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ACUTE HEMOLYSIS IN ASSOCIATION WITH HEPATITIS B INFECTION IN A CHILD WITH BETA–THALASSEMIA TRAIT*

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Autoimmune hemolytic anemia may occur in the course of some viral diseases such as Coxsackie virus, cytomegalovirus, Epstein Barr virus, Influenza A, herpes simplex virus, and rarely hepatitis B virus infection. The role of being heterozygous for beta-thalassemia in hemolysis during acute viral hepatitis is not known.

In this report, we present an eight-year-old boy with jaundice and anemia. The diagnoses of hepatitis B virus infection and hemolytic anemia were made on the basis of physical and laboratory findings. A hemoglobin electrophoresis revealed that the child was heterozygous for beta-thalassemia. No specific etiology could be found for hemolytic anemia. It remained unclear whether hemolytic anemia in this patient was merely a coincidental finding or whether hepatitis B virus infection and beta-thalassemia trait had played a role in causing hemolysis. *Key words: hemolysis, hepatitis B infection, thalassemia trait.*

Shortening of the erythrocyte life span occurs in the course of some viral diseases such as Coxsackie virus, cytomegalovirus, Epstein Barr virus, Influenza A and herpes simplex virus[1]. Autoimmune hemolytic anemia in the course of acute hepatitis B virus (HBV) infection has been reported rarely[2-4]. In this report, we present a child with acute, self-limited hemolysis during hepatitis B infection.

Case Report

An 8-year-old boy was brought to Hacettepe Children's Hospital for evaluation of severe anemia and hepatitis. Twenty days prior to admission he had abdominal pain, nausea, vomiting, jaundice accompanied by pallor, and passing of dark urine. Physical examination revealed a well-developed boy (75^{th} percentile for height and weight) with yellow sclera. The liver was palpable 2 cm below the right costal margin. Kayser-Fleischer ring was absent and other physical findings were unremarkable.

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The laboratory examination demonstrated a severe anemia (hemoglobin 4.04 g/dl, hematocrit 13%) and elevated reticulocyte count (18%). The peripheral blood smear showed polychromasia, anisocytosis and basophilic stippling, as well as hypochromia in some of the red cells. Total serum bilirubin was 3.1 mg/dl with a direct bilirubin of 1.6 mg/dl. Glucose-6-phosphate dehydrogenase (G_6PD) was 250 U (normal: 80-100 units). Hemoglobin electrophoresis at pH 8.6 showed an elevated Hb A_2 band. Hb A_2 was quantitated by microcolumn chromatography and was present at 6.7%. The patient's father also had beta thalassemia trait (HbA_2 5.2%). Serum copper, ceruloplasmin, direct, indirect and complement-mediated Coombs, pyruvate kinase, erythrocyte osmotic resistance, autohemolysis, cold agglutinin, methemoglobin, unstable hemoglobin, erythrocyte, urine and fecal porphyrin levels, acidified serum lysis and the sucrose hemolysis test were all normal. Hepatitis A virus antibody IgM (HAVAb IgM) was negative. Hepatitis B surface antigen (HBsAg) was positive, while anti-HBs was negative. Other laboratory tests done during the follow-up period are displayed in Table I.

The patient's hemolysis was self-limited, thus required no blood transfusion. Levamisole was given as a nonspecific immunostimulant agent for two months for the hepatitis B infection. Hemolytic anemia and hepatitis resolved over the following two months. The patient was then completely healthy. liver function tests were normal and HBsAg was negative.

Discussion

Aplastic anemia, thrombocytopenia and autoimmune hemolytic anemia may occur during or following acute hepatitis B virus infection[1,5,6]. The presented patient's clinical course, serologic findings of hepatitis B [HBsAg (+), anti-HBsAb (−)] and the disappearance of HBsAg in the fourth month of the disorder were consistent with an acute hepatitis B infection. Previously, autoimmune hemolytic anemia has been reported in three patients with viral hepatitis[2-4]. Autoimmune hemolytic anemia was not considered because of the patient's self-limited hemolysis and absence of markers for autoimmune hemolytic anemia, including Coombs tests and cold agglutinin. Autoimmune hemolytic anemia associated with viral hepatitis usually requires emergency measures including blood transfusion, steroid therapy and plasmapheresis[2-4], but none of these was given to the patient. Only levamisole, a nonspecific immunostimulant, was administered, and may have accounted for the patient becoming HBsAg negative[7]. The presence of the beta thalassemia trait in the patient is interesting. It is not known whether or not heterozygosity of beta thalassemia can play a role in hemolysis during acute viral hepatitis.

Table I: Selected Laboratory Findings

Day	Hb g/dl	Ret %	Normoblast %	MCV fl	Plasma Hb mg/dl	Haptoglobin mg/dl	AST U/L	ALT U/L	Alk.phos U/L	T.bil mg/dl	HBsAg	Anti-HBs	Anti-HBc IgM	Anti-HBc IgG	HBeAg	Anti-HBe
1	4.64	18.8	3	86	13.9	0	366	598	176	3.1	+	–				
4	6.28	19.2	2	–	–	–	–	–	–	–						
7	6.86	15.2	3	–	–	–	–	–	–	–						
14	8.68	10.4	1	–	–	–	–	–	–	–						
26	10.0	2.2	0	–	8.0	0	342	445	260	2.5						
55	11.8	0.2	0	–	–	63	46	27	316	0.6	+					
65	12.4	0.4	0	62	0.0	70	32	25	–	–	+					
131	11.9	0.4	0	62	–	–	–	–	–	–	–	–	–	+	–	+

Hb : Hemoglobin.
Ret : Reticulocyte.
MCV : Mean corpuscular volume.
AST : Aspartate amino transferase.
ALT : Alanine amino transferase.
Alk.Phos. : Alkaline phosphatase.
T.bil : Total billirubin.
HBsAg : Hepatitis B surface antigen.
Anti-HBs : Hepatitis B surface antibody.
Anti-HBc : Hepatitis B core antibody.
HBeAg : Hepatitis B e antigen.
Anti-HBe : Hepatitis B e antibody.

Possible mechanisms for HBV-associated hemolytic anemia in the patient may be immune-mediated hemolysis that could not be demonstrated, or direct destruction of red cells due to HBV. Another possibility is that the simultaneous occurrence of hemolytic anemia and viral hepatitis was a coincidental finding.

In conclusion, we recommend that screening for HBV in addition to G_6PD be done in children with hemolytic anemia during viral hepatitis.

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