Hemophagocytic Lymphohistiocytosis: A Confusing Problem of the Diagnosis of Visceral Leishmaniasis

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Introduction

15-month-old boy was referred to our clinic for evaluation of fever and pancytopenia for 10 days. Physical examination was normal except pallor and hepatosplenomegaly (HSM). Laboratory investigation revealed hemoglobin 7.9 g/dL, leukocyte count $3.2 \times 10^9/L$, absolute neutrophil count $0.6 \times 10^9/L$ and platelet count $35 \times 10^9/L$. The peripheral blood smear demonstrated 10% atypical lymphocytes resembling virocytes; other blood cells were normal appearance. Serum lactate dehydrogenase level was 1596 U/L, triglyceride 262 mg/dL, fibrinogen 102 mg/dL, and ferritin level was 9356 ng/mL. Vitamin B12 level was very low (65 pg/mL). There was no serological evidence of infection, such as hepatitis A, hepatitis B and hepatitis C, cytomegalovirus, Epstein-Barr virus, human immunodeficiency virus, and toxoplasmosis. The first bone marrow aspirate was hypercellular with the presence of dysmyelopoiesis, numerous histiocytes engulfing erythroid cells, neutrophils and lymphocytes leading to a suspicion of hemophagocytic lymphohistiocytosis (HLH) (Fig. 1). No parasites were detected.

Prompt wide spectrum antibiotics, intravenous immune globulin and intramuscular vitamin B12 therapies were started, nevertheless fever and HSM were not resolved and HLH 2004 protocol was added to his treatment and evaluation of familial HLH mutations were planned. Though his clinical condition was well, his fever and laboratory finding worsened in spite of etoposide, cyclosporine and dexamethasone combinations and antibiotic modifications. Bone marrow aspiration was repeated 4th week of HLH protocol. Several amastigote form of *Leishmania* was demonstrated (Fig. 2). Because the patient was not from an endemic area for leishmaniasis, no serological test was performed before second bone marrow. His fever, pancytopenia and organomegaly were resolved with liposomal amphotericin B therapy and HLH protocol was discontinued after 8th week.

Visceral leishmaniasis is a chronic and frequently lethal disease caused by protozoal parasites of the *Leishmania donovani* [1]. Usually manifests by fever, hepatosplenomegaly, and pancytopenia. The clinical spectrum of visceral leishmaniasis is highly variable. Several reports of HLH secondary to leishmaniasis have been published. Amastigote sequestration and chronic intracellular infection of macrophages trigger uncontrolled macrophage activation, with secretion of proinflammatory cytokines and subsequent HLH development [2].

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Fig. 1 Prominent hemophagocytosis with histiocytes engulfing erythrocyte, lymphocyte and normoblast

Fig. 2 Macrophages with intracellular forms of *Leishmania* amastigotes

Previous reports have shown that the first bone marrow aspirate often fails to establish the presence of *Leishmania* amastigotes in 36.3% of cases and immunosuppressive therapy usually increases the number of amastigotes present on a bone marrow smear [3, 4]. Especially in endemic areas, *Leishmania* infection must be considered as part of the differential diagnosis in patients presenting with hemophagocytosis, and reevaluation of bone marrow and serologic tests required for accurate diagnosis.

Compliance with Ethical Standards

Conflict of Interest The authors report no conflict of interest.

References

1. Cançado GGP, Freitas GG, Flavia FHF, Van de Macedo A, Nobre V (2013) Hemophagocytic lymphohistiocytosis associated with visceral leishmaniasis in late adulthood. *Am J Trop Med Hyg* 88:575–577
2. Freeman HR, Ramanan AV (2011) Review of haemophagocytic lymphohistiocytosis. *Arch Dis Child* 96:688–693
3. Rajagopala S, Dutta U, Chandra KS, Bhatia P, Varma N, Kochhar R (2008) Visceral leishmaniasis associated hemophagocytic lymphohistiocytosis—case report and systematic review. *J Infect* 56:381–388
4. Gagnaire MH, Galambrun C, Stéphan JL (2000) Hemophagocytic syndrome: a misleading complication of visceral leishmaniasis in children—a series of 12 cases. *Pediatrics* 106:E58