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CASE REPORT

A Case of Visceral Leishmaniasis Characterized by Fever of Unknown Origin and Nodular Lesions in the Spleen

Nedeni Bilinmeyen Ateş ve Dalakta Nodüler Lezyonlar ile Karakterize Bir Visseral Leishmaniasis Olgusu

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ABSTRACT

Introduction: Leishmaniasis is a zoonosis caused by Leishmania spp. parasites through the bite of infected female sandflies, and has three main forms: visceral (VL), cutaneous (CL) and mucocutaneous (MCL). VL is endemic in many countries around the world. It is on the World Health Organization's (WHO) list of neglected diseases and is difficult to diagnose due to its non-specific clinical manifestations. VL is characterized by fever, hepatosplenomegaly and bone marrow suppression. The diagnosis is made by the presence of amastigotes in tissue or blood samples or serological and DNA-based techniques.
Case: Our patient was a 30-year-old male who did not have any immunodeficiency. He was characterized by persistent fever, pancytopenia, hepatosplenomegaly and multiple millimetric hypoechoic solid nodules in the spleen. The diagnosis of VL was confirmed using all three parasitological, serological and molecular methods. Cure was achieved by treatment with liposomal amphotericin B (L-AmB).
Conclusion: VL should be considered in the differential diagnosis of patients with fever of unknown cause, pancytopenia and hepatosplenomegaly. The presence of solid nodular lesions in the spleen may also shed light in favour of VL.

Keywords: Fever of unknown cause, hepatosplenomegaly, pancytopenia, splenic nodule, visceral leishmaniasis

ÖZ

Giriş: Leishmaniasis, enfekte dişi tatarcık sineklerinin ısırması sonucu Leishmania spp. parazitlerinin neden olduğu bir zoonoz olup visseral (VL), kutanöz (KL) ve mukokutanöz (MKL) olmak üzere üç ana formu vardır. VL dünyada birçok ülkede endemik olarak bulunur. Dünya Sağlık Örgütü'nün (DSÖ) dikkat çektiği ihmal edilen hastalıklar listesinde olup, spesifik olmayan klinik bulguları nedeniyle tanı konulması zor bir hastalıktır. VL ateş, hepatosplenomegali, kemik iliği süpresyonu ile seyreder. Tanı doku ya da kan örneklerinde amastigotların görülmesi veya serolojik ve DNA esaslı tetkikler ile konur.
Olgu: 30 yaşında immün yetmezlik öyküsü olmayan erkek hastada persistan ateş, pansitopeni, hepatosplenomegali ve aynı zamanda dalakta çok sayıda milimetrik hipoekoik solid nodüller mevcuttu. Parazitolojik, serolojik ve moleküler yöntemlerin üçü de kullanılarak VL tanısı kesinleştirildi. Lipozomal amfoterisin B (L-AmB) ile tedavi edilerek kür sağlandı.
Sonuç: Nedeni bilinmeyen ateş, pansitopeni ve hepatosplenomegali olan hastalarda ayırıcı tanıda VL düşünülmelidir. Dalakta solid nodüler lezyonların varlığı da VL tanısına ışık tutabilir.

Anahtar Kelimeler: Dalakta nodül, hepatosplenomegali, nedeni bilinmeyen ateş, pansitopeni, visseral leishmaniasis

Introduction

Leishmaniasis is a parasitic zoonotic disease transmitted by the bite of infected female sandfly (Phlebotomus), one of the tropical diseases considered important by the World Health Organization (WHO). Dogs, foxes, jackals and other Canidae are reservoirs of the parasite in nature. There are 3 main forms: visceral (kala-azar) (VL), cutaneous (CL) and mucocutaneous (MKL). CL is the most common form. VL is the most serious form and is fatal if not diagnosed and treated. Leishmaniasis is endemic in 99 countries, including Türkiye and other countries in the Mediterranean region, as well as underdeveloped countries in America, East and North Africa, and West and Southeast Asia. Increased travelling, migration movements and climate change as a result of global warming increase the prevalence of leishmaniasis worldwide. According to WHO data, it is estimated that between 50.000 and 90.000 new cases of visceral leishmaniasis develop annually in the world, but it is thought that less than half of them is reported. VL is characterized by fever attacks, weight loss, hepatomegaly, splenomegaly and pancytopenia. Definitive diagnosis is made by demonstration of amastigotes in tissue or blood samples. However, various serological tests based on the detection of specific anti-Leishmania antibodies and DNA-based molecular techniques are also used (1-4). In this case report, we present a patient who was initially suspected to have haematological malignancy due to persistent fever, bone marrow suppression and the presence of multiple nodular solid lesions in the spleen, but was diagnosed with VL in the clinical progress.

