

CASE REPORT

FIRST REPORT OF CUTANEOUS LEISHMANIASIS CAUSED BY *Leishmania (Leishmania) infantum chagasi* IN AN URBAN AREA OF RIO DE JANEIRO, BRAZIL

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SUMMARY

American tegumentary leishmaniasis (ATL) is an infectious disease caused by protozoa of the genus *Leishmania*, and transmitted by sandflies. In the state of Rio de Janeiro, almost all of the cases of American tegumentary leishmaniasis (ATL) are caused by *Leishmania (Viannia) braziliensis*, while cases of visceral leishmaniasis (VL) are caused by *Leishmania (Leishmania) infantum chagasi*. The resurgence of autochthonous VL cases in Rio de Janeiro is related to the geographic expansion of the vector *Lutzomyia longipalpis* and its ability to adapt to urban areas. We report the first case of leishmaniasis with exclusively cutaneous manifestations caused by *L. (L.) infantum chagasi* in an urban area of Rio de Janeiro. An eighty-one-year-old woman presented three pleomorphic skin lesions that were not associated with systemic symptoms or visceromegalies. Multilocus enzyme electrophoresis identified *L. (L.) infantum chagasi*, but direct smear and PCR of bone marrow were negative for *Leishmania sp.* (suggesting exclusively cutaneous involvement). We discuss the different dermatological presentations of viscerotropic leishmaniasis of the New and Old World, and the clinical and epidemiological importance of the case. Etiologic diagnosis of ATL based upon exclusive clinical criteria may lead to incorrect conclusions. We should be aware of the constant changes in epidemiological patterns related to leishmaniasis.

KEYWORDS: Cutaneous leishmaniasis; *Leishmania (Leishmania) infantum chagasi*.

INTRODUCTION

Leishmaniasis are antrozooses caused by protozoa of the genus *Leishmania* and comprise a complex of diseases with varied clinical spectrum and epidemiological diversity, whose transmission occurs during blood feeding of infected female sandflies²¹. In the state of Rio de Janeiro, almost all of the cases of American tegumentary leishmaniasis (ATL) are caused by *Leishmania (Viannia) braziliensis*³, while visceral leishmaniasis (VL) is caused by *Leishmania (L.) infantum chagasi*. The resurgence of autochthonous VL cases in the state of Rio de Janeiro since 2010 is related to the geographic expansion of the vector *Lutzomyia longipalpis* and to its ability to adapt to urban areas^{7,12}. In the city of Rio de Janeiro, dogs are the main reservoir of *L. (L.) infantum chagasi*. Canine enzooties have preceded the occurrence of human cases, and infection in dogs has been more prevalent than in humans^{8,13}. The patient we describe lived in Caju neighborhood, located near downtown, in an area without forest remnants. The emergence of VL in the urban area of Rio de Janeiro is highly relevant, since it represents an important public health problem. While in Central America cutaneous manifestations of *L. (L.) infantum chagasi* are quite common, in Brazil they are extremely rare. We report the first case of

leishmaniasis with exclusively cutaneous manifestations caused by *L. (L.) infantum chagasi* in an urban area of Rio de Janeiro, discussing its clinical importance and possible epidemiological consequences.

CASE REPORT

An eighty-one-year-old woman, from Rio de Janeiro, residing for the previous two years in a nursing home in Caju neighborhood, reported the appearance of skin lesions about seven months earlier. She had cardiac disease and chronic renal failure (CRF) and was referred to the Laboratory of Leishmaniasis Surveillance of the Evandro Chagas National Institute of Infectious Diseases, of the Oswaldo Cruz Foundation. Dermatological examination revealed the presence of three pleomorphic lesions that measured between 3 and 4 cm in diameter and were located in the frontal and left malar regions of the face, and in the right elbow (Fig. 1 and 2). The lesions were not associated with systemic symptoms such as fever, weight loss or poor general condition. The patient had no lymphadenopathy or visceromegalies. Laboratory tests were within normal range, except for increased urea (135 mg/dL) and creatinine (2.65 mg/dL) due to pre-existing CRF. Electrocardiogram showed cardiac arrhythmia and

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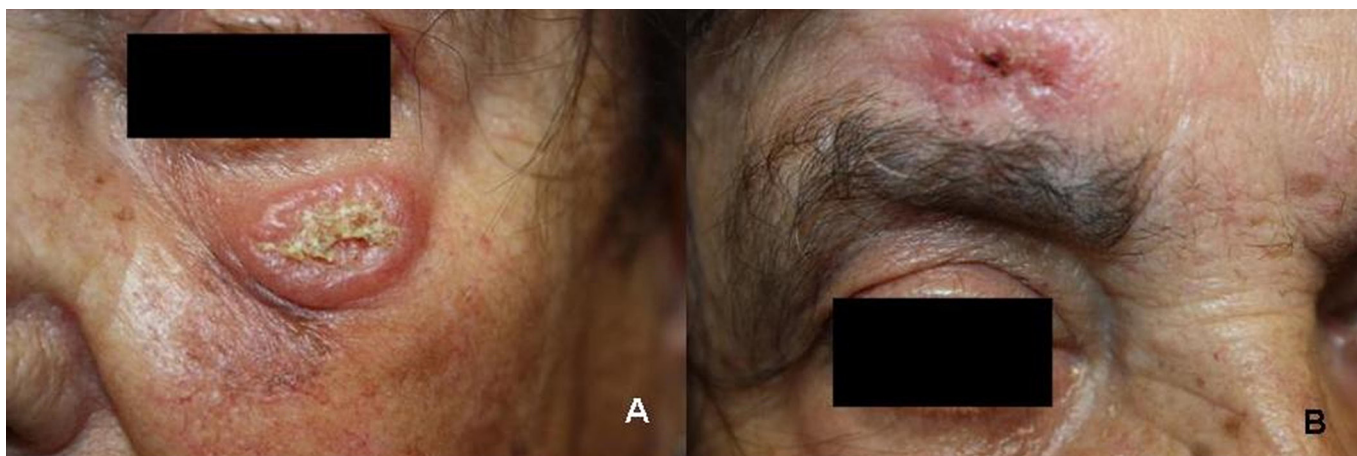


Fig. 1 - A) Ulcerative and vegetating lesion in the left infra-orbital region. B) Infiltrative exulcerated plaque in the frontal region.



Fig. 2 - Round ulcer with infiltrated borders in the right elbow.

enlargement of the corrected QT space (QTc) (0.50 seconds). Abdominal ultrasound did not reveal the presence of hepatomegaly or splenomegaly. Histopathology, direct smear, culture in McNeal, Novy, Nicolle (NNN) medium, and polymerase chain reaction (PCR) performed on cutaneous lesions fragments confirmed the clinical diagnosis of ATL. Montenegro skin test and enzyme-linked immunosorbent assay (ELISA) serology for leishmaniasis resulted positive. Since no previous cases of ATL were known in this neighborhood, and a recent case of VL had been described in this location¹⁸, we performed the multilocus enzyme electrophoresis assay as previously described⁵, and the identification of *L. (L.) infantum chagasi* was confirmed (Fig. 3). Culture and PCR of a bone marrow sample were negative for parasite isolation or *Leishmania* DNA detection. Since the patient presented a history of heart disease and chronic renal failure, we discarded the use of meglumine antimoniate. The patient received liposomal amphotericin B 4 mg/kg/day with a cumulative dose of 1.25 g. During hospitalization, the patient did not present any systemic manifestations compatible to VL. Two months post-treatment, the facial lesions had healed and the lesion of the arm was partially epithelialized.

DISCUSSION

Only two cases of ATL caused by species other than *L. (V.)*

