

Kala-Azar: A Case Report

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Abstract

Leishmaniasis is a zoonosis caused by unicellular protozoans *Leishmania*. The transmission can be zoonotic or anthroponotic, depending on the species, and the main vector is the phlebotomine sandfly. The disease is endemic in the tropics of Asia and Africa but is considered rare in Portugal, especially in immunocompetent hosts. Its main clinical syndromes constitute cutaneous leishmaniasis, mucocutaneous disease, and visceral leishmaniasis. The latter is also known as *kala-azar* and is caused by the infection of the phagocytes of the reticuloendothelial system, causing the typical symptoms: fever, hepatosplenomegaly, and pancytopenia. The clinical manifestations are non-specific, frequently causing a delay in the diagnosis, especially in nonendemic areas and immunocompetent hosts. Early diagnosis and treatment are essential, given the high mortality rate in untreated patients. The diagnosis is based on the direct visualization of the protozoan and molecular methods, such as polymerase chain reaction tests. Amphotericin B is considered the first-line treatment. We present a case of visceral leishmaniasis in an immunocompetent patient with fever, hepatosplenomegaly, and pancytopenia.

Categories: Infectious Disease

Keywords: unintentional weight loss, immunocompetent adult, high fever, "pancytopenia", visceral leishmaniasis (vl)

Introduction

Visceral leishmaniasis, also known as *kala-azar*, is a systemic disease caused by unicellular protozoans of the genus *Leishmania* (principally *Leishmania donovani* (*L. donovani*) and *Leishmania infantum* (*L. infantum*), depending on the geographical area), transmitted by phlebotomine sandflies [1-3]. The disease is endemic in the rural areas of the tropics of Asia, East Africa, and Brazil [3] but is hypoendemic in Portugal [4]. The principal clinical syndromes associated with the *Leishmania* infection are cutaneous leishmaniasis, mucocutaneous leishmaniasis, and visceral leishmaniasis, caused by systemic dissemination of the parasites through the reticuloendothelial system [1-3]. Clinical manifestations of visceral leishmaniasis are non-specific [3], and a high index of suspicion is necessary to diagnose the disease in non-endemic areas. When untreated, the disease is associated with a high mortality rate [2].

Case Presentation

We present a case of a 38-year-old woman with a history of primary hyperparathyroidism, having undergone parathyroidectomy and depression, for which she was medicated with escitalopram and bromazepam. The patient presented with vespertine fever, night sweats, weight loss (6.1% of the total body weight), anorexia, and non-productive cough, which started about a month before the hospitalization. The patient was of African descent and had moved to Portugal from the Democratic Republic of São Tomé and Príncipe (not an endemic area for leishmaniasis) three years before the hospitalization and had traveled there six months before the onset of symptoms. There was no other relevant epidemiologic history, such as insect bites, contact with dogs, or other domesticated or wild animals.

At admission, pallor of the mucosa and splenomegaly were identified. Laboratory investigations revealed new-onset pancytopenia (normocytic anemia 10.3g/dL, leukopenia 2700/μL, and thrombocytopenia 90000/μL) and C-reactive protein elevation (14mg/dL) (Table 1).

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Laboratory test	Value at admission	Normal range
Hemoglobin	10.3g/dL	12-15.3g/dL
Leukocytes	2700x10 ⁹	4000-11000x10 ⁹
Platelets	90000 x10 ⁹	150-450 x10 ⁹
CRP	14mg/dL	<0.5 mg/dL
IGRA	Negative	-

TABLE 1: Laboratory tests performed at admission, showed pancytopenia
CRP: C-reactive protein; IGRA: Interferon-gamma release assay

The peripheral blood smear was unremarkable, and blood infectious serologies, including human immunodeficiency virus (HIV), hepatitis B and C, cytomegalovirus (CMV), parvovirus B19, Epstein-Barr virus (EBV), as well as *Brucella*, *Coxiella burnetii*, *Rickettsia conorii* and the enzyme-linked immunoassay test for *Leishmania*, were all negative (Table 2). Malaria parasites were not found on the peripheral blood smear. The Interferon-γ release assays (IGRA) test was negative as well.