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Case

A 30-year-old male patient living in a rural area of Konya presented to our outpatient clinic with complaints of fever, weakness and weight loss for ten days during the summer months. In his anamnesis, he had no history of travelling anywhere other than the district where he lived. He had a history of tick bite one week ago. There was no known underlying disease. On physical examination, fever was 39°C, pulse 94/minute, BP 110/70 mmHg, and hepatosplenomegaly was determined. Laboratory examination revealed haemoglobin 13.9 g/dl, leukocyte 3830/mm3, platelet 95 thousand/mm3, erythrocyte sedimentation rate (ESR) 27 mm/h, CRP 120.5 mg/L, AST 62 U/L, ALT 57 U/L, LDH 597 U/L, CK 61 U/L, INR 1.35 and ferritin 4599 µg/L. Brucella and Salmonella agglutination test and Crimean-Congo haemorrhagic fever ELISA test, Hbs Ag, anti HCV, anti-HIV, CMV IgM, toxoplasma IgM, EBV VCA IgM, HSV IgM and VDRL tests ordered for differential diagnosis were negative. Thyroid function tests were normal. His chest X-ray was normal with no infiltrations. No pathological findings were found on echocardiography. Respiratory tract microarray polymerase chain reaction (PCR), including COVID, was performed and nothing was detected. Spleen long axis was 170 millimeters (mm) on abdominal ultrasonography.

During the follow-up of the patient who was followed up due to fever of unknown origin, bone marrow suppression increased and AST, ALT, ALP, GGT and CK levels continued to increase among biochemical parameters. Persistent fever (>38 °C) continued. No growth was detected in the blood culture samples taken. Abdominal computed tomography (CT) showed liver size of 180 mm in vertical dimension, spleen size of 190 mm, and hypoechoic solid nodular foci with heterogeneous parenchymal appearance. Abdominal magnetic resonance imaging (MRI) showed multiple millimetric nodular lesions in the splenic parenchyma less than 10 mm in size, which were less contrasted with the parenchyma in arterial phase imaging and had equal signal with the parenchyma in other phases (Figure 1). Blood examination was performed for malaria and it was not detected. No atypical cell was detected in peripheral blood smear. Considering that the etiology of the lesions in the spleen and fever had not yet been elucidated, it was decided to perform a bone marrow biopsy to exclude or demonstrate hematological malignancy. No growth was detected in the blood culture sent from the bone marrow aspirate. On examination of the bone marrow aspirate, findings suggestive of haemophagocytic syndrome were found. In the follow-up, Leishmania spp. IgG and PCR results were found positive by dipstick in serum and blood samples sent to the National Microbiology Reference Laboratory of Public Health of Türkiye, and peripheral blood smear and bone marrow preparations were examined by an expert parasitologist and Leishmania spp. amastigote forms were detected in the microscopic examination (10x100) of Giemsa-stained smears (Figure 2). Parenteral 3mg/kg/day liposomal amphotericin B (L-AmB) was started with the diagnosis of VL. After 72 hours of treatment, the patient's fever decreased and other complaints regressed. On laboratory examination, bone marrow suppression findings and biochemical parameters regressed. Control peripheral blood smear examination on the fifth day showed rare amastigotes. The patient was discharged after five days of L-AmB treatment. L-AmB dose was repeated on the 14th and 21st days of treatment initiation and terminated. No Leishmania amastigotes were observed in the peripheral blood smears performed at the end of the treatment. Abdominal ultrasonography showed regression of hepatosplenomegaly. No pathological findings were found in the third month outpatient clinic control and the patient was considered cured.

