

CASE REPORT

Visceral leishmaniasis in a six-year-old patient – unexpected diagnosis: case study

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ABSTRACT

Visceral leishmaniasis is a parasitic disease caused by protozoa of the *Leishmania* genus and transmitted by the bites of phlebotomine sandfly species. The disease may be a diagnostic challenge in nonendemic countries. The following study presents a case of a six-year-old girl with recurrent fever, hepatosplenomegaly, lymphadenopathy, and pancytopenia. During the diagnostic work-up acute leukaemia, metabolic diseases, and connective tissue diseases were excluded. A second examination of the bone marrow revealed macrophages containing inclusions typical of *Leishmania* amastigotes. The diagnosis was confirmed by identification of the parasite's DNA in a PCR test of a bone marrow sample and serologic detection of antibodies to *Leishmania* spp. Treatment with liposomal amphotericin B was administered with good effect.

KEY WORDS:

visceral leishmaniasis, parasitic disease, child.

INTRODUCTION

The leishmaniasis are a group of parasitic diseases caused by protozoa of the *Leishmania* genus and transmitted by the bites of phlebotomine sandfly species. Visceral leishmaniasis (VL), also known as kala-azar, is the most severe form of leishmaniasis. Approximately 50,000 to 90,000 new cases of VL are detected worldwide annually. The major risk factors for VL are malnutrition, poor housing, human migration, and environmental and climate changes. Although there are 75 endemic countries for VL, about 90% of all global cases are limited to the following seven: Brazil, Ethiopia, India, Kenya, Somalia, South Sudan, and Sudan [1, 2]. This potentially fatal systemic infection is mainly characterised by irregular fever and splenomegaly. Nevertheless, affected patients may present an array of other symptoms including weight

loss, hepatomegaly, pancytopenia, and lymphadenopathy. Hypergammaglobulinaemia is common; however, the presence of autoimmune antibodies may confuse the presentation, especially in travellers or migrants [3]. Febrile splenomegaly occurs in many infectious diseases; therefore, a suspicion of VL needs to be confirmed by *Leishmania*-specific laboratory tests. The classical test is based on microscopic observation of the amastigote form of the parasite in tissue aspirates. The specificity of the method is high, but the sensitivity of microscopy varies between different tissues and is highest for spleen and bone marrow aspirates [4]. Serological tests based on the detection of antibodies to *Leishmania* from patients' serum are currently the gold standard and the most widely used method for control of VL in endemic areas [5, 6]. The major limitation of serological diagnosis is the persistence of the antibodies for several years after cure and

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therefore the inability to reliably control relapse or distinguish between current, asymptomatic, or past infections [4, 5]. The detection of parasite DNA by polymerase chain reaction (PCR) in aspirates of blood or bone marrow is the most sensitive and specific method, but it is restricted to research centres [4, 6]. The treatment of VL is based on chemotherapy. The primary drugs are pentavalent antimonials, but clinical resistance and treatment failure is becoming more pronounced. Alternative medications such as miltefosine, paromomycin, and amphotericin B are increasingly used worldwide [7]. Furthermore, the development of a vaccine that prevents *Leishmania* infection, halts its progression, or limits transmission are research priorities. Currently, only three vaccines are being tested in clinical trials [3], and several in are in preclinical development [8].

