Atypical presentation of visceral leishmaniasis (kala-azar) from non-endemic area

Yatendra Singh, Paramjeet Singh, Subhash Chandra Joshi, Mohammad Khalil

ABSTRACT

Leishmaniasis is a major public health problem in various parts of the world; it has also emerged in new geographic areas and host populations. Visceral infection can remain subclinical or become symptomatic, with an acute, subacute or chronic course. Kala-azar, or visceral leishmaniasis (VL), presents as fever, pancytopenia and hypergammaglobulinaemia. The presence of splenomegaly is characteristic of VL. It may be absent in immunocompromised patients, who may present atypically. Absence of splenomegaly is rare in immunocompetent patients, though it may occur in the early stages. Atypical presentations can be challenging to the clinician. This paper presents an atypical presentation of kala-azar, with multi-organ failure in the absence of splenomegaly or fever.

Key words: kala-azar without splenomegaly, multi-organ failure, pancytopenia, visceral leishmaniasis

INTRODUCTION

Leishmaniasis is a vector-borne zoonosis with variable clinical presentations, in the form of visceral, cutaneous (of localized or diffuse types) and mucocutaneous types, depending upon the Leishmania species and immune responses of the hosts. Visceral leishmaniasis (VL) is endemic in various parts of India, mainly Bihar, West Bengal and Orissa, as well as neighbouring countries such as Nepal and Bangladesh. Recent increases in the number of cases have been reported from non-endemic areas of India.1 Atypical presentation of VL in a nonendemic area can lead to a diagnostic dilemma. This paper reports VL in a patient from a nonendemic region of India, who presented with pancytopenia and multi-organ failure in the absence of splenomegaly or fever.

CASE HISTORY

The patient gave written informed consent for publication.

The patient was a 32-year-old woman, who did not smoke or consume alcohol and who worked as a labourer in her native region, Uttarakhand, India. She was admitted to hospital with a 4-week history of weakness, vomiting, abdominal pain, progressive dyspnoea, loss of appetite and weight loss. She was severely anaemic and two units of packed red blood cells had been transfused prior to admission. Intravenous ceftriaxone at 1 g twice a day had been administered by her general practitioner for the past 5 days, but brought no symptomatic relief. No significant past history was present. She had never visited any area endemic for VL.

On physical examination, the patient was tachypnoeic and tachycardic, with mild jaundice and severe pallor. Abdominal examination revealed early medical renal disease and mild hepatomegaly.

Laboratory investigations revealed that haemoglobin was 38 g/L and normocytic normochromic anaemia with pancytopenia was observed on peripheral smear examination; total serum bilirubin was 54.72 µmol/L and serum creatinine was 291.7 µmol/L. The transaminases were raised (serum glutamic oxaloacetic transaminase [SGOT] – 766 IU, serum glutamic pyruvic transaminase [SGPT] – 555 IU). Total serum proteins were 65 g/L and albumin was 15 g/L. Others tests, including arterial blood gas analysis, were in the normal range. Tests for enteric fever, dengue, malaria, HIV and viral hepatitis (A, B, C and E) were negative. The thyroid profile,
iron profile and vitamin B₁₂ values were normal. Antinuclear antibodies (ANA), cytoplasmic and perinuclear antineutrophil cytoplasmic antibodies (c-ANCA and p-ANCA) and direct Coombs' tests were negative.

The patient had a working diagnosis of pyrexia with pancytopenia, so Napier’s aldehyde test was done and found to be positive. To confirm the diagnosis of VL, a rK39 strip test and bone marrow examination were carried out. The rK39 immunochromatographic strip was positive for anti-K39 antibody. Intracellular and extracellular amastigotes (Leishman–Donovan bodies) were visualized directly in Giemsa-stained bone-marrow aspirate.

The patient was started on amphotericin B, at a dose of 0.5 mg/kg/day after 1 week and this was continued for 3 weeks. By the seventh day of treatment, she had improved symptomatically as well as biochemically. Three units of whole blood were also transfused to maintain her haemoglobin levels. At discharge, the spleen tip was just palpable and the liver was not palpable. The patient is under regular follow-up and is asymptomatic.

**DISCUSSION**

VL ranges over the intertropical zones of America and Africa, and extends into temperate regions of South America, Southern Europe and Asia. There are an estimated 12 million cases worldwide, with one and a half to two million cases occurring each year. Ninety per cent of the VL cases in the world are in Bangladesh, India, Nepal, Sudan and Brazil. VL is a chronic infectious disease caused by *Leishmania donovani* and characterized by irregular fever, hepatosplenomegaly, weight loss, pancytopenia and hypergammaglobulinaemia. There is infiltration of the reticuloendothelial system with amastigotes, which gives rise to the clinical and biochemical features. Splenomegaly is an important feature of the clinical presentation, owing to the hyperplasia of the reticuloendothelial cells that are filled with parasites. In one series, splenomegaly was reported to be present in 100% of patients, but it may be absent in immunocompromised patients, such as those who are HIV positive, renal transplant recipients, those with haematological malignancies and those on long-term steroids. Rarely, it may be absent in acute cases, or in the early stages of the disease.

Milder forms of liver involvement occur in 17% of individuals with VL, and are structurally and functionally reversible after treatment. Pathophysiologically, liver involvement in VL is typically self-limiting and involves a mononuclear cell-dominated granulomatous inflammation mediated by cytokines, chemokines and reactive oxygen and nitrogen species. Several authors have described renal pathological changes in VL. The main pathophysiological mechanism responsible for renal impairment in VL probably includes the deposition of immune complexes. The most frequent pathologies found are proliferative glomerulonephritis and interstitial nephritis. The development of acute kidney injury is an important clinical complication in individuals with VL, which appears to increase the mortality rate in this group of patients. The patient in this study had both hepatic and renal involvement.

VL misdiagnosed as connective tissue disorders is well reported in the literature. Haematological abnormalities found in systemic lupus erythematosus, namely anaemia, leukepna, lymphocytopenia and thrombocytopenia due to the presence of auto-antibodies, can also be found in kala-azar. *Leishmania donovani* infection induces nonspecific and specific antibody production, much of which is probably due to parasite-released substances, which act as B-cell mitogens. As a consequence of B-cell hyperactivity, *Leishmania donovani* infection may cause hypergammaglobulinaemia and production of auto-antibodies such as ANA. This may cause confusion in diagnosis. For this reason, a careful clinical approach is required to reach a definitive conclusion. For similar reasons, the patient in this study was also investigated for these biochemical markers and antibodies.

**CONCLUSION**

The case is presented to highlight the atypical presentation of VL in a nonendemic region where the index of suspicion is low. The patient presented with pancytopenia and multi-organ failure, in the absence of splenomegaly and fever, which is an unusual presentation of kala-azar.

Delayed diagnosis due to atypical manifestations can lead to fatal outcomes for patients. Instead of relying solely on the classical clinical features of VL, simple laboratory findings like pancytopenia, altered albumin/globulin ratio and positive aldehyde and rK39 strip tests can help make an early diagnosis, even in atypical cases, thereby reducing the mortality of VL.

**REFERENCES**


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