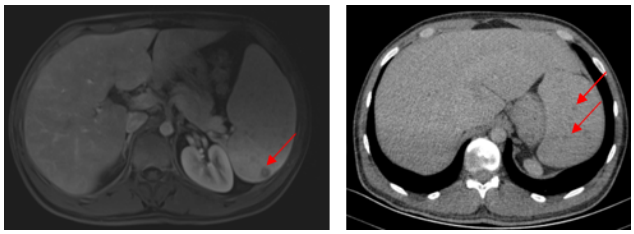

Figure 1. Nodular lesions in the spleen on MRI (1a) and CT (1b) imaging

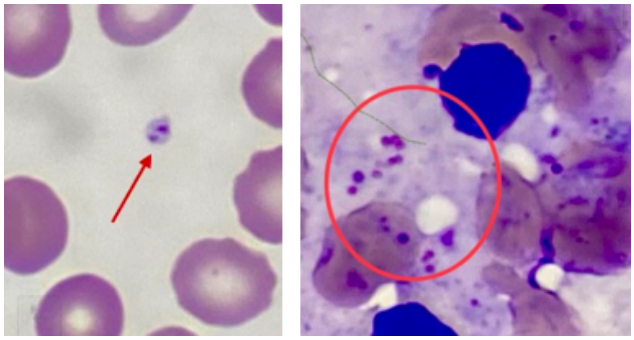

Figure 2. Amastigotes in peripheral blood smear (2a) and bone marrow aspirate (2b)

Discussion

Leishmaniasis is one of the zoonotic diseases which is endemic in the Mediterranean region including Türkiye and is caused by more than 20 species. However, VL is observed as sporadic cases in Türkiye, mainly in the Aegean and Mediterranean regions (5-8). Therefore, it may not be considered in the differential diagnosis outside these regions. Since our patient lived in Konya, a Central Anatolian city and had no history of travelling outside the province, VL was not primarily considered. When the literature was analyzed, the presence of vector flies in this region was found (9). Considering the presence of vector flies and reservoir dogs, our patient may have been infected.

Visceral leishmaniasis is characterized by fever, hepatosplenomegaly and pancytopenia. Due to its non-specific clinical findings, the diagnosis is delayed and may cause morbidity and mortality. It may also be confused with haematological malignancies. The gold standard in diagnosis is the observation of amastigotes in the infected material on microscopic examination

in preparations stained with giemsa. Serological and molecular methods are also used in diagnosis (3, 6). In the literature, although similar findings including fever, hepatosplenomegaly, anaemia, leucopenia and weight loss are common, few cases have nodules in the spleen or liver on abdominal imaging (10-14). Our patient had similar clinical and laboratory findings. In addition, multiple solid nodules were found in the spleen on abdominal imaging. The presence of hypoechoic nodules in the spleen is generally associated with lymphoma, splenic infarction, metastatic disease, septic embolism and granulomatous diseases (15). However, we saw that there may be a similar image in VL. We think that it should be included in the possible differential diagnosis of these focal lesions in the spleen and liver.

While malignancy was considered in the foreground in the patient, the diagnosis was made when Leishmania amastigotes were observed in the bone marrow aspirate sample examined upon positive Leishmania IgG test in the serum blood sample. The presence of Leishmania was also demonstrated by PCR method.

Currently treatment of VL, antimony compounds and amphotericin B compounds are used. However, L-AmB has been preferred recently because of its less side effects and toxicity. In a non-immunosuppressed patient, parenteral L-AmB 3mg/kg/day on days 1-5 and days 14 and 21, totalling 21mg/kg (3, 4). L-AmB was also used in our patient and a dramatic improvement was observed in his complaints after 72 hours.

In conclusion, VL should be considered in the etiology of fever of unknown origin in non-endemic regions and it should be kept in mind that the disease may be confused with haematological malignancies because of pancytopenia, hepatosplenomegaly and solid nodule findings in the spleen. In addition, considering the presence of vector flies in our region and the fact that dogs, which are frequently found in our living areas, are the reservoir host of the parasite, it should be taken into consideration by the authorities that sporadic cases of Leishmaniasis in stray, uncontrolled, stray dogs may cause an important public health problem for our region.

Patient Consent: A consent form was obtained from the patient included in our study.

Conflict of Interest: The authors declare no conflict of interest regarding this article.

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