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Case Report

A Case Report of Leishmaniasis and HIV Co-Infection in Pernambuco, Brazil

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Abstract

Leishmaniasis is a recurrent pathology in underdeveloped countries, being neglected among political bodies. Visceral leishmaniasis, known as Calazar, is due to the infection of the protozoan of the genus *Leishmania* and subspecies *donovani*. It has systemic involvement and chronic evolution in its host. Among the main manifestations are the most cited: prolonged fever, weight loss, hepatomegaly, splenomegaly, hypergammaglobulinemia and pancytopenia. At the same time, the incidence of HIV/aids is increasing progressively in the world, especially in poor countries such as Brazil, India and Sudan. In this way, it is not uncommon to find patients with both pathologies. As a consequence of immunosuppression, different clinical manifestations are observed, such as gastrointestinal and respiratory tract symptoms, which can often be confused as a consequence of HIV infection.

In view of the high prevalence of these diseases, in addition to being frequently associated, it is important to have knowledge of the clinical condition, in order to make the diagnosis early and propose appropriate therapy for the patient.

ABBREVIATIONS

VL: Visceral Leishmaniasis; HIV: Human Immunodeficiency Virus; AIDS: Acquired Immunodeficiency Syndrome; WHO: Worldwide Organization of Health; IIFT: Indirect Immunofluorescence Test

INTRODUCTION

The Leishmaniasis is one of the most neglected diseases of the world. The Visceral Leishmaniasis (VL) known as Calazar is a zoonosis of systemic development and chronic evolution that compromises the man and several mammals [1]. Its etiological agent is the protozoan of the *Trypanosomatidae* family, type *Leishmania* and species *donovani*. Several subspecies were identified causing this pathology, being those of bigger incidence L. (L.) *donovani,* L. (L.) *infantum* and L. (L.) *chagasi* [2]. The parasite can be transmitted through the prick of the insect phlebotomine, taking the dog as a main reservoir in the urban environment. There are other forms of contamination, through contaminated blood transfusion and vertical transmission [3,4]. The pathophysiology is determined, initially, by the invasion of dendritic and macrophage cells. The parasite manages to survive and to multiply by blocking the macrophage phagolisossomes. The interaction between virulence of the parasite and the immune cellular response, as well a mediated by antibodies immune response is complex and responsible for the different clinical forms of the disease [5,6].

The leishmaniasis has a worldwide distribution, compromising several regions of the globe, like Europe, the Americas, Asia and Africa [7]. It is considered an endemic disease in tropical and subtropical regions of 88 countries [8]. The predominance of *L. donovani*, the main form of transmission among humans, is limited to the countries of Asia, mainly India, and east of Africa. Meanwhile, *L. infantun*, sometimes called of *L. chagasi*, are prevalent in the Mediterranean, its region of origin, and Latin America [9].

The Worldwide Organization of Health (WHO) estimates that 350 million people are under the risk of contracting leishmaniasis and that approximately 2 million new cases occur annually. In accordance with the last report of the Worldwide Organization of Health, in 2014, there were 30.758 notified cases of VL in a group

of 14 countries. Six countries are responsible for 90% of the cases in the whole world: India, Bangladesh, Sudan, Sudan of the South and Brazil [10]. In 2015, 3.289 cases were confirmed, being 1, 6 cases for 100.000 inhabitants in Brazil. In the same period, the moderate number of deaths was 272, whose rate of lethality was 7, 8. In Pernambuco, in the year of 2015, 123 cases were confirmed, which means an incidence of 1, 3 cases for 100.000 inhabitants. Regarding the number of deaths, there were 11, making the lethality rate 8, 9 bigger than the national rate [11].

If not diagnosed and treated early, VL can be lethal. Among the main clinical demonstrations presented by the patient diagnosed with the visceral form are prolonged fever, loss of weight, hepatomegaly, splenomegaly, hypergammaglobulinemia and pancytopenia [12].

