Pediatric Oncall Journal (July-Sept 2020)
Volume 17, Issue 3: 90-91
DOI: https://doi.org/10.7199/ped.oncall.2020.27

PEDIATRIC ONCALL
CHILD HEALTH CARE

CASE REPORTS

HEPATITIS A AND E DUAL INFECTION WITH SEVERE HEMOLYTIC ANEMIA AND G6PD DEFICIENCY IN AN INDIAN FEMALE CHILD

Radhey Shyam Sharma, Kusum Kalla, Ravi Sharma, Rajiv Kumar Bansal.

Department of Pediatrics, Santokba Durlabhji Memorial Hospital, Jaipur, Rajasthan, India.

ABSTRACT
Dual infection with Hepatitis A and E has been reported. Its co-existence with Glucose 6-Phosphate Dehydrogenase (G6PD) deficiency is rare, especially in females. We present an 8 years old female child with Hepatitis A and E dual infection with severe anemia due to intravascular hemolysis due to G6PD deficiency. She responded to conservative treatment and packed red blood cells (PRBC) transfusion.

ARTICLE HISTORY
Received 9 March 2020
Accepted 29 May 2020

KEYWORDS
G6PD deficiency, Dual infection, intravascular hemolysis, severe anemia

Introduction

Acute viral hepatitis is a major public health problem worldwide.[1,2] Hepatitis A virus (HAV) and Hepatitis E virus (HEV) are the most common cause of acute viral hepatitis that mainly affects the pediatric age group. Both HAV and HEV are transmitted through the enteral route and there are postulations that their co-infection might be associated with a more severe natural course of illness and increased mortality especially in pediatric patients. Incidence of infection is more in non-affluent countries like India due to sub-optimal hygiene and sanitary conditions.[3] Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency is inherited in an X-linked recessive manner and rarely as autosomal recessive manner.[4] The prevalence of G6PD deficiency in the Indian population is low, reported approximately 2.2-14% (as in a study in northern Indian population), and in females' prevalence is much lower.[5] In India, many cases of acute viral hepatitis (HAV/HEV) with G6PD deficiency have been reported in adults[5,6,7,8] and no such case has been reported in a female child with the best of our knowledge. We are reporting an unusual case of dual infection: HAV and HEV coinfection with G6PD deficiency in a female child who presented as an acute liver failure with severe hemolysis.

Case Report

An 8 years old female child from Rajasthan, India, presented in the emergency department with fever followed by vomiting, upper abdominal pain, yellowish discoloration of the body for a week along with altered sensorium for 2 days. She was admitted in the pediatric intensive care unit (PICU). On admission, she was normothermic with a Glasgow Coma Scale (GCS) of 13/15, heart rate of 90/min, respiratory rate of 18/min, blood pressure of 102/66 mmHg. On systemic examination, she had deep jaundice with tender hepatomegaly. Other systems were normal. Investigations are depicted in table 1. Ultrasonography (USG) of the abdomen showed altered hepatic echotexture with minimal bilateral pleural effusion and ascites. Both Hepatitis A and E IgM by Elisa were positive. She was treated with maintenance intravenous fluid, multivitamins, and lactulose. On the second day of admission, the child developed severe anemia with hemoglobinuria and negative direct comb's test with reticulocytosis. G6PD deficiency was diagnosed by dye test as the dye did not decolorize in 24 hours. Rapid malaria antigen test, dengue serology (NS1, IgG and IgM), anti-leptospiral IgM, scrub typhus IgM, Widal tests were negative. She was treated with one unit of packed red blood cells (PRBCs).

Patient improved clinically as well as by laboratory parameters normalized in 2 weeks.

Discussion

In India, the prevalence of Hepatitis A virus (HAV) infection is high (31-67%) in comparison to Hepatitis E virus (HEV) infection (16-66%) in children, whereas the prevalence rate of HAV and HEV co-infection is 10.4%.[3] HAV infection is acquired early in life with various community-based studies demonstrating the presence of anti-HAV antibodies in nearly 80% of children by the age of 5 years. Although serological positivity of HEV infection is higher in adults than children, it might be due to the possibility of asymptomatic/subclinical HEV infection in early childhood which has led to their under-diagnosis as suggested by Handa et al.[3] They have also suggested the possibility of under-diagnosis of HEV infection even in symptomatic young children due to the presence of some other acute co-infection like HAV. It is very difficult to distinguish the co-infection with HAV and HEV viruses as a cause of viral hepatitis and cannot be differentiated from mono-infection but the laboratory diagnosis either by serology or polymerase chain reaction (PCR) can be a useful tool in the diagnosis of the simultaneous presence of both.[6]

A minor degree of hemolysis that is associated with decreased red blood cell survival could be there in the

CONTACT Dr Radhey Shyam Sharma

Email: theradheyshyamsharma@gmail.com

Address for Correspondence: Dr. Radhey Shyam Sharma, D-74B, Siwad area, Bapu Nagar, Jaipur, Rajasthan 302015, India.

