

Visceral Leishmaniasis with Splenic Nodules: Case Report

Visseral Leşmanyaziste Dalakta Nodüller

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ABSTRACT Visceral leishmaniasis (VL) is transmitted to humans by the bite of sandflies. VL is an endemic parasitic disease which is characterized by fever, splenomegaly and pancytopenia in most of the cases. Delays in diagnosis of VL are common because of nonspecific symptoms and variable incubation time. Specific serology and polymerase chain reaction are useful for the diagnosis. Anti-K39 strip test is highly sensitive. Splenic multifocal hypoechoic nodules should be evaluated for VL with clinical and laboratory features in patient. Herein we report a twenty-two month-old female infant with diagnosis of VL who presented with recurrent fever, pancytopenia and ultrasonography revealed enlarged spleen with multifocal hypoechoic nodules. We considered that splenic nodules can help to diagnosis of VL in children as literature case reports support to this situation.

Key Words: Fever; pancytopenia; leishmaniasis, visceral

ÖZET Visseral leishmaniasis (VL) insanlara dişi kum sineklerinin (sandfly) ısırmasıyla bulaşmaktadır. VL olguların çoğunluğunda gözlenen ateş, splenomegali ve pansitopeni ile karakterize, endemik paraziter bir hastalıktır. Özgül olmayan semptomlar ve değişken inkübasyon süresinden dolayı tanıda gecikme siktir. Özgül serolojik testler ve polimeraz zincir reaksiyonları tanıda kullanılmaktadır. Anti-K39 testinin duyarlılığı çok yüksektir. Klinik ve laboratuvar bulguları uyumlu olan hastalarda ultrasonografide görülen dalaktaki çoklu sayıda hipoekoik nodüller VL'ı akla getirmelidir. Bu olgu sunumunda tekrarlayan ateş, pansitopenisi olan, ultrasonografide dalak büyüklüğü ve çok sayıda hipoekoik nodüller saptanan yirmi iki aylık bir kız hastayı sunduk. Biz olgumuz ve literatürde yayımlanmış olan vaka sunumları ışığında, dalakta saptanan nodüllerin çocuklarda VL tanısı koymada yardımcı olabileceği düşüncesindeyiz.

Anahtar Kelimeler: Ateş; pansitopeni; leşmanyazis, visseral

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Visceral leishmaniasis (VL) is a systemic parasitic disease that is caused by the *Leishmania donovani* (South Asia and East Africa) or *Leishmania infantum* (Mediterranean basin, Middle East, Western Asia and Brazil) and is transmitted by sand flies (genus *Phlebotomus*). Fever and splenomegaly are detected in more than 80% of patients as the most common clinical manifestations. Neutropenia, anemia, thrombocytopenia, elevated sedimentation and hypergammaglobulinemia are the most common laboratory abnormalities of this disease. Without treatment VL is nearly always lethal due to infectious and haemorrhagic complications.¹⁻³

CASE REPORT

A twenty-two month-old female was admitted to our hospital with complaints of vomiting, coryza and fever during seven days which were not controlled with antibiotic therapy. She had no infectious disease history up to the present. She was living in village with her parents and there was no specific history to explain fever focus. The pale patient's physical examination revealed blood pressure 100/60 mmHg, body temperature of 38.7°C, respiratory rate of 25/ minute, pulse rate of 130/minute. Rash or enlarged lymph nodes and focus of fever were not detected. Her primary laboratory data was as follows: White blood cells counts (WBC) $6.3 \times 10^3/\text{mm}^3$, neutrophils 56%, lymphocytes 43%, eosinophils 1%, hemoglobin (Hb) 11 g/dL, platelets $181.000/\text{mm}^3$, erythrocyte sedimentation rate 35 mm/hr, C-reactive protein (CRP:39 mg/dL), aspartate aminotransferase (74 U/L), alanine aminotransferase (26 U/L), creatine kinase (40 U/L), lactate dehydrogenase (565 U/L), prothrombin time (1.2), activated partial thromboplastin time (34), albumin, total protein and routine kidney function test results were within normal limits. When *Escherichia coli* (100.000 colony/ mm^3) was detected in the urine culture, antibiotic treatment (cefoperazone-sulbactam) was started. Blood and throat cultures were negative. Serologic test results were as follows: Rose Bengal and Grubel-Widal tests were (-). Recent infection with cytomegalovirus, Epstein-Barr virus, parvovirus, or toxoplasma were excluded by serological enzyme immunoassay. Although urine findings improved with antibiotic treatment, fever was continued so antibiotic was stopped on tenth day of treatment. Echocardiography was evaluated as normal for performed to rule out Kawasaki disease. On abdominal ultrasonography, the spleen was enlarged with multiple nodular lesions which were hypoechoic in nature (the largest was 10 mm). On rheumatological examinations; there was no pathology in ocular fundus examination evaluation and antinuclear antibodies (ANA) (-), anti-dsDNA (-), C3, C4, immunoglobulins, peripheral lymphocyte subsets and phagocyte system were normal.