In the last decades, an increase of the lethality of the disease was noted in several regions of the country. Factors such as age higher than 60 years, weakness, co-infection of *Leishmania*/HIV, bleeding, jaundice and other symptoms were associated with the increase of mortality [12]. VL can be diagnosed by the clinical presentation and the straight visualization of the parasite through the microscopy of lymphatic ganglia, bone marrow and spleen by needle aspiration. Other diagnostic tests also can be used such as the indirect immunofluorescence test (IIFT), the immunocromatographic test (Kalazar Detect) and molecular biology techniques [6]. In Brazil the drugs used for the treatment of the VL are: N-metil glucamine antimoniate, Amphotericin B deoxycholate and Liposomal amphotericin B. The choice of the drug depends, among other reasons, on the severity and evolution of the disease, age group, pregnancy, associated comorbidities and the toxicity profile of the drug [13].

It is not rare to find the association of the VL and infection with HIV virus, an infection rising in the endemic countries of the leishmaniasis. 35 countries have been reported with this co-infection, being Ethiopia the country with the leading numbers, reporting 569 cases between 2003 and 2008. Brazil is the country of America with the most number of cases (91) in the same period. That is justified due to high predominance of VL and the growing numbers of cases of HIV [14,15]. 151 deaths were reported in patient diagnosed with these two infections between 2010 and 2015 in Brazil [16]. The clinical manifestations can be similar, in most of the cases reported with VL, like fever, pancytopenia and hepatosplenomegaly. Besides, the incubation period can be shorter and the varied forms of the disease have already been reported [17]. Gastrointestinal and respiratory symptoms may confuse the diagnosis very often as consequences of HIV infection. Besides, the co infection of VL/HIV has been associated with the biggest rate of mortality and risk of recurrence of the disease [17].

We describe a case of coinfection of Leishmaniasis and HIV with an atypical presentation and immune reconstitution inflammatory syndrome.

CASE PRESENTATION

Patient F.J.S., masculine sex, 34 years, horse tamer, born in the metropolitan region of Recife. Was admitted in the service of infectious diseases of the University Hospital Oswaldo Cruz to investigate local adenomegaly, associated with pain, heat, blush and local edema, and by daily, predominantly nocturnal, fever with sweating and a weight loss of 10 kg.

During the investigation, laboratory tests confirmed an unknown until then infection with the HIV virus, serologies showed previous immunity for toxoplasmosis and cytomegalovirus, and blood count presented anemia and lymphopenia. The immunocromatographic test was negative for the RK39 antigen. The CD4 T lymphocyte count was 62 cells/mm3 and the viral HIV load was 1.157.231 copies/ml.

Due to suspicion of ganglionar tuberculosis, the chosen treatment was rifampicin, isoniazid, ethambutol and pyrazinamide and was recommended to proceed the investigation with ganglionar biopsy.

Evolution

After a week, the patient evolved with hepatic toxicity (GOT of 113 and GPT of 142). The biopsy of the cervical lymph node resulted in acute and chronic lymphadenitis associated with the presence of Leishmaniasis parasites, no signs of malignancy, and a negative bacilloscopy for mycobacterium.

Guided by to the laboratory tests, the patient started on Liposomal amphotericin B in the dosage of 3 mg/kg, for 7 days. The complications were alteration of the renal function and nosocomial pneumonia. The patient was started on antiretroviral therapy with lamivudine, tenofovir and efavirenz two months after the beginning of symptoms, and maintained a weekly secondary prophylaxis with Amphotericin B.

After three months the patient presented with an increase of cervical lymph nodes, in several chains, without other signs and associated symptoms. Laboratory tests showed significant improvement in the T CD4 cell count and HIV viral load. The antiretroviral therapy was maintained, as well as the secondary prophylaxis and the patient evolved well without any more complications.