Infectious serologies	Result
Human immunodeficiency virus (HIV)	Negative
Hepatitis B	Negative
Hepatitis C	Negative
Parvovirus B-19	Negative
Cytomegalovirus (CMV)	Negative
Epstein-Barr virus (EBV)	Negative
<i>Brucella</i> spp.	Negative
<i>Rickettsia conorii</i>	Negative
<i>Coxiella burnetii</i>	Negative
<i>Leishmania</i> spp.	Negative

TABLE 2: Infectious serologies solicited

The whole-body computerized tomography (CT) showed discrete hepatosplenomegaly and para-aortic lymphadenopathy (Figure 1). Given the persistent fever and pancytopenia during the hospitalization, a positron emission tomography (PET) was solicited, and intense metabolic activity of the spleen and bone marrow was detected.

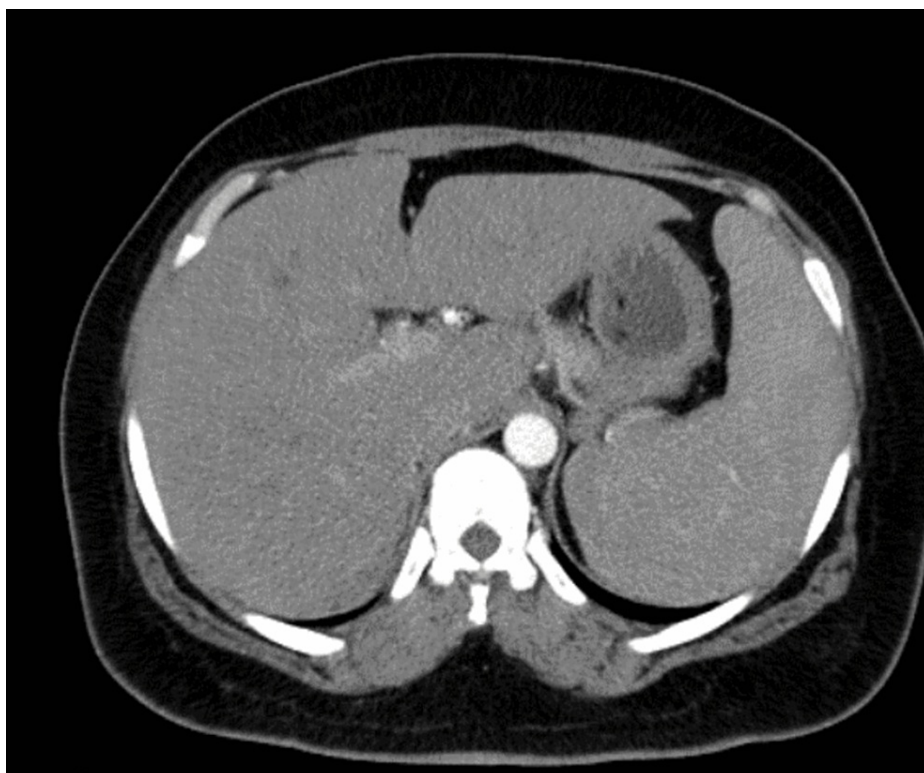


FIGURE 1: Abdominal CT scan showing hepatosplenomegaly

CT: computerized tomography

A myelogram and bone marrow biopsy were performed, evidencing multiple *Leishmania*, thus confirming the diagnosis of visceral leishmaniasis or kala-azar (Figure 2).

