Unexpected diagnosis of visceral leishmaniasis in a patient presenting with an infected ICD lead

D.H. van Raalte*, H.M. Wesselius, G. de Klerk

Department of Internal Medicine, Kennemer Hospital, Haarlem, the Netherlands, *corresponding author: tel.: +31 (0)23 5453545, fax: +31 (0)23 5453759, e-mail: d.vanraalte@vumc.nl

ABSTRACT

Visceral leishmaniasis (VL) is a rare disease in Western countries. Infection with Leishmania parasites usually remains asymptomatic, but may cause significant disease in children and immunocompromised adults in endemic areas. Here, we report a case of sporadic VL caused by Leishmania infantum in an immunocompetent patient who had visited Southern France one year ago and presented with implantable cardioverter defibrillator (ICD) lead infection.

KEYWORDS

Sporadic visceral leishmaniasis, immunocompetent, Mediterranean

INTRODUCTION

Visceral leishmaniasis (VL) is caused by the protozoan 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). L. infantum has a zoonotic form of transmission with the domestic dog as main reservoir. Infections usually remain asymptomatic with an estimated 30-100 asymptomatic infections for every symptomatic case in the Mediterranean region.1 Until recently, endemic VL in Southern Europe occurred mainly in young children. With increased incidence of immunosuppression due to HIV infection, transplantation and chemotherapy, about half the cases are now in adults.4 Sporadic VL may occur in non-indigenous people of any age who have visited endemic areas. The incubation period may be lengthy and ranges from weeks to years. Symptoms include malaise, prolonged irregular fever and weight loss with hypersplenism. Anaemia may develop due to haemolysis, bone marrow suppression and splenic sequestration. Darkening of the skin is typically found in India, but not in Europe (the Hindi name, kala-azar, means ‘black fever’). Without treatment, VL is nearly always lethal due to infectious and haemorrhagic complications.1 However, with liposomal amphotericin B treatment or pentavalent antimonials, high cure rates are reached.4 Here, we report a case of VL in an immunocompetent patient with a seemingly insignificant travel history, who presented with a bacterial infection.

CASE REPORT

A 69-year-old autochthonous Dutch patient presented with complaints of malaise, rigors, night sweats and weight loss over the past three weeks. Medical history included diabetes mellitus and a myocardial infarction with cardiac
arrest, after which percutaneous transluminal coronary angioplasty (PTCA) was performed and an ICD was placed. History was otherwise unremarkable and travel history did not include visits to tropical areas. Physical examination revealed a pale man with a diastolic heart murmur and splenomegaly. No rash or enlarged lymph nodes were observed. Laboratory analysis showed a pancytopenia, with haemoglobin 5.8 mmol/l, mean corpuscular volume 84 fl, reticulocyte count 240 x 10⁹/l, thrombocytes 133 x 10⁹/l and leukocytes 1.7 x 10⁹/l. Furthermore, non-immune haemolysis was observed with 35% elliptocytes in the blood smear. Due to suspicion of endocarditis, a transoesophageal echocardiography was performed which demonstrated vegetations on the ICD lead. Blood cultures were positive for S. hominis and S. epidermidis. He was treated with flucloxacillin and the ICD lead, from which S. hominis, S. epidermidis as well as propionibacterium were cultured, was removed.

Despite appropriate treatment and repetitively negative blood cultures, he continued to suffer from spiking fever, profuse perspiration, weight loss and general malaise. Blood tests showed persistent pancytopenia with haemolysis.

Additional diagnostic tests were performed. Recent infection with cytomegalovirus, Epstein-Barr virus, parovirus, or toxoplasma could be excluded by serological tests. Enzyme immunoassay for HIV-1 and -2 was negative. A positron emission tomography (PET) scan revealed increased uptake in bone marrow and spleen. A bone marrow biopsy did not show a haematological malignancy. A more detailed travel history revealed regular visits, the last one nearly a year ago, to Southern France, the Cévennes region. He recalled that in this region dogs are advised to wear insecticidal collars to protect against sand fly bites. This comment led us to suspect VL. Bone marrow samples were reviewed and Leishmania species amastigotes were identified (figure 1). L. infantum infection was confirmed with direct agglutination test and polymerase chain reaction. Treatment with liposomal amphotericin B for a total dose of 20 mg/kg was given, which resulted in immediate clinical improvement. At follow-up visits, no more periods of fever were reported, splenomegaly was reduced and leucocytes and thrombocytes had normalised. He still had a well-compensated non-immune haemolytic anaemia, which was ascribed to previously unknown hereditary elliptocytosis, which was also found in one of his two daughters.

**DISCUSSION**

We describe a case of sporadic VL caused by L. infantum in an immunocompetent autochthonous Dutch patient. Although leishmaniasis (L. infantum) is endemic in Mediterranean areas, cases of VL are relatively rare. In the Netherlands, incidence of VL is estimated at 5-10 patients per year. However, exact incidence is unknown since there is no obligation to mention cases to Health Authorities. In these sporadic VL patients the infection is contracted while visiting an endemic region, not seldom a long time ago. Since the vector is not present in the Netherlands, there is no risk for local transmission. However, due to climate change, the sand fly vector is increasingly found in more northern European regions. Therefore VL incidence in the Netherlands might increase in the next decades.

In endemic countries many people are infected with Leishmania species, but only a few develop symptoms, predominantly children and immunocompromised individuals, most notably HIV patients. Following initial infection, Leishmania parasites evade immune responses by several strategies, including neutralisation of complement factors, preventing release of macrophage superoxide, and suppression of induction of T lymphocytes, thereby surviving in host macrophages without causing symptoms. The mechanisms involved in parasite reactivation leading to the clinical syndrome of VL, in particular in relation to host immune status, are presently unknown.

Remarkably, our patient was immunocompetent. Diabetes mellitus has not been recognised as a risk factor for VL. The relationship between infection of his ICD lead and reactivation of L. infantum is uncertain. Most likely, VL-induced immune suppression had made our patient susceptible for infections. Indeed, VL-associated morbidity and mortality is mostly driven by infectious complications. Liposomal amphotericin B at a total dose of 15-25 mg/kg is the reference treatment in the Mediterranean region with 90-98% efficacy. A relapse in successfully treated patients occurs in 5% of patients.

In conclusion, VL should be considered in patients with persisting fever, weight loss, splenomegaly and
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pancytopenia, when more common diagnoses have been excluded and when there is a travel history to an endemic area. This also holds true for patients who are immunocompetent and for patients with a travel history restricted to the Mediterranean region, where *L. infantum* is endemic. As the incidence of leishmaniasis is expected to increase in Europe over the next decades and VL is usually lethal when untreated, increased awareness and early recognition by carefully taking the travel history are of utmost importance.

REFERENCES


