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CASE REPORT

Epidemiology of human immunodeficiency virus-visceral leishmaniasis-co-infection

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In Brazil, the rates of mother-to-child-transmission (MTCT) of human immunodeficiency virus (HIV) decreased from 20% to 1—2% in some regions. However, the country contains 90% of individuals infected with visceral leishmaniasis (VL) in Latin America, and the west region of São Paulo state faces an alarming expansion of the disease. We describe the epidemiological aspects of the expanding infection of VL and a case report of an HIV-VL-co-infected child from the west region of São Paulo state. The patient was an AIDS-C3 with low levels of CD4, high viral load, severe diarrhea, oral and perineal candidiasis, severe thrombocytopenia, and protein-caloric malnourishment. She evolved with sepsis, renal and cardiac failure. An rK rapid diagnosis test, indirect fluorescent antibody test (IFAT), and bone marrow aspirate were performed for VL. Her symptoms improved significantly after liposomal amphotericin B administration. From the 45 municipalities that compose the Regional Health Department of Presidente Prudente, *Lutzomyia longipalpis* vectors were found in 58% of them. VL infected dogs were found in 33% of those municipalities, infected dogs and humans were found in 29%, 20% are starting and 33% of the municipalities are preparing VL investigation. It is likely, in this patient, that VL advanced the clinical progression of the HIV disease and the development of AIDS severity. Supported by favorable conditions, the region becomes a new frontier of VL in Brazil.

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Introduction

Brazil was one of the first developing countries to adopt measures against mother-to-child-transmission (MTCT) of human immunodeficiency virus (HIV) and in some regions rates decreased from 20% to 1—2%.[1] Despite all the efforts made by public and private organizations, MTCT still arises, mainly from drug users and women living in poor settings.[2] HIV-infected children with irregular use of antiretroviral therapy (ART) are predisposed to opportunistic and pathogenic agents, such as tuberculosis and leishmaniasis. Visceral leishmaniasis (VL) is a chronic and frequently lethal disease distributed worldwide. Brazil contains about 90% of individuals infected with VL in Latin America.[3] In 2003, the sandfly was found in Dracena, the west region of São Paulo state and in 2004, the Adolfo Lutz Institute diagnosed infected dogs with *Leishmania (Leishmania) infantum chagasi* by polymerase chain reaction (PCR). In 2005, the first human case with VL was found in Dracena.[4,5]

The HIV-infection increases the risk of developing VL by 100—2320 times in endemic areas.[3] VL associated HIV-AIDS is becoming an important public health problem, however, few reports of HIV-VL co-infection are described in São Paulo state. Our aim was to analyze the epidemiological aspects of the expanding infection of VL and to describe a case report of an HIV-VL-co-infected child from the west region of São Paulo state.

