

## Case Reports

### Hemophagocytic Syndrome Associated with Visceral Leishmaniasis

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*Hemophagocytosis, either primary (familial) or secondary (reactive), is a life threatening condition in childhood. Etiology should be vigorously searched to avoid a diagnosis of primary hemophagocytosis and treatment with cytotoxic drugs. A child with visceral leishmaniasis causing hemophagocytosis is presented.*

**Keywords:** Hemophagocytosis, Leishmaniasis.

Visceral leishmaniasis (kalaazar) is a systemic disease caused by the dissemination of the intracellular parasite of genus leishmania, through the reticuloendothelial system. The infection is endemic in most Mediaterranean countries, southern Europe, Middle East, East Africa, China, India and Turkey(1,2). It may mimic or lead to several types of hematological disorders including pancytopenia

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and hemolysis. Recently, hemophagocytic syndrome has been reported(3-9).

Differentiation between primary and secondary hemophagocytic syndrome is extremely important. Hemophagocytosis associated with such infectious illnesses resolves with treatment of the underlying infections, while cytotoxic drugs are used for the treatment of primary cases. We report a child with visceral leishmaniasis as a rare cause of the hemophagocytic syndrome.

#### Case Report

A previously healthy 18 month-old-girl presented with fluctuating fever (39-40°C) for one month. Physical examination revealed pallor and distended abdomen with hepatomegaly and splenomegaly (6 cm and 4 cm below the costal margins respectively). Neither lymphadenopathy nor any bleeding signs were observed. Serological markers for Epstein-Barr virus, cytomegalovirus, toxoplasmosis, hepatitis A and B viruses were negative; salmonella and brucella agglutinins were negative and blood cultures could not demonstrate any infectious agent.

Blood counts showed pancytopenia with hemoglobin concentration of 7.1 g/dL, white blood cell count 2400/mm<sup>3</sup> and platelet 33000/mm<sup>3</sup>; red cell morphology was normal. Serum levels of aspartate aminotransferase (AST) 492 IU/L, alanine aminotransferase (ALT) 315 IU/L, gamma-glutamyltransferase (GGT) 303 IU/L, triglycerides 297 mg/dL, erythrocyte sedimentation rate 68 mm/hour, C-reactive protein 12.2 mg/dL and ferritin 15000 ng/mL, were all elevated. Fibrinogen level (214 mg/dL) was normal. On bone marrow aspiration marked erythrocyte and

lymphocyte phagocytosed histiocytes and leishmania amastigotes were observed. Liposomal amphotericin B (AmBisome®) was administered immediately (starting with 0.5 mg/kg/day and gradually increased to 2 mg/kg/day was given on the first 3 days. Treatment was continued with 2 mg/kg/day on the following 2 days and an additional 2 mg/kg/day on day 15). Treatment was well tolerated. Symptoms and clinical findings improved gradually. Fever was controlled and hepatosplenomegaly regressed. One month after the end of therapy, physical examination revealed further regression of hepatosplenomegaly (3 cm below costal margins). Marked improvement of hemoglobin (10.7 g/dL), white blood count (9800/mm<sup>3</sup>) and platelet count (358000/mm<sup>3</sup>) were observed.

### Discussion

Hemophagocytic syndrome is a disorder characterized by nonmalignant infiltration of vital organs by activated lymphocytes and macrophages. Engulfment of any hematological cell type in bone marrow and reticuloendothelial system by these activated cells, called hemophagocytosis is the hall mark of the disease(3). This may result in pancytopenia, fever, organ enlargement, neurological dysfunction and disseminated intravascular coagulation(3). Hemophagocytic syndrome may be classified as primary, which may be further, subclassified as sporadic and familial and secondary that is reactive to an underlying medical illness(3). Identification of an etiological cause may not be easy and moreover the clinical course of the triggering infection and hemophago-cytosis may coincide and lead to delay in diagnosis.

Visceral leishmaniasis has been rarely defined as an etiological cause of hemophagocytic syndrome. Pancytopenia, hemolysis, megaloblastic findings, fibrinolysis, cold

agglutinin syndrome and hemophago-cytic syndrome are some of the hemato-logical abnormalities observed in visceral leishmaniasis(3-9). Diagnostic delay might cause severe complications and death occurs in 90% patients without specific antileishmanial treatment(8). Definitive diagnosis of visceral leishmaniasis is established by isolating the organism from spleen, bone marrow and liver. Amastigotes and hemophagocytic cells were seen on bone marrow smears of our patient. Particularly in young children visceral leishmaniasis presenting with hemophagocytic syndrome may cause considerable diagnostic difficulty since its clinical signs coincides with hemophagocytic syndrome and results in over treatment with cytotoxic drugs(9). Clinical signs and laboratory abnormalities of our case were compatible with the proposed diagnostic criterion for hemophagocytic syndrome(3).

Treatment of reactive hemophagocytic syndrome depends on the treatment of underlying cause. Liposomal amphotericin B provides sufficient drug levels in tissue and persistent detectable levels are observed 14 days after treatment(10). Our patient also improved under liposomal amphotericin B treatment. The drug was well tolerated with no side effects.

In conclusion the early diagnosis and appropriate treatment of visceral leishmaniasis is important. Although the prominent bone marrow hemophagocytosis, high fever and pancytopenia may lead to diagnostic confusion, patients with hemo-phagocytic syndrome should be vigorously screened for visceral leishmaniasis, before accepting the case as primary hemophago-cytosis and starting cytotoxic therapy.

*Contributors:* NK, ME and AY did the clinical work up. FG did hematological work up. AY reviewed the final draft and will be the guarantor.

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## Unusual Cause of Acute Renal Failure in Infancy

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*Acute renal failure due to intratubular obstruction is uncommon in infants. Two infants presenting with acute renal failure associated with acute gastroenteritis were found to have bilateral global nephrocalcinosis secondary to oxalosis.*

**Key words:** Nephrocalcinosis, Renal biopsy, Oxalosis.

Acute renal failure (ARF) is frequent in newborns and infants. Clinical conditions causing hypovolemia, hypoxemia and hypotension in newborns and infants may lead

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