Case Report

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TANAFFOS

Visceral Leishmaniasis in Two Brothers; Diagnostic Dilemma Due to Hemophagocytic Syndrome

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Visceral Leishmaniasis (VL), a systemic infection of the reticuloendotherlial system, is caused by a parasitic infection.

The co-occurrence of VL and hemophagocytic syndrome (HPS) has been previously reported in several studies. In this report we present two cases of HPS and VL among members of the same family.

Key words: Visceral leishmaniasis, Hemophagocytosis, Endemic, Bone marrow aspiration

INTRODUCTION

Visceral Leishmaniasis (VL), a systemic infection of the reticuloendothelial system, is caused by a parasite endemic in the Middle East and Mediterranean regions (1,2). The disease has been reported almost from all countries except Australia and Antarctica. VL is an endemic disease very common in northwestern and southern parts of Iran. Asymptomatic infection occurring in close contacts of VL patients has a prevalence of 36.4%.Hemophagocytic syndrome (HPS) is a lethal condition featured by drastic activation of histiocytes and hemophagocytosis. VL manifestations have an overlap with HPS (2-4,5). Secondary type HPS can develop after infections with EBV, HSV, HCV, HBV, bacterial sepsis and leishmaniasis, malignancies, or collagen vascular diseases (1, 2). Hemophagocytosis in visceral leishmaniasis is rare and often mild (6-8), but without initiation of appropriate treatment the outcome would be fatal (1).The co-occurrence of VL and HPS has been previously reported in several articles. Herein we report two cases of HPS and VL among members of the same family.

CASE SUMMARIES

Case 1

A 16 year-old boy (older brother) was admitted with fever, sweating and loss of appetite since 4 months ago. He mentioned history of travel to an endemic area for VL in a province located in north of Iran 4 months ago. On physical examination, he was ill and febrile and systemic physical exam revealed huge hepatosplenomegaly. Laboratory findings showed elevated liver enzymes with pancytopenia and increased ESR and positive CRP. Blood and urine culture were negative for infectious disease. Abdominal sonography and CT-scan of the abdomen

demonstrated huge hepatosplenomegaly with retroperitoneal and paraaortic lymphadenopathy. The initial diagnosis of HPS associated with VL was made. For confirmation of diagnosis, bone marrow aspiration (BMA) was performed 4 times. The first three BMAs were reported negative and surprisingly on the fourth BMA Leishman Donovan bodies were observed within bone marrow macrophages (Figures 1 and 2).

Specific therapy for VL and HPS was instituted and patient's clinical condition and laboratory findings improved.

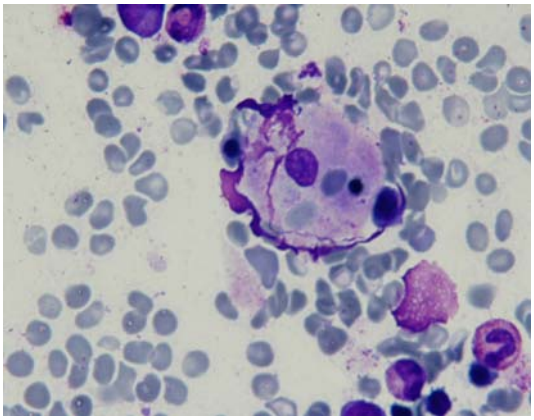

Figure 1. Hemophagocytosis in the bone marrow. An activated macrophage engulfing blood cells; Papanicolaou's stain (oil immersion)

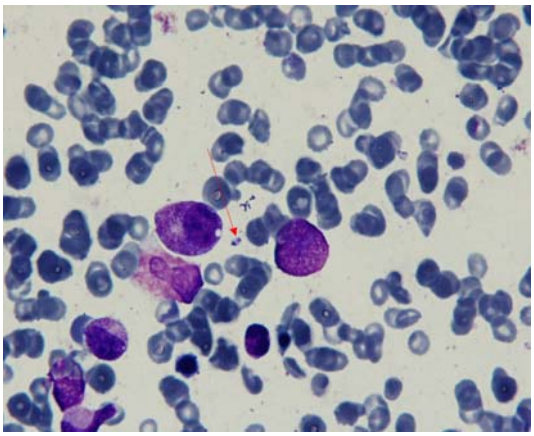

Figure 2. Leishmania sp. Amastigote in bone marrow aspiration; Papanicolaou's stain (oil immersion).

Case 2

An 8 year-old boy from Tehran (younger brother) presented with prolonged fever, abdominal pain and jaundice since 2 months ago. He had history of travel to an endemic area for VL in a province located in north of Iran 4 months ago. He had been previously hospitalized for 14 days and he had been monitored in the intensive care unit; however, no cause could be ascertained for his fever. He was then referred to our center. At the time of admission, the child was febrile, with toxic appearance and marked jaundice. On physical examination he had hepatosplenomegaly .His kidney function tests and respiratory and cardiovascular systems were normal.

Laboratory tests at the time of admission revealed pancytopenia (hemoglobin 5.4, WBC<1000, PLT 63,000). The patient had deranged liver function (serum bilirubin 2.4 mg%, AST 152,000, ALT 147,000, LDH 601, ALK-P 1443). Blood and urine cultures were sterile and peripheral smear was negative for malaria parasite. The patient was also found to be negative for antibodies to HIV, hepatitis A, B, C, D virus, CMV, EBV, Borrelia and malaria. Ultrasonography of the abdomen revealed diffuse hepatosplenomegaly without any focal lesion. CT scan of abdomen revealed hepatosplenomegaly with para-aortic lymphadenopathy and pleural effusion. Laboratory findings included pancytopenia, hyperlipidaemia, elevated levels of ferritin and LDH. Bone marrow Aspiration (BMA) was performed three times .All of them were negative but his brother had a positive BMA for Leishman Donovan bodies and numerous histiocytes showing hemophagocytosis. With the final diagnosis of HPS associated with VL, The child was treated with glucantime/cyclosporine and corticosteroids .His condition was cured following treatment.

Unfortunately after one year of treatment two brothers expired due to HPS relapse.

DISCUSSION

VL is an infectious disease of endemic regions. Although the co-occurrence of HPS and VL has been evaluated in many studies but to the best of our knowledge familial form of this concurrence has not been reported. In this study 2 siblings were diagnosed with HPS based on

physical examination, lab tests and manifestations. HPS can occur following immunologic or infectious diseases; therefore, patients were evaluated for CGD, AIDS and other infectious diseases.

In a study in Spain, it has been suggested that CGD is a predisposing condition for co-occurrence of these two diseases. Immunologic work-up for CGD was normal in the two patients presented in this paper (8).

HPS has accompanied VL in non endemic regions in patients with immunodeficiencies such as AIDS (9). These two patients had negative results for infection etiology such as HIV, Borrelia, Malaria or Hepatitis. To rule out VL in differential diagnosis, BMA was performed in both cases. The older brother who became symptomatic sooner had a positive BMA (Leishman Donovan body was detected) and subsequently the diagnosis of VL was made based on the BMA result. Although the younger brother did not have positive BMA result, he was suspected for VL because of having manifestations similar to those of his brother's and history of recent traveling to an endemic region of leishmaniasis. Treatment for Leishmaniasis was initiated for both of them and they showed a temporary response.

VL has been supported to have genetic predisposition (10) and many studies have discussed familial hemophagocytosis syndrome (11-13) but there are no reports of co-occurrence with VL in the same family. It appears that this study may be the first reporting an association between VL and HPS in one family.

Since both children had Leishmaniasis and hemophagocytosis at the same time, genetic evaluation should be performed in similar cases.

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