No acid-fast bacilli was detected in sputum smear and tuberculin skin test with purified protein derivative was negative. The patient was evaluated for tick-transmitted diseases because living in village; Crimean-Congo hemorrhagic fever, lyme, tularemia serologic tests were negative. Thick blood smear test was evaluated for Babesiosis and Ehrlichiosis, parasite could not be detected. Ferritin, triglycerides, fibrinogen levels were normal. Because of patient's fever had continued during fifteen days, bone marrow aspiration was planned for obtain culture and exclude hemophagocytic histiocytosis. But we could not get permission from her family. The patient's fever and acute phase reactants were regressed spontaneously on seventeenth day of illness. The patient who had good general condition was discharged and recommended to polyclinic control after two days. Abdomen computerized tomography (CT) scans were planned for splenic nodules.

Three weeks later, the child was readmitted to the pediatric university hospital with fever and vomiting complaints. Laboratory analysis showed a pancytopenia, following values: hemoglobin, 7.3 g/dL; hematocrit, 22%; white blood cell count, 3800 cells/ mm^3 (61% neutrophils, 6% band forms with toxic granulations and 29% lymphocytes); platelet count, 43.000 cells/ mm^3 ; and CRP, 66 mg/dL. At physical examination, the pale patient had a distended abdomen and enlarged splenomegaly. Patient had septic appearance so vancomycin, meropenem therapy was started. Q fever and rickettsial serology, control Brucella tube agglutination test and cultures were negative. On abdominal ultrasonography splenic multiple nodular lesions still persisting which were thought to be associated with the splenic lymphoma or an infectious processes. A contrast-enhanced abdominal CT scan displayed numerous hypodense nodules with the largest one 10 mm in diameter within splenic parenchyma (Figure 1).

Diagnostic tests for tuberculosis were negative. There was neither any clinical evidence to support the diagnosis of a granulomatous disease (sarcoidosis, tuberculosis, cat-scratch disease) nor lymphoma or other tumoral pathology. A bone



FIGURE 1: Abdominal computerized tomography: The parenchyma of the spleen contained hypodense nodules (arrow).

marrow aspirate showed an intact and no amastigotes or signs of malignancy. Bone marrow aspirate cultures were found negative for *Brucella* and *Salmonella spp.* Immunoglobulin G (1.8 g/L) levels were increased. Leishmaniasis was considered clinically, because she was living in an endemic area and the fever was refractory although broad-spectrum antibiotics. Leishmania serology and polymerase chain reaction (PCR) had sent to an external center before switched to liposomal amphotericin B (LAMB-3mg/kg/day) to therapy. Within 4 days of treatment, the child's temperature fell to $<38^{\circ}\text{C}$ and her condition improved dramatically. At follow-up visits, no more periods of fever were reported, splenomegaly was reduced, leucocytes and thrombocytes became normal. Control hemoglobin level was 12.3 mg/dL, the WBC count was 10300 cells/mm³ and the platelet count was 353.000 cells/mm³. General condition of the patient improved rapidly, treatment lasted after ten day. After seven day termination of treatment, results came back from external center. *Leishmania* antibodies titer was high titer (1:64) and rK39 rapid diagnostic test was positive. One month later after discharge, evaluation abdominal CT was normal.

DISCUSSION

Visceral leishmaniasis (VL) is a severe disease associated with considerable mortality, characterized by fever, hepatosplenomegaly, pancytopenia, and hypergammaglobulinemia. The hepatosplenomegaly is

a result of the accumulation of mononuclear phagocytic cells which cause hyperplasia in reticulo-endothelial system. Pancytopenia occurs secondary to bone marrow involvement and hypersplenism. The role of imaging techniques as diagnostic tools remains to be established in visceral leishmaniasis.⁴ The finding of multiple hypoechoic splenic nodules commonly relates with lymphoma, splenic infarction, metastatic disease, septic emboli or abscesses. Though less frequent granulomatous diseases (tuberculosis, sarcoidosis, cat-scratch disease), cysts, hemangiomas, hamartomas, lymphangiomas or disseminated *Pneumocystis carinii* infection also have to be considered.⁵ In the literature patients who VL were described contain hypoechoic halo and hypoechoic lesions on the liver and spleen, caused by amastigote stage of the leishmanial parasite. Melchionda et al. reported 4 cases of young children in northern Italy presenting with persistent fever of unknown origin and diagnosed with VL by serological and molecular methods. These patients showed multiple iso-hypoechoic nodules associated with splenomegaly. Spleen nodules completely resolved after 1 to 3 months after medical treatment.⁶ Raeymaeckers et al. present a case of 15-month-old Moroccan girl detected multiple hypoechoic nodular splenic lesions who diagnosed VL. Her nodules had completely resolved four months after the start of the treatment.⁷ Our patient was presented prolonged and intermittent fever with splenic nodules. Delays in diagnosis of VL are common because of variable incubation time. In our cases, microscopic examination of bone marrow smear failed to detect amastigotes. Spleen nodules responded quickly to LAMB treatment. One month after treatment splenic nodules resolved completely. By the time result of serologic and PCR tests came back, we had completed treatment with LAMB.

Literature case reports support that this peculiar ultrasound finding, in association with clinical and laboratory criteria, as fever, hepatosplenomegaly, anemia, leucopenia and weight loss, may corroborate the suspicion of VL. That should be confirmed by serological and/or molecular tests.⁶ We suggest that spleen nodules may be an indicator for diagnosing of leishmaniasis.

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