A Severe Form of Pediatric Visceral Leishmaniasis - A Case Report

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Abstract

According to the World Health Organization, leishmaniasis is one of the seven most important tropical diseases, and it is a major global health concern. In Armenia, it is a re-emerging disease. We present a case of a one-year-old child from active visceral leishmaniasis (VL) focus with a history of intermittent fever and anemia, progressive weakness, abdominal distension with loss of appetite for 3 months. The case was confirmed as VL by a positive result for the rK39 test. Considering the symptoms and signs a combination of VL and secondary hemophagocytic lymphohistiocytosis (HLH) was suspected. The patient was treated with a 21 mg/kg total dose of AmBisome. The child responded positively to treatment, and HLH syndrome was excluded.

Keywords

Visceral leishmaniasis, Active foci, rK39, AmBisome, Public health concern

Introduction

Leishmaniasis is a protozoal vector-borne disease affecting both humans and animals. The pathogen is an intercellular parasite of the genus Leishmania and is transmitted by the bite of certain species of sandflies, mainly Phlebotomus and Lutzomyia [1,2]. Dogs are mainly responsible for maintaining and circulating these species [3].

Different Leishmania species cause a wide range of clinical manifestations, varying in severity from self-resolving cutaneous lesions to hazardous conditions. The outcome is set by the interaction of parasite and vector characteristics and host's factors, the effectiveness of the immune response particularly [4]. There are 3 main forms of leishmaniasis: Cutaneous, mucocutaneous, and visceral or kala-azar [1]. Visceral leishmaniasis (VL) is the most serious, systemic type of disease, which is normally lethal if not treated [4]. It is transmitted either by the species Leishmania donovani (anthroponotic VL) or Leishmania infantum (zoonotic VL) [2]. The main symptoms of visceral leishmaniasis are fever, hepatosplenomegaly, and pancytopenia. Severe disease can lead to skin hyperpigmentation, leading to the name Kalaazar (Hindi "black skin") [3]. Medical characteristics of the disease in an endemic region support the diagnosis of visceral leishmaniasis, which is verified by either indication of the parasite in the splenic, bone marrow aspirate, or indirect studies. The rK39-based immunochromatographic test is currently in widespread use [5].

Leishmaniasis is one of the seven most important tropical diseases, according to the World Health Organization (WHO), and it is a major global health issue with a wide range of clinical symptoms and a potentially lethal outcome. According to the estimates of WHO, 2 million new cases are diagnosed each year (75% for cutaneous leishmaniasis and 25% for visceral leishmaniasis) and 12 million people are affected globally [2].

Leishmaniasis has always had a special place in Armenian infectious pathologies. In the past, both VL and CL cases were reported in Armenia, but no new cases were recorded between 1969 and 1999. Due to the re-emergence of VL in Armenia, this disease has now become a significant and ongoing problem [6]. In Armenia, the causative agent of VL is L. infantum [7]. The first-choice drug for this species according to WHO is liposo...
Our patient was from an active VL focus, the Syunik region, in Armenia. In contrast, a VL case was recorded in 1999 after a long elimination period, and from 1999 to 2016, 116 local and 99 imported cases of VL were observed in Armenia mostly in the regions Syunik, Tavush, Lori, and Yerevan [6]. The majority of VL cases in Armenia occurred in children aged 1 to 3 years. The first sero-epidemiological studies performed in active Armenian VL foci (Yerevan, Armariv, Ararat, Lori, Tavush, and Syunik) in 2015 and 2016 revealed that the seroprevalence in the ~1200 studied children under the age of ten years was relatively low (0.3 percent). Furthermore, seroprevalence in dogs ranged from 3 to 16 percent, with the highest percentages in Tavush (16.1 percent), Syunik (9.3%), and Lori (6.5 percent), highlighting the importance of dogs as a reservoir in these VL foci [9].

The antifungal amphotericin B has been used as a leishmaniasis treatment option but its high toxicity is a major deterrent [8]. Liposomal amphotericin B (AmBisome) is less toxic due to the incorporation into a liposome bilayer [10] and despite its high cost is the most commonly used drug for the treatment of VL [8].

Pentavalent antimonials are available as sodium stibogluconate and N-methyl glucamine antimoniate [8]. Drug resistance, high toxicity, particularly cardiotoxicity causing cardiac arrhythmias, ventricular tachycardia, ventricular premature beats, ventricular fibrillation, prolonged QTc interval, are the challenges of antimonials treatment [11].