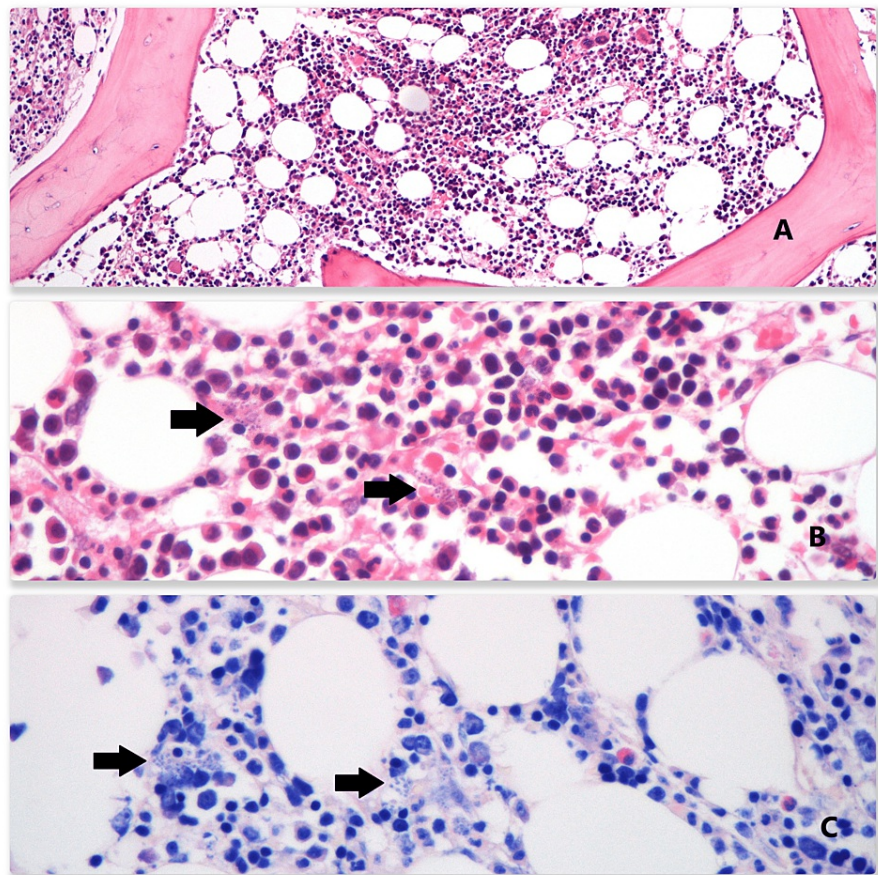


FIGURE 2: Microscopical analysis of the bone marrow that shows normal cellularity (A). At 40x magnification, numerous macrophages with round and basophilic intracytoplasmic organisms that corresponded to *Leishmania* amastigotes are seen (B). These organisms are also readily visualized in a Giemsa staining (C)

Treatment with intravenous liposomal amphotericin B (3mg/kg/day, for five days) was started, with the resolution of the fever, thrombocytopenia, and leucopenia, maintaining only anemia (10g/dL) on hospital discharge.

Discussion

Visceral leishmaniasis (VL) is a systemic disease caused by unicellular protozoans from the *Leishmania* genus, typically transmitted by female phlebotomine sandflies [1]. Although nearly 90% of all worldwide cases occur in Bangladesh, India, Nepal, Sudan, and Brazil, *Leishmania* is endemic in some Mediterranean and Middle East countries [5]. VL is typically caused by *L. donovani*, found almost exclusively in the Old World, and *L. infantum*, endemic in Latin America and the Mediterranean [6]. The transmission is either anthroponotic, in the case of *L. donovani*, or zoonotic, as in *L. infantum*, with dogs, rodents, foxes, and other animals serving as the main reservoir [2,6]. Despite the geographic localization, visceral leishmaniasis is hypoendemic in Portugal, with an incidence rate of 0.1 cases per 100,000 inhabitants [4], and is more frequently diagnosed in the pediatric population and immunocompromised patients [7].