Case report

Written consent was obtained from the family for publication of this case report. On November 1, 2011, an 11 year-old girl, native of Pilar county, Alagoas state, northeast of Brazil and residing in Paulicéia county, the west region of São Paulo state [Fig. 1A and C, on the border with Mato Grosso do Sul (MS), circled in blue] was referred to the Regional Hospital (RH) of Presidente Prudente, São Paulo state. The city harbors the Regional Health Department (DRS XI). In the preceding 2 months, she lived with her grandparents. The girl's mother, an HIV-seropositive, chronic alcoholic, and street-living woman, remained in Alagoas state. Contrary to the hospitalization, the girl's grandparents were convinced of her condition, due to the seriousness of her health status. However, the high level of fear, stigma, discrimination, and negative aspect of the disease expressed by them was clear. The child was an MTCT-HIV-AIDS-C3-exposed patient with irregular use of ART, presenting with diarrhea for several days characterized by being liquid, with no blood or pus. On physical examination, she was uncommunicative, hypoactive, severely malnourished, pale, eupneic, afebrile, showing moderate dehydration with pasty turgor and petechiae distributed in the trunk and face. With a painless excavated abdomen, a mild hepatomegaly was present and extending to 5 cm below the costal margin. Lymphadenopathy and splenomegaly were not detected. She presented perineal and oral candidiasis, difficulties in eating and walking and precarious teething, weighing 15 kg. Laboratory investigations showed leukocytes 4,69 $\times$ 10^3/mL, 84% neutrophils, 6% lymphocytes, and 10% monocytes. The hemoglobin level was 9.7 g/L. Severe thrombocytopenia (18,000/mL) and hypoalbuminemia (1.98 g/mL) were found. A urine sample showed 5 $\times$ 10^3 of leukocytes/mL and 5.0 $\times$ 10^3 of erythrocytes/mL. Serum creatinine was at 0.21 mg/dL. Hepatic enzymes alanine/aspartate transaminases resulted in 30 U/L and 15 U/L, respectively. Serum sodium, potassium, and phosphorus electrolytes resulted in 113 mEq/L, 4.8 mEq/L, and 3.68 mEq/L, respectively. HIV-viral load resulted in 45,089 copies/mL. CD4 and CD8 levels resulted in 12 (2.2%) cells/mm^3 and 371 (68.71%) cells/mm^3, respectively. An abdominal ultrasound revealed hepatomegaly with spleen in the normal range; an echocardiogram resulted in normal values. After clinical and laboratory assessments, her initial diagnosis was AIDS/C3 with irregular lamivudine + tenofovir + lopina/ritonavir treatment (ART), plus severe protein-caloric malnourishment, electrolyte disturbance (hyponatremia), oral and perineal candidiasis, chronic diarrhea, precarious teething, and depression. The patient was treated by a multidisciplinary staff and evolved with persistent diarrhea, decreased consciousness level, fluctuating in periods of drowsiness and stupor. A mild hepatic enlargement was detected, secondary to congestive cardiac insufficiency. On the 17th day of hospitalization, she was sent to the pediatric intensive care unit (ICU), with a sepsis of unknown origin, remaining 4 days and receiving antibiotic therapy (vancomycin 40 mg/kg/day and meropenem 120 mg/kg/day) during 21 days; methylprednisolone (1 mg/kg/day) during 5 days and human intravenous IgG immunoglobulins (400 mg/kg/day) during 5 days. On the 23rd day of hospitalization, she had not improved and developed severe fever, a marked decrease of diuresis, moderate tachydyspnea and tachycardia with presence of bilateral stertor in the base of the lung, cardiac and renal failure. The patient was admitted again into the pediatric ICU, with a diagnosis of septic shock of the blood of fungal origin.

The origin and destination of the patient from the endemic area of Alagoas state to another emerging area of VL, the west region of São Paulo, was considered. Furthermore, due to her clinical symptoms (hepatomegaly, petechiae, renal failure, and sepsis of fungal origin) and laboratorial results of thrombocytopenia, liposomal amphotericin B deoxycholate (ampho B, 5 mg/kg/day) was introduced. Simultaneously, an rK rapid diagnosis test (Kalazar detect™, InBios, Seattle, Washington, USA), indirect fluorescent antibody test (IFAT; Bio-Manguinhos/FIOCRUZ, Rio de Janeiro, Brazil) and bone marrow aspirate by direct parasitological (DP) were performed for VL. Even though the rapid diagnosis test and IFAT results were negative, liposomal ampho B (2 mg/kg/day) was maintained. No pathogens were isolated from different culture samples. Later, DP bone marrow aspirate showed macrophages filled with intracytoplasmatic *Leishmania* spp. amastigotes parasites (Leishman-Donovan bodies) on Giemsa staining.

The patient's clinical symptoms gradually improved, with moderate weight gain, and she was interacting with other children of the pediatric ward, with an easy smile, active, collaborative, and communicative. After the 47th day of hospitalization, she relapsed with thrombocytopenia and a retreatment with ampho B and intravenous human IgG immunoglobulin was applied, but was not sufficient for platelets normalization. On admission, she weighed 15 kg; after 71 days of hospitalization, she weighed 23.8 kg, with a gain of 8.8 kg in the period. On