CASE REPORT

The case report refers to a six-year-old girl who was admitted to a paediatric oncology clinic with a suspicion of acute leukaemia. Symptoms had started five months prior to admission when mild anaemia and thrombocytopenia were found in control blood count. The patient was treated with iron therapy, folic acid, and vitamin B6 by the primary care physician. Over the following months subsequent symptoms appeared – malaise, lower extremity pain, epistaxis, bruising tendency, abdominal distension, recurrent fever, and pancytopenia. The child was referred to the clinic for further diagnostics. On admission, the physical examination revealed pallor, caput medusae, tachycardia, hepatosplenomegaly, and cervical lymphadenopathy. Laboratory tests confirmed pancytopenia (WBC $3.79 \times 10^9/l$, RBC $3.34 \times 10^{12}/l$, Hb 7.3 g/dl, PLT $53 \times 10^9/l$), lymphocytosis on peripheral blood smear, and increased values of inflammatory markers, liver enzymes, and D-dimer levels. Hypergammaglobulinaemia and elevated levels of autoimmune antibodies were also detected. Abdominal computed tomography (CT) showed massive splenomegaly, moderate hepatomegaly, and multiple, polycyclic structures along the celiac trunk, which might suggested pathological lymph nodes (Fig. 1). Thoracic CT revealed mediastinal and axillary lymphadenopathy. On the basis of bone marrow examination acute leukaemia was excluded. The patient was consulted with a rheumatologist; after negative tests of double-stranded DNA, anticardiolipin, and lupus anticoagulant, differential diagnosis of systemic lupus erythematosus was excluded. Subsequently, the girl was referred to the Department of Metabolic Diseases, where inherited metabolic disorders were ruled out, including the most probable – Gaucher disease. Despite the use of broad-spectrum antibiotics, and antiviral and antifungal drugs, irregular fever persisted and the patient required regular transfusions of blood. At that time, re-examination of bone marrow was carried out and it showed inclusions in

macrophages typical of amastigote forms of *Leishmania* (Fig. 2). The diagnosis was confirmed by identification of the parasite's DNA by PCR and serologic detection of antibodies to *Leishmania* spp. The infection was probably acquired two years earlier during holidays in Cro-

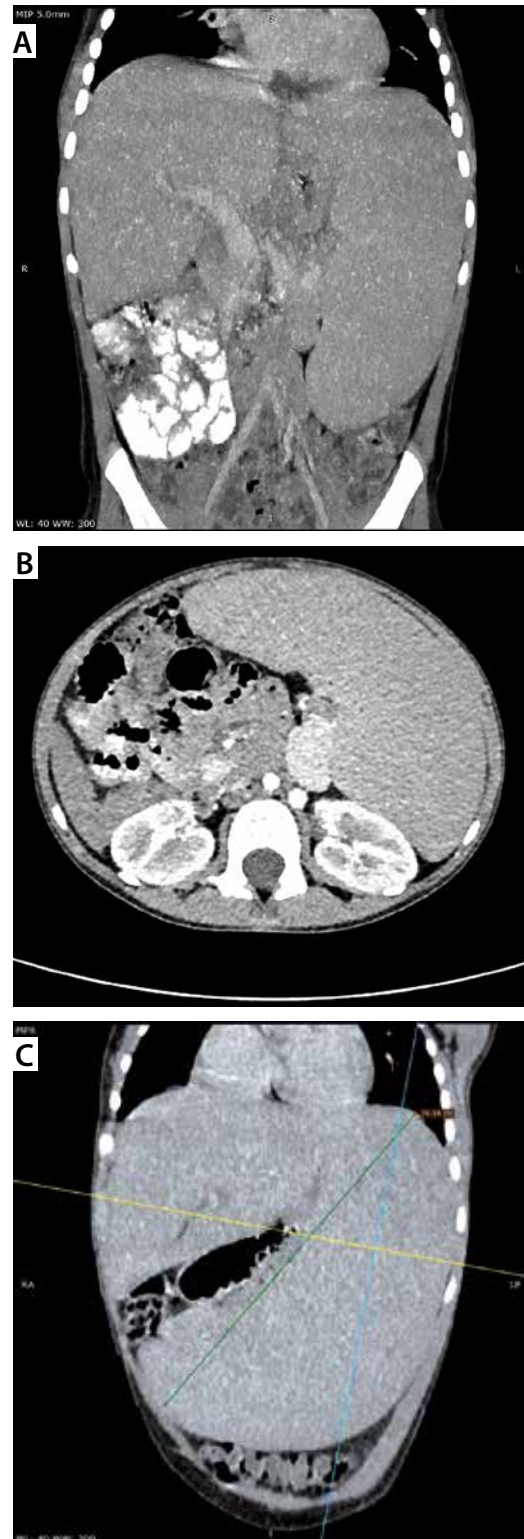


FIGURE 1. Abdominal CT of the patient showing: **A)** massive hepatosplenomegaly, **B)** enlargement of the spleen visualised on the axial projection, and **C)** and enlargement of the spleen visualised with bipolar splenic diameter