The incubation period can vary between 2 weeks and 18 months, but the disease can take years to become symptomatic [6]. After the inoculation of the promastigote form into the skin, the parasites are internalized by phagocytes (dendritic cells and macrophages) in the skin, where they transform into amastigotes, replicate, and later disseminate through lymphatic and blood vessels and infect the phagocytes of the reticuloendothelial system [2-3], resulting in infiltration of the bone marrow and hepatosplenomegaly [3]. The most common clinical manifestations are fever, weight loss, fatigue, and hepatosplenomegaly [8], but the symptoms may be atypical in immunocompromised (especially AIDS-acquired immunodeficiency syndrome) patients [2]. As the disease progresses, fatigue aggravation due to anemia and abdominal pain due to hepatosplenomegaly may occur [2-3,8]; gastrointestinal involvement, causing diarrhea, pleural effusion,

and pulmonary nodules, are also described [5].

Typical laboratory findings include anemia, leukopenia, pancytopenia, increased transaminases, and hypergammaglobulinemia [5,8]. A high index of suspicion is necessary to diagnose VL since its clinical presentation is non-specific and can be associated with other infectious diseases, such as tuberculosis, malaria, and brucellosis, as well as hematologic malignancies and macrophage activation syndrome [5,8].

Traditionally, the gold standard for the diagnosis has been direct visualization of the parasite on microscopy or culture of invasive samples [9,10]. Still, molecular methods have the highest sensitivity and specificity [10]. Therefore, a step-wise approach is recommended in the diagnosis of VL [9]; non-invasive tests, such as serology and polymerase chain reaction (PCR) tests, should be the first to be performed [9]. In contrast to immunocompromised patients, serology has good sensitivity and specificity (80%-100%) in immunocompetent patients [5,9]. When the diagnosis can't be ruled out or reliably confirmed, bone marrow, lymph nodes, or spleen samples should be obtained [9]. Spleen biopsy has the best sensitivity (93%-99%) [9], but because of the risk of spleen hemorrhage, bone marrow aspirate is preferred, despite the lower sensitivity (53%-86%) [5,9]. RK39 and rK28-based rapid diagnostic tests have been implemented, but their sensitivity and specificity vary according to the geographical location, being highest in the Indian continent [9-10] and, thus, not very useful to diagnose VL in Portugal.

Our patient was of African descent and had moved to Portugal from the Democratic Republic of São Tomé and Príncipe three years before the hospitalization; she had visited the country about six months before the hospitalization. According to the World Health Organization (WHO), no autochthonous cases have been reported in the country up until now [11]. No insect bites or contact with dogs or other domesticated or wild animals were reported. She presented with typical symptoms of intermittent fever, weight loss (6.1%), night sweats and fatigue, and splenomegaly was observed at admission. The laboratory results confirmed pancytopenia. Although she presented a typical clinical picture, it is not specific to leishmaniasis, and the patient did not refer high-risk epidemiologic history for leishmaniasis.

Other parasitic and bacterial infections were excluded, including malaria, an endemic disease in São Tome, tuberculosis, brucellosis, and rickettsiosis. Viral infections, causing fever and pancytopenia, were also ruled out. The serology for *Leishmania* in the peripheral blood was negative. Further investigation was performed to confirm leishmaniasis and exclude eventual hematologic disease. Hepatosplenomegaly was documented on the CT scan; intense metabolic activity of the spleen and bone marrow was detected on the PET scan. Given the high risk of post-procedure hemorrhage, a bone marrow biopsy and myelogram were performed instead of a spleen biopsy. Multiple *Leishmania* parasites were observed on microscopy, confirming the diagnosis of VL.

When not treated, VL is associated with a high mortality rate [10]. Therefore, all symptomatic patients should be treated according to the current guidelines, and the treatment should be adapted to the patient's immune status and the geographic location where the infection was acquired [1,9]. Currently, amphotericin B and miltefosine (for *L. donovani*) are considered the first-line treatment, with pentavalent antimony being an alternative treatment in patients that do not tolerate the treatments mentioned above [1,9]. Clinical parameters correlate with the response to the treatment, and invasive methods are not recommended to monitor the response [1]. Our patient was started on liposomal amphotericin B (3mg/kg/day intravenously for five days, and on days 14 and 21) after an infectious disease consult, with the resolution of fever and normalization of thrombocytopenia and leukopenia, maintaining discrete anemia.

