Immune Hemolytic Anemia in Association with Visceral Leishmaniasis

Viseral Layşmanya ile Birlikte Görülen İmmün Hemolitik Anemi

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Summary
Despite the fact that anemia is one of the most striking clinical features of visceral leishmaniasis (kala-azar), the factors involved in the pathogenesis are not fully understood. The cause of anemia seen in these patients is often multifactorial including sequestration and destruction of the erythrocytes in the enlarged spleen, hemophagocytosis and alterations in erythrocyte membrane permeability. Anemia due to immune hemolysis is rarely seen in patients with kala-azar. We present here 4 year-old girl diagnosed as kala-azar associated with autoimmune hemolytic anemia. No signs of hemolysis had remained after kala-azar was successfully treated with meglumine antimonate. *(J Pediatr Inf 2007; 1: 36-8)*
Key words: Immune hemolytic anemia, kala-azar

Özet
Anemi viseral layşmanyazın (kala-azar) en göze çarpan klinik bulgularından biri olsa da patogenezindeki faktörler halen tam olarak anlaşılamamıştır. Bu hastalarda görülen aneminin büyüyen dalakta sekestrasyon ve eritrosit yıkımı, hemofagositoz ve eritrosit membran permeabilite değişiklikleri gibi çok çeşitli nedenleri vardır. Kala-azar'lı hastalarda immün hemolize bağlı anemi nadiren görülür. Bu yazıda kala-azara eşlik eden otoimmün hemolitik anemili 4 yaşında kız hasta sunulmuştur. Kala-azar'ın meglumin antimonat ile tedavisi sonrası hastanın hemolizi de düzelmiştir. *(Çocuk Enf Derg 2007; 1: 36-8)*
Anahtar kelimeler: İmmun hemolitik anemi, kala-azar

Introduction

Visceral leishmaniasis (kala-azar), an infection caused by the protozoan parasites called Leishmania spp, is a potentially fatal parasitic disease and a public health problem in most countries bordering the Mediterranean basin, including Turkey. Visceral leishmaniasis may mimic or lead to several types of hematological disorders including pancytopenia, hemolysis, megaloblastic findings, fibrinolysis, and also rarely, it may cause autoimmune hemolytic anemia and cold agglutinin syndrome (1). Anemia is almost always present and may be severe. It is usually normocytic and normochromic. It appears to be due to a combination factors including hemolysis, marrow replacement with leishmania infected macrophages, hemorrhage, splenic sequestration of erythrocytes, hemophagocytosis, hemodilution and marrow suppressive effects of cytokines such as TNF-α (2-4).

Case Report

A previously healthy four-year-old girl was admitted to our hospital with complaints of fever and fatigue for 1-month. She lived in a small village at Adana. The patient had not received any medications before the admittance to the hospital.

Physical examination on admission revealed poor general condition, beside hepatomegaly and splenomegaly (6 cm and 4 cm below the subcostal marnins, respectively).

In admission, laboratory values revealed pancytopenia with hemoglobin concentration

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of 5.8 g/dL, white blood cell count 2800/ mm^3, platelet count 39,000/mm^3; elevated liver function tests with aspartate aminotransferase 518 IU/L, alanine aminotransferase 247 IU/L, gamma glutamyltransferase 51 mg/dL, elevated bilirubin levels, C-reactive protein 48 mg/dL, and hypergammaglobulinemia. Signs of hemolysis were appeared in peripheral blood smear and reticulocyte count was %6 as haptoglobin decreased to 2 mg/dL, direct Coombs reaction was 2 (+), free hemoglobin in plasma and urine were 2 (+) at the onset of admission. The warm and cold reactive antibodies could not be detected.

Serologic studies have shown no evidence of brucellosis, toxoplasmosis, Epstein-Barr virus, cytomegalovirus, hepatitis A and B viruses and human immunodeficiency virus infection. Extracelullar or intracellular leishmania amastigotes were not seen and also no evidence of malignancy or dysplasia appeared in bone marrow aspiration. Kala-azar dipstick (rk-39) was positive.

After her active hemolysis, hematocrit fell to level of 15% and because of cardiac insufficiency, erythrocyte transfusion was done. Specific treatment of meglumine antimonate (Glucantime®) at a dose of 20 mg/kg body weight was started. At the 10th day of treatment of meglumine antimonate, WBC and platelet count increased to 6200/mm^3 and 265,000/mm^3 also the signs of hemolysis were disappeared and direct Coombs test became negative.

Discussion

Kala-azar is characterized by fever, hepatosplenomegaly, weight loss, diarrhea, and severe hematologic alterations. Anemia is the constant feature in this disorder. The cause of the anemia is multifactorial; sequestration and destruction of the red blood cells in the enlarged spleen, immune mechanism, increased plasma volume due to splenomegaly, dyserythropoietic changes of bone marrow, concomitant infections, malnutrition leading to folic acid, vitamin B12, or iron deficiencies, and alterations in erythrocyte membrane permeability have been implicated (1), Hemolytic anemia in kala-azar has been reported in literature rarely (5,6). In our case, because the spleen was not enlarged to huge dimensions, so it was not responsible for anemia only. Also hemophagocytosis was not seen in bone marrow aspiration. So hemophagocytosis must not be the reason of the anemia. As hemolysis findings were positive, autoimmune hemolytic anemia was considered in the patient and after treatment of infection hemolysis had resolved spontaneously. Bone marrow aspiration is safer and less sensitive in diagnosis of kala-azar. Amastigotes are seen in approximately two thirds of patients in this method. Recombinant kinesin protein of 39 kDa called rK 39 is the most promising molecules. The antigen used in various test formats has been proved highly sensitive and specific for visceral leishmaniasis (7). It is useful in the diagnosis of HIV-Leishmania co-infection and as a prognostic marker (8). We used this technique in our clinic. Although leishmania amastigotes were not seen in the bone marrow aspiration smears, stick test was positive and the patient's clinic improved with the treatment of Glucantime, quite well.

In fact, according to suggestion from ferrokinetic studies and erythrocyte survival studies anemia in leishmaniasis is due to hemolysis. These studies have also shown very little evidence of ineffective erythropoiesis, beside reduced plasma iron stores in spite of increased iron stores. This is because of reticuloendothelial hyperplasia with iron retention. As a result, bone marrow cannot respond to hemolysis adequately. However, a different clinical picture may be seen in especially babies and young infants as severe hemolysis at the onset of disease. Although both IgG and complement components are found on the red cells mostly, there is no immune hemolysis. Hemolysis is because of macrophages in the liver and spleen without immune component (9).

Immune hemolysis in visceral leishmaniasis may be seen rarely as in our case. Nevertheless, in previous study it has found that immune complexes on the erythrocyte surface are a result of non-specific adsorption secondary to polyclonal hypergammaglobulinemia mostly (1). However, cold and mostly warm antibodies have detected in some studies (1,10). The number and type of immunoglobulin molecules may affect hemolysis, despite the correct relation is still unclear (1). In our case, it has found that because intravascular hemolysis findings were positive it was accepted as hemolysis secondary to kala-azar infection and the hemolysis was not expected with erythrocyte with non-specific adsorbed immune complexes secondary to polyclonal hypergammaglobulinemia.

Anemia is seen because of multiple mechanisms in visceral leishmaniasis. Although immunoglobulins on erythrocytes are not specific in most cases, in presence of significant hemolysis, physician must consider that it is different from previous conditions and some other therapeutic options must be considered when the treatment of visceral leishmaniasis is not sufficient.

As a conclusion in case of anemia in patients with kala-azar, increased destruction must be taken into consideration and keep in mind for the appropriate treatment management.

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