Unusual occurrence of hemophagocytic lymphohistiocytosis in HIV-positive person with visceral leishmaniasis

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Abstract

Introduction: Visceral leishmaniasis is a well-recognized opportunistic infection in people living with HIV (PLHIV). Unlike adults, in children this infection is frequently associated with hemophagocytic lymphohistiocytosis (HLH). We report a case of HLH in HIV-positive person with visceral leishmaniasis.

Case description: A 25-year-old man known living with HIV since 2013 was admitted to infectious diseases department in March 2017. His clinical examination was clear. His initial viral load was 630,000 copies/mm³ and CD4+ cells count was 12/mm³. No opportunistic infections were noted. The patient was started on antiretroviral therapy. During hospitalization, he developed fever, asthenia, rhinorrhea, and odynophagia. The diagnosis of HLH was retained because of pancytopenia, cytolyis, hyponatremia, high level of ferrinemia, and hemophagocytosis. Etiological investigations revealed positive Leishmania PCR. Also, Leishmania was detected in sternal puncture. Patient received meglumine antimoniate (glucantime) 20 mg/kg/day for 21 days with favorable outcomes. To prevent relapse, he received meglumine antimoniate 20 mg/kg/month as long as his CD4+ count was less than 100 cells/mm³. After 1-year follow up, no relapse was detected.

Conclusions: Clinical and laboratory presentation of visceral leishmaniasis in PLHIV may differ from classic kala-azar. In our case, HLH was the reason for VL discovery.

Key words: HIV, hemophagocytic lymphohistiocytosis, visceral leishmaniasis.

Introduction

Visceral leishmaniasis (VL) is a vector-borne parasitic disease, caused by Leishmania donovani species complex, predominantly affecting macrophages [1]. It is a well-recognized opportunistic infection in people living with HIV (PLHIV). Majority of HIV-Leishmania co-infected cases show classic features of VL. Hemophagocytic lymphohistiocytosis (HLH) is a rare reactive hyperplastic disease of mononuclear phagocytic cell system. It is a life-threatening syndrome, clinically divided into 2 types: primary HLH and secondary HLH. Infection is the most common etiology underlying secondary HLH [2], which can be induced by viruses, bacteria, fungi, parasites, and protozoa. It is frequently associated with VL in immunocompetent children. For PLHIV, this syndrome is rarely associated with VL. In the present paper, we describe a patient with stage 3 HIV infection and atypical features of VL.

Case description

A 25-year-old man was known living with HIV since 2013 and was lost to follow-up. He was admitted in our de-
The prevalence of patients with both HIV and VL infection in Africa is emerging [3], whereas the prevalence of HIV-VL co-infection depends on parts of the world, with 17% found in Ethiopia. Age, residence, and employment were factors associated with this co-infection [4]. In Tunisia, this HIV-VL co-infection occurrence is rare. Various clinical features are observed, including irregular bouts of fever, substantial weight loss, swelling of the spleen and liver, and anemia [5]. For PLHIV, the most frequent symptoms are weight loss, fever, and cough [6]. For our patient, it was HLH.

HLH is a systemic disease characterized by overwhelming activation of normal T lymphocytes and macrophages, leading to clinical and hematologic alterations. This disorder clinically manifests as fever, hepatosplenomegaly, and less frequently, lymphadenopathy, jaundice, and rash. Pancytopenia, elevated levels of serum ferritin and triglycerides, coagulopathy with hypofibrinogenemia, and abnormal liver enzymes are commonly present. This syndrome is frequent in children, and it is a common circumstance of VL in this population [7]. In adults, VL has various symptoms, but HLH is rare [7]. In our case, VL was discovered unexpectedly after bone marrow investigation due to confirmation of HLH diagnosis. Because of side effects of meglumine antimoniate and efficiency of liposomal amphotericin B (LAB), it was the first line of VL treatment. The World Health Organization recommends LAB as the first line treatment at a dose of 40 mg/kg in 10 doses [8].

However, in our patient due to lack of LAB and pancytopenia, the use of meglumine antimoniate was preferable.
Several studies have shown that meglumine antimoniate caused severe adverse events (cardiotoxicity, nephrotoxicity, hepatotoxicity, and pancreatitis), resulting in high case fatality rates. Antimonies have also been shown to stimulate HIV-1 replication in vitro [4]. For our patient, no side effect was noted.

With treatment, VL usually present favorable outcome; however, in case of HIV co-infection, the outcome is poor [3]. Mortality rate is high in HIV-VL individuals [9]. This can be easily explained by pathophysiology of the two diseases, as both HIV and VL lead to a compromised immune status of a patient. Delays in diagnosis and treatment are the main causes of poor treatment outcomes. Therefore, mortality rate is comparable with stage 3/4 HIV monoinfection.

However, in our patient treated with meglumine antimoniate, the outcome was favorable.

The risk of a relapse is high in patients with CD4+ count less than 200 cells/mm³. That is why some experts recommend secondary prophylaxis [10].

For our patient, to prevent relapse, meglumine antimoniate 20 mg/kg/month was administered as long as his CD4+ count was less than 100 cells/mm³. After 1-year follow-up, no relapse was detected.

**Conclusions**

HIV-VL co-infection in Tunisia is rare. Clinical and laboratory presentation of VL in HIV-co-infected patients may differ from classic kala-azar. These differences may be partly responsible for the delay in diagnosing and treating leishmaniasis. In our case, HLH was the circumstance of VL discovery. It was an unusual presentation, therefore PCR leishmaniasis must be performed in such patients, even with minor VL symptoms.

**Conflict of interest**

The authors have no conflict of interest.

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