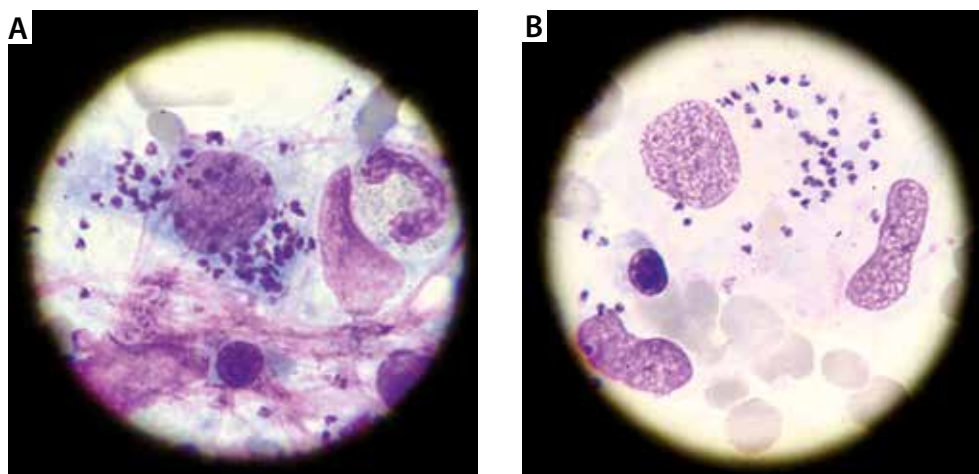


FIGURE 2. Microscopy findings of amastigotes of *Leishmania* in macrophages of the patient (A and B)

atia and Bosnia and Herzegovina, which are endemic regions for VL. Therapy of liposomal amphotericin B was administered (at a dose of 3 mg per kg, for 10 days) [9–12]. We observed good parasitological response to the treatment: improvement of the patient's overall condition, reduction of the size of the spleen, and normalisation of the peripheral blood cell count [12].

DISCUSSION

Due to the increasing number of people undertaking long-distance travel, the incidence of cases of endemic diseases imported to nonendemic countries is on the rise [13]. The diagnosis of VL in nonendemic areas, including Poland, may be challenging, although the clinical presentation is usually similar to that in endemic areas. This is mainly due to the fact that the clinical possibility of VL in the differential diagnosis is very low in patients from nonendemic regions [14, 15]. Delay in diagnosis and treatment may lead to serious complications and even a fatal outcome of VL [16]. European endemic countries are located mainly in the Mediterranean basin. Nonetheless, leishmaniasis is still considered as a tropical disease by many European physicians and public health experts [17]. It is noteworthy that the data on cases of the disease in children are limited, so the discussion is difficult. Chandra *et al.* analysed 27 cases of VL in nonendemic regions [18]. The study showed that fever and hepatosplenomegaly were the most common clinical presentations of VL. According to haematological findings, all patients were anaemic, and pancytopenia was observed in 96.2%. The diagnosis of VL was not initially suspected in 81.4% of the cases. The study indicated that the substantial delay between the onset of symptoms and the final diagnosis is mainly caused by its presence in a nonendemic region and overlapping clinical features of other conditions typical of this area. Interestingly, several European studies [19–21] showed that very few of the imported infections have been acquired in countries that account for over 90% of VL cases worldwide (Brazil, Ethiopia, India, Ken-

ya, Somalia, South Sudan, and Sudan). The recorded data emphasise the differences in the epidemiology of VL in travellers and inhabitants of epidemic regions. Most of the patients with travel-acquired VL were successfully treated with liposomal amphotericin B [19–21]. To date, no vaccines or preventive drugs are available, so personal protective measures are recommended to travellers to minimise exposure to sandfly bites with the following: protective clothing, insect repellent to exposed skin, and minimising nocturnal outdoor activities [9, 10].

CONCLUSIONS

Visceral leishmaniasis is a rare cause of prolonged, irregular fever, hepatosplenomegaly, and pancytopenia in children in nonendemic regions. The clinical manifestation of VL may mimic symptoms of other paediatric conditions, including oncological, metabolic, and connective tissue diseases. This case report reinforces the need for consideration of VL in the differential diagnosis whenever the symptoms occur, even in nonendemic areas.

DISCLOSURE

The authors declare no conflict of interest.

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