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CASE REPORT

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

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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

What was known on this topic?
Visceral leishmaniasis is a common disease in Southern and Western Asia, Ethiopia, Sudan and Brazil. It is mostly seen in children and in immunocompromised patients.

What does this case add?
Visceral leishmaniasis can be underlying or concurrent with a bacterial infection and should also be considered in patients who are immunocompetent and have a travel history restricted to Mediterranean countries.

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.[2] 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.[3] 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

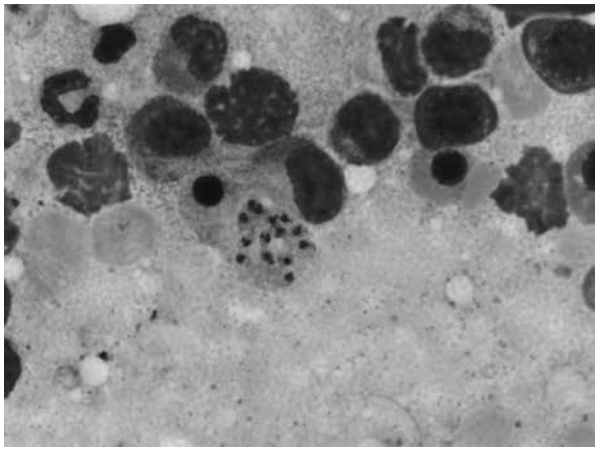
A 69-year-old autochthonous Dutch patient presented with complaints of malaise, rigors, night sweats and weight loss over the past three weeks. Medical history included diabetes mellitus and a myocardial infarction with cardiac

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 10^9/l, thrombocytes 133 x 10^9/l and leukocytes 1.7 x 10^9/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 proprionibacterium 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, parvovirus, 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.

Figure 1. *Bone marrow aspirate showing Leishmania species amastigotes*



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.[5] 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.[6] 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.[6] 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.[7]

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.[7] 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.[8]

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.[9]

Liposomal amphotericin B at a total dose of 15-25 mg/kg is the reference treatment in the Mediterranean region with 90-98% efficacy.[2] A relapse in successfully treated patients occurs in 5% of patients.[8]

In conclusion, VL should be considered in patients with persisting fever, weight loss, splenomegaly and

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.

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