DISCUSSION

The classic triad of the visceral leishmaniasis is also the commonest clinical manifestation in the co-infection *Leishmania*/HIV, hepatosplenomegaly, anemia and pancytopenia can be observed in 75% of the reported cases, but the splenomegaly is less frequent in patient's co-infected [18]. Adenopathy is present in 12 to 57% of the cases, in general associated to other more common symptoms of the disease. We report a case of co-infection of *Leishmania*/HIV which presented with the atypical form showing cervical adenomegaly and bicytopenia that evolved with an immune reconstitution inflammatory syndrome after three months of antiretroviral therapy. In Brazil, the tegumentary leishmaniasis is present in all regions, however the visceral form is seen with more frequency in the south-east and northeast regions of the country, being the last one the place of origin of the patient [19,20].

Patients with the binomial leishmaniasis-HIV can present atypical signs and symptoms that result from a low T CD4 lymphocytes count, presenting a variety of clinical manifestations and when the parasites are located in places such as: the pleura, lymph nodes and the gastrointestinal tract. Such manifestations,

very often, are confused with the symptoms of other opportunistic infections, which constitutes a diagnostic challenge [21]. In the case reported, initially, the patient presented with palpable lymphadenopathy in the left anterior and posterior cervical chains, movable, painless and fibroelastic, the biggest measuring 2 cm, presenting with edema, blush, local heat and ipsilateral increase in the volume of the sternocleidomastoid muscle, accompanied by nocturnal fever, sweating and weight loss. This clinical presentation mimics a case of ganglionary tuberculosis. The ganglionary involvement can take place in any lymph node chain, although anterior cervical chain involvement has been reported as more common [22]. The ganglionary tumefaction generally is painless, unilateral and involves several ganglia of the same chain. The clinical manifestation is characterized by the presence of nocturnal fever, weight loss and nocturnal sweating [23,24].

Cytopenias are common demonstrations found in cases of visceral leishmaniasis. In the case reported the anemia and leukopenia are, probably, multifactorial. The direct effect of the virus, the infiltration of the bone marrow, nutritional deficiencies, peripheral destruction and toxic pharmacological effects might be related with origin of these findings. The constitutional symptoms (asthenia, anorexia and weight loss) are observed in most of the infected patients [25].

In spite of its severity, VL has treatment. It is free, available in the Health System service and is based on the use of three drugs, depending on the medical indication: N-metil glucamine antimoniate Liposomal amphotericin B and Amphotericin B deoxycholatel [26]. In the reported case, the treatment was with Liposomal amphotericin B, the more powerful leishmanicidal drug commercially available [27-29]. However, co-infected patients present lower rates of treatment success and higher rates of recurrences than the cases reported as HIV negative, but the patient of the reported case responded well to the treatment and remained using secondary prophylaxis. Therefore it is primordial to guarantee the viral and immune control, through the negativation of the viral charge and the increase of the T CD4+ cell count. The patient responded well to the antiretroviral treatment, with the initial T CD4+ lymphocyte cell count of 62 cells/mm3 and a viral charge of the HIV of 1.157.231 copies/ml in the moment of diagnosis, evolving for CD4+ of 221 cells/mm3 and viral charge of less than 40 copies/ml in his last dosage.

The sum of unspecific symptomatology, poorly sensitive laboratory tests and the gap between the scientifical knowledge about these, potentially fatal, comorbidities, demand creation of more appropriate diagnostic and therapeutic protocols to the management of this co-infection [30,31]. Visceral Leishmaniasis must be a part of the differential diagnosis of opportunistic infections, although the clinical manifestations show up in the not so common forms and that the immunological tests present negative, especially in countries with high predominance of *leishmania*, such as the case of Brazil. The physician must be aware of the possibility of immune reconstitution inflammatory syndrome after the beginning of the antiretroviral therapy, a differential diagnosis with recurrence of the disease. On the other side, all individuals carriers of visceral leishmaniasis must be tested for HIV in order to identify patients with bigger chances to evolve into more severe situations, with high potential of recurrence and risk of death. The presented case reports a co-infection of *Leishmania*/HIV with an atypical presentation and immune reconstitution inflammatory syndrome that had a positive evolution with the resolution of the disease and a good viral and immune control after the introduction of the antiretroviral therapy.

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