In the beginning, considering the following symptoms and signs: hepatosplenomegaly, pancytopenia, elevated levels of ferritin, fibrinogen, triglycerides, and AST, we calculated the H-Score (it was 220) [12] and suggested that VL is complicated with secondary hemophagocytic lymphohistiocytosis (HLH).

Activation and unregulated non-malignant proliferation of T-lymphocytes and macrophages are the main characteristics of HLH. Secondary HLH has been linked to a variety of infections, including viral, bacterial, fungal, and parasitic infections, as well as autoimmune diseases and malignancies [13]. A growing number of HLH cases have been identified as a result of tropical infections, including VL cases [14]. The diagnosis of leishmaniasis as the inciting etiology can be difficult, even in endemic areas, since the hematologic features seen in VL can be very similar to those seen in HLH.

We began a VL-specific therapy, and the results were promising. The laboratory tests and clinical signs improved after a total dose of 21 mg/kg AmBisome, and the diagnosis of HLH was ruled out. In such cases when a negative dynamic is observed, there is a need for bone barrow puncture for differentiation of resistance to AmBisome and HLH.

Our patient was from an active VL focus, the Syunik region. The diagnosis was delayed and the patient was admitted to the hospital in a heavy condition. At nine months a diagnosis of anemia was made, and iron mal Amphotericin B. Current WHO recommended dose is 3-5 mg/kg per daily given by infusion over 3-6 days, up to a total dose of 18-21 mg/kg [4]. Pentavalent antimonials have been used to treat visceral leishmaniasis since the 1940s and continue to be effective, except for India, where resistance is high [8].

Case Details
In this case, a one-year-old girl from Syunik region, village Shrenvants, was admitted to the isolation unit of “Muratsan” University Hospital Complex from Kapan Medical Center in April 2021 with a preliminary diagnosis of “leishmaniasis”. The current symptoms, according to her mother, began three months ago and included: Pallor, cough, increased abdominal size, fatigue, reduced appetite, peripheral edema, oral cavity lesions. Considering the complaints, anamnestic data (episodes of fever were observed periodically in the child for about 3 months, anemia was diagnosed at nine months), epidemiological anamnasis (the Syunik region is endemic for VL), objective examination (general weakness, pallor of skin and mucous membranes, edema of the limbs and cheeks, enlargement of abdomen, hepatomegaly (about 2 cm below the costal margin), splenomegaly (the lower margin reached to pelvic cavity)), and the results of present laboratory and instrumental examinations (Complete Blood Count: WBC/NEU - 1.63/0.26 [10^3/uL], PLT - 20 [10^3/uL], RBC - 2.00 [10^12/uL], HGB - 49 g/L); Coagulation Tests: PI/PT- 21.2%/34.4, INR - 3.65, fibrinogen A - 1.09 g/L, aPTT/TT - 43.5/25.1; Biochemical Analysis: Total protein/albumin - 56.3/24.4 g/L, LDH - 1239, GGT- 104.1, AST- 70.2 U/L, CRP- 32.4; abdominal ultrasound - hepatosplenomegaly; positive immunochromatographic test), “visceral leishmaniasis” was diagnosed. Stool and blood cultures were negative. The treatment scheme included AmBisome with 21 mg/kg (200 mg) total dose, antibacterial therapy, vitamin K, hemotransfusion, symptomatic treatment, vitamin B12 (examinations revealed its deficiency). Due to the specific therapy, a clinical and laboratory improvement was observed.

Discussion and Conclusion
After sleeping sickness and Chagas disease, leishmaniasis has the third highest mortality rate among all neglected tropical diseases [2]. It is present in about 89 countries around the world. Excluding Oceania, it can be found on any continent and is endemic in limited geographic regions of Northeast Africa, Southern Europe, the Middle East, Southeast Mexico, Central, and South America. Despite its high epidemiological significance, leishmaniasis is regarded by the WHO as a disease that has been overlooked by various public and private organizations funding health improvement and research [1].

Since 1999 no cases of cutaneous leishmaniasis have been identified in Armenia. In contrast, a VL case was recorded in 1999 after a long elimination period, and
preparation was prescribed, but the underlying cause was ignored. Anemia in endemic foci for visceral leishmaniasis should be an alarm for primary care physicians.

References