Table 1. Laboratory investigations of the child

DAY(D)	D1	D2	D3	D4	D5	D6	D7	D8	D9
AST (IU/L)	3735					321			
ALT (IU/L)	2395					570			
S. Bilirubin (mg/dl) (direct bilirubin)	24.7 (2.4)		25.5 (2.0)			12.2 (1.3)			
Blood Ammonia (mcg/dl)		69							
INR	2.52	1.87	1.66	1.64	1.51	1.54	1.54	1.38	1.28
Hemoglobin (gm/dl)	7.6	5.8	6.0		10.1 (post transfusion)				
LDH (IU/L)			1338						
Reticulocyte count			14%						
S. Ceruloplasmin (mg/dl)			23.0						

Note: AST - aspartate transaminase, ALT - alanine transaminase, INR - international normalized ratio, LDH - Lactate dehydrogenase

patients of acute viral hepatitis[8] but is seldom of clinical significance. Our patient had severe intravascular hemolysis as evidenced by a fall in hemoglobin, reticulocytosis, unconjugated hyperbilirubinemia, hemoglobinuria, and high serum LDH levels suggestive of the hemolytic process. The presence of severe hyperbilirubinemia in patients with viral hepatitis and G6PD deficiency has also been previously reported in adults as well as pediatric population. In a case-control study, Gotsman and Muszkat[9] evaluated the impact of G6PD deficiency on patients with HAV infection in adult patients. They also found that although the patients with G6PD deficiency had a more severe initial clinical presentation, the clinical outcome was not affected. The mechanism behind hemolysis in G6PD deficiency is believed to be through decreased levels of glutathione in RBCs because of the accumulation of oxidants due to hepatic dysfunction, thus causing hemolysis in presence of G6PD deficiency.[7] As the deficiency of enzyme G6PD is mainly inherited in an X-linked recessive manner, the prevalence of its presence in a female is quite uncommon. In females, a possible mechanism of mutation is random X-Chromosome inactivation, diagnosed by Beutler test and Glucose Phosphate Dehydrogenase (GPD) enzyme quantitative assay.[4]

Treatment is supportive with serial monitoring of the signs of acute liver failure and in rare cases, a liver transplant is the end treatment. For hemolysis, transfusion of PRBC in severe cases and avoidance of potential hemolysis triggering drugs is recommended. Although serum bilirubin level in patients with viral hepatitis along with intravascular hemolysis is quite high, the overall prognosis is usually favorable and mainly related to the degree of hepatic injury.

In conclusion, in every pediatric patient who is presenting with acute viral hepatitis and unexplained severe anemia with jaundice (unconjugated hyperbilirubinemia), the possibility of intravascular hemolysis should always be considered and G6PD deficiency should be ruled out.

Compliance with Ethical Standards

Funding: None

Conflict of Interest: None

References:

1. Arora NK, Nanda SK, Gulati S, Ansari IH, Chawla MK, Gupta SD. Acute viral hepatitis types E, A, and B singly and in combination in acute liver failure in children in North India. J Med Virol. 1996;48:215-22.
2. Rawat SK, Jain A. Seroprevalence of Hepatitis A and E virus IgM in children suffering from acute hepatitis. J Med Sci Cli Res. 2015;3:4616-20.
3. Handa S, Wasim S, Kalra BP, Rawat A, Chandar V, Gupta A. Clinico-epidemiological profile of hepatitis A virus and hepatitis E virus co-infection in pediatric age group: a hospital based retrospective study. Int J Contemp Pediatr. 2019;3:588-592.
4. Au WY, Lam V, Pang A, Lee WM, Chan JL, Song YQ, et al. Glucose-6-phosphate dehydrogenase deficiency in female octogenarians, nanogenarians, and centenarians. J Gerontol Biol Sci Med Sci. 2006;61:1086-1089.
5. Sheikh UR, Datta K, Khan SM, Das I, Mittal D. G6PD Deficiency as a Precipitant of Hemolysis in Hepatitis E Patients. Ind J Emerg Med. 2017;7:3:325.
6. Lapp RT, Rochling F. Acute cholestatic hepatitis a virus infection presenting with hemolytic anemia and renal failure: a case report. Case Reports Hepatol. 2013;2013:438375.
7. Rodriguez Lay LD, Quintana A, Villalba MC, Lemos G, Corredor MB, Moreno AG, et al. Dual infection with hepatitis A and E viruses in outbreaks and in sporadic clinical cases: Cuba 1998-2003. J Med Virol. 2008;80:798-802.
8. Monga A, Makkar RP, Arora A, Mukhopadhyay S, Gupta AK. Case report: acute hepatitis E infection with co-existent Glucose-6-phosphate dehydrogenase deficiency. Can J Infect Dis. 2003;14:230-1.
9. Gotsman I, Muszkat M. Glucose-6-phosphate dehydrogenase deficiency is associated with increased initial clinical severity of acute viral hepatitis A. J Gastroenterol Hepatol 2001;16:1239-43.