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Hepatitis E Associated Autoimmune Hemolytic Anemia – A Rare Case Presentation

KEYWORDS: Autoimmune haemolytic anemia, Hepatitis E virus, Warm autoimmune antibodies, Coomb's test.

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ABSTRACT *Autoimmune haemolytic anemia (AIHA) is a rare disease characterised by hemolysis, requiring varying degrees of blood transfusions. Autoantibodies are directed against red blood cells which cause their premature destruction by macrophages from the reticuloendothelial system leading to anemia. Warm antibody type autoimmune haemolytic anemia is the most common AIHA. Secondary autoimmune haemolytic anemia due to various viral infections has been documented. Hepatitis viruses A, B and C have been commonly implicated in causing AIHA. Hepatitis E virus (HEV) causing AIHA is rare. We present a case of AIHA, in which the patient tested positive for HEV IgM antibodies, demonstrating association of acute HEV infection with AIHA.*

INTRODUCTION

Autoimmune haemolytic anemia (AIHA) is caused by hemolysis induced by the reaction of autoantibodies with red blood cells (RBCs)[1]. Various viral infections including influenza [2], Ebstein-Barr virus[3], Hepatitis A, Hepatitis B[4] and Hepatitis C[5] viruses are associated with AIHA. Association of Hepatitis E virus (HEV) with AIHA is rare. We report a case of a 7 year old child with coomb's positive haemolytic anemia in association with acute HEV infection.

CASE REPORT

A seven years old male child presented with a 6 days history of fever, nausea, vomiting, abdominal pain, dark coloured urine and yellowish discolouration of sclera.

On examination he was jaundiced and severely pale. There was no stigma of chronic liver failure and no lymphadenopathy. He had hepatomegaly palpable 2cm below the subcostal margin and palpable splenomegaly. Cardiovascular, respiratory, and neurological examinations were normal. No Kayser -Fleisher rings were seen on slit lamp examination.

Laboratory investigations revealed a hemoglobin level of 5.1 g/dl (normal range 13 to 18g/dl). The reticulocyte count was 5.0% (1 to 2.5%). Peripheral blood smear showed microcytic hypochromic RBC morphology, with sphrecytosis. There was no abnormality of the red cell membrane and no malarial parasite was seen. Liver function tests showed a bilirubin level of 5.0 mg/dl (0 to 1.2mg/dl) with a predominant conjugated component, alanine aminotransferase of 2500 IU/L (0 to 45IU/L) and alkaline phosphatase of 295 IU/L (80 to 306 IU/L). Serum albumin was 4.5 g/dl (3.5 to 5 g/dl). Serum lactate dehydrogenase was 1200 IU/L (200 to 400 IU/L). Renal function tests were within normal limits.

Table 1: Laboratory values

	Patient value	Normal range
Hemoglobin (g/dl)	5.1	13 to 18
Reticulocyte count (%)	5.0	1 to 2.5
Serum bilirubin (mg/dl)	5.0	0 to 1.2
Serum albumin (g/dl)	4.5	3.5 to 5.0
ALT (IU/L)	2500	0 to 45
ALP (IU/L)	295	80 to 306
LDH (IU/L)	1200	200 to 400

ALT - alanine aminotransferase, ALP -alkaline phosphatase, LDH - lactate dehydrogenase.

Blood and urine cultures were negative and viral markers for hepatitis A, B and C, Ebstein-Barr virus, cytomegalovirus, herpes simplex, measles, varicella zoster and parvovirus were all negative. Hepatitis E virus IgM was strongly positive.

Biochemical tests for Glucose 6 phosphate dehydrogenase (G6PD) deficiency were negative.

Abdominal ultrasound demonstrated hepato-splenomegaly with no intrahepatic duct dilatation, normal common bile duct and patent vessels with forward flow. There was no ascites. Gall bladder was normal.

A blood transfusion was suggested. In the blood bank the patient's blood failed to show compatibility with blood group compatible donors. Direct and indirect Coomb's tests were carried out, both of which were found to be positive. Subsequently the patient was put on intravenous steroids for and he responded to the treatment well with an improvement in hemoglobin levels (10.0 g/dl). He was discharged ten days after initial presentation. At a four weeks review his liver functions returned to within normal ranges but the coomb's test was positive.

DISCUSSION

Hepatitis E virus (HEV) infection is an important public health problem in the developing world. According to the fact sheet on HEV, published by the World Health Organization (WHO) and updated in July 2015, every year there are an estimated 20 million hepatitis E infections, over 3 million symptomatic cases of hepatitis E and 56,600 hepatitis E-related deaths.[6]

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Hepatitis E virus (HEV) is a non-enveloped RNA virus responsible for large epidemics of acute hepatitis and sporadic hepatitis cases in southeast and central Asia.[7] HEV is transmitted by fecal-oral route and there is very low person to person transmission rate. The incubation period ranges from 2 to 10 weeks. The illness is usually self limiting lasting 1 to 4 weeks but may develop into fulminant hepatitis (acute liver failure). As the illness subsides, serum aminotransferases and bilirubin decrease, returning to normal after 6 weeks in most patients. In acute HEV hepatitis, IgM appears during the early phase of clinical symptoms, preceding IgG by several days, and disappears over 4 to 5 months. IgG persists for several years after infection.[7]

Extra-hepatic manifestations of HEV include acute pancreatitis, neurological disorders (with primarily dominant peripheral nerve involvement, most commonly manifested as Gullain-Barre syndrome, followed by neuralgic amyotrophy), haematological disorders, glomerulonephritis, and mixed cryoglobulinemia. Hemotological disorders include autoimmune haemolytic anemia, haemolytic anemia due to G6PD deficiency, severe thrombocytopenia, hepatitis-associated aplastic anemia, pure red cell aplasia, and secondary hemophagocytic syndrome. [8]

A two-step mechanism could explain virus involvement in the development of experimental haemolytic anemia. The development of anemia during the course of viral infection may require two independent stimuli, in which the first triggers autoantibody production and the second enhances the pathogenicity of these autoantibodies.[9]

Three documented cases of AIHA associated with HEV infection have been published. These cases revealed sudden and rapid drops in hemoglobin levels during the course of illness, similar to our present case and were diagnosed after excluding other cases of anemia and hemolysis.[10-12] Two patients were treated supportively with good outcomes[11,12] and the treatment administered to the third patient was not mentioned.[10]

Our patient responded well to steroid therapy. The hemoglobin levels of the patient improved drastically from 5.1 g/dl on admission to 10.3 g/dl after steroid therapy.

CONCLUSION

Although rare, HEV infection may be associated with AIHA and can be treated with intravenous steroid therapy.

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