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Is Visceral Leishmaniasis the same in HIV-coinfected adults?

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ABSTRACT

Introduction: Visceral Leishmaniasis (VL) is the most severe form of disease caused by the *Leishmania donovani* complex, with significant morbidity and mortality in developing countries. Worse outcomes occur among HIV-positive individuals coinfected with Leishmania. It is unclear, however, if there are significant differences on presentation between VL patients with or without HIV coinfection.

Methods: We reviewed medical records from adult patients with VL treated at a reference healthcare center in Fortaleza – Ceará, Brazil, from July 2010 to December 2013. Data from HIV-coinfected patients have been abstracted and compared to non-HIV controls diagnosed with VL in the same period.

Results: Eighty one HIV-infected patients and 365 controls were enrolled. The diagnosis in HIV patients took significantly longer, with higher recurrence and death rates. Kala-azar's classical triad (fever, constitutional symptoms and splenomegaly) was less frequently observed in VL-HIV patients, as well as jaundice and edema, while diarrhea was more frequent. Laboratory features included lower levels of hemoglobin, lymphocyte counts and liver enzymes, as well as higher counts of blood platelets and eosinophils. HIV-infected patients were diagnosed mainly through amastigote detection on bone marrow aspirates and treated more often with amphotericin B formulations, whereas in controls, rK39 was the main diagnostic tool and pentavalent antimony was primarily used for treatment.

Conclusions: Clinical and laboratory presentation of VL in HIV-coinfected patients may differ from classic kala-azar, and these differences may be, in part, responsible for the delay in diagnosing and treating VL, which might lead to worse outcomes.

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Introduction

Leishmaniasis is the second most prevalent cause of protozoal diseases in the world and visceral presentation (VL or kala-azar) is the most severe form. World Health Organization (WHO) estimates 300 million new cases each year worldwide, with over 20,000 deaths.[1] In Brazil, between 2001 and 2013, 46,642 cases were reported, and seven states (Ceará, Minas Gerais, Maranhão, Bahia, Piauí, Tocantins, and Pará) contributed with nearly 75% of notifications. In the same period, at least 3058 deaths due to the disease occurred throughout the country. Among VL patients, the number of cases reported in HIV-infected individuals has increased substantially. Between 2007 and 2013, 1602 cases of leishmaniasis in HIV-infected individuals were reported in Brazil.[2]

Most cases of VL in HIV-coinfected patients are caused by reactivation of a latent infection which becomes clinically apparent as the immunosuppression progresses and the parasite overcomes the contingency capacity of the host's immune system.[3,4] Classic kala-azar, characterized by prolonged fever, constitutional symptoms, hepatosplenomegaly, cytopenias and hypergammaglobulinemia is not always manifested in immunocompromised individuals. In general, the clinical presentation is similar to the non-coinfected, although there is a tendency to involve organs and systems not usually parasitized, like lungs, skin, and gastrointestinal (GI) tract.[5–7] It is unknown if potential differences in clinical and laboratory presentations might hinder the inclusion of VL in the differential diagnosis, potentially leading to delayed diagnosis and therapy, which might lead to more severe course of the disease and poorer outcomes.

In Brazil, Ceará is the state with more cases of kala-azar reported in the period of 2007–2013, with or without HIV-coinfection.[2] Local data describing clinical features peculiar to coinfected individuals are scarce. Our goal was to identify such features in relation to monoinfected patients with VL, in order to alert clinicians about differences and similarities in clinical presentation that might expedite diagnosis and treatment initiation.

Material and methods

Study design

This was a cross-sectional study in adult patients with VL and HIV-coinfection, aiming to describe their epidemiological, clinical and laboratory presentations at diagnosis, as well as the drug prescribed for therapy. All data gathered from coinfected subjects were compared to monoinfected VL controls.

Population and study place

Medical records of all patients with confirmed VL diagnosis treated at São José Infectious Diseases Hospital (Hospital São José de Doenças Infecciosas), in the period of July 2010 to December 2013 were reviewed. São José Hospital is the reference healthcare center for treatment of infectious diseases in the state of Ceará. Individuals under 18 years, patients not tested for HIV, and those who had prior diagnosis of leishmaniasis or had been previously treated with amphotericin B for any disease were excluded.

Data collection

Epidemiological data (age, gender, education level, and origin), clinical information (comorbidities, duration of symptoms, clinical symptoms at diagnosis), laboratory tests (complete blood count, biochemical blood tests, and diagnostic tests) and treatment of HIV-coinfected patients (VL-HIV group) were compared with HIV-negative controls (VL group) diagnosed at the center during the same period.

The symptoms were considered present if reported by the patient at diagnosis or verified on physical examination by the doctor who assisted the patient. In addition, signs or symptoms within the first 24 h of hospitalization were considered, unless observed after the first dose of therapy. Regarding laboratory tests, only those collected immediately before the first dose of therapy were considered; for blood count, urea and creatinine (more sensitive to changes in medical interventions non-directly related with the treatment, such as intravenous hydration), we opted for the corresponding examination on arrival at the hospital or immediately previous to that moment.

Patients were treated at the discretion of their assisting physicians and most patients received treatment according to national guidelines at the time.

Diagnostic criteria

Diagnosis of HIV infection was performed in accordance to the Brazilian Health Ministry guidelines, and included Enzyme-Linked Immunosorbet Assays (ELISA), plus a confirmatory method (usually Indirect Immunofluorescence or Immunoblot). Immunochromatographic rapid tests were only considered as diagnostic if confirmed by one of the confirmatory method previously cited.

Visceral Leishmaniasis confirmation criteria included: (1) visualization of amastigotes in bone marrow aspirate or other clinical materials (except when detected exclusively on skin or nasal/oral mucous membranes); (2) serology (detection of anti-rK39 antibodies by immunochromatography or indirect immunofluorescence reaction in a title equal or greater than 1:80), associated with clinical and laboratory findings compatible with the disease.

Statistics

Data were compiled in Microsoft Excel version 2007 and the statistical analyses were performed using Stata SE, version 11.2. Numerical variables were described as median and range and were compared using Mann–Whitney test. Categorical variables were described as frequencies and analyzed by Pearson's chi-square test or 2-tailed Fisher exact test. For statistical significance, p-value of less than 0.05 was admitted.

Ethics

The research project was approved by the Research Ethics Committee of São José Hospital (CAAE 26007713.3.0000.5044)

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