Conclusions

Visceral leishmaniasis is a systemic, potentially fatal disease caused by protozoa of the *Leishmania* genus. It is transmitted by sandflies, and its natural reservoir is dogs, foxes, and rodents. Due to its non-specific clinical presentation, a high index of suspicion is necessary to diagnose the disease, especially in non-endemic areas and immunocompetent patients. A prompt diagnosis and exclusion of other infectious and hematologic diseases are crucial. The timely institution of treatment has a direct impact on the prognosis. Direct visualization and molecular tests are the most sensitive and specific tools for diagnosis.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Aronson N, Herwaldt BL, Libman M, et al.: Diagnosis and treatment of leishmaniasis: Clinical practice guidelines by the Infectious Diseases Society of America (IDSA) and the American Society of Tropical Medicine and Hygiene (ASTMH). *Clin Infect Dis*. 2016, 63:1539-57. [10.1093/cid/ciw742](https://doi.org/10.1093/cid/ciw742)
2. B.S. MCGWIRE and A.R. SATOSKAR: Leishmaniasis: clinical syndromes and treatment . *Q J Med*. 2014, 107:7-14. [10.1093/qjmed/hct116](https://doi.org/10.1093/qjmed/hct116)
3. Chappuis F, Sundar S, Hailu A, et al.: Visceral leishmaniasis: what are the needs for diagnosis, treatment and control?. *Nat Rev Microbiol*. 2007, 5:873-82. [10.1038/nrmicro1748](https://doi.org/10.1038/nrmicro1748)
4. Almeida M, Maia C, Cristóvão JM, et al.: Seroprevalence and risk factors associated with leishmania infection in dogs from Portugal. *Microorganisms*. 2022, 10: [10.3390/microorganisms10112262](https://doi.org/10.3390/microorganisms10112262)
5. Buonomano R, Brinkmann F, Leupin N, Boscacci R, Zimmermann A, Müller N, Fux CA: Holiday souvenirs from the Mediterranean: three instructive cases of visceral leishmaniasis. *Scand J Infect Dis*. 2009, 41:777-81. [10.1080/00365540903104127](https://doi.org/10.1080/00365540903104127)
6. Ready PD: Epidemiology of visceral leishmaniasis. *Clin Epidemiol*. 2014, 6:147-54. [10.2147/CLEP.S44267](https://doi.org/10.2147/CLEP.S44267)
7. Maia C, Campino L: Leishmaniose em Portugal no início do século XXI . *Anais IHMT*. 2014, 13:25-28. [10.25761/anaisihmt.167](https://doi.org/10.25761/anaisihmt.167)
8. Safavi M, Eshaghi H, Hajihassani Z: Visceral leishmaniasis: Kala-azar. *Diagn Cytopathol*. 2021, 49:446-8. [10.1002/dc.24671](https://doi.org/10.1002/dc.24671)
9. van Griensven J, Diro E: Visceral leishmaniasis: Recent advances in diagnostics and treatment regimens . *Infect Dis Clin North Am*. 2019, 33:79-99. [10.1016/j.idc.2018.10.005](https://doi.org/10.1016/j.idc.2018.10.005)
10. Kassa M, Abdellati S, Cnops L, et al.: Diagnostic accuracy of direct agglutination test, rK39 ELISA and six rapid diagnostic tests among visceral leishmaniasis patients with and without HIV coinfection in Ethiopia. *PLoS Negl Trop Dis*. 2020, 14:e0008963. [10.1371/journal.pntd.0008963](https://doi.org/10.1371/journal.pntd.0008963)
11. World Health Organization: Leishmaniasis. (2021). Accessed: January 11, 2023: https://apps.who.int/neglected_diseases/ntddata/leishmaniasis/leishmaniasis.html.