test will be negative. Arrangement of multiple blood transfusions and dialysis should be of utmost priority.

AHEV vaccine (Hecolin) has recently been developed and is in phase III clinical trials in China, which has given a promising result in preventing HEV.[11,12] Further studies and clinical trials are needed to validate its safety.

Conclusion

The severe haemolysis and renal failure precipitated by hepatitis E virus in the G6PD Deficient patients

necessitate a multi-disciplinary team of haematology, hepatology and nephrology for timely diagnosis and aggressive management.

Consent of Patient: Written informed consent of patient was taken for publishing this case and ethical approval letter was provided by the head of gastroenterology department.

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Conflict of Interest: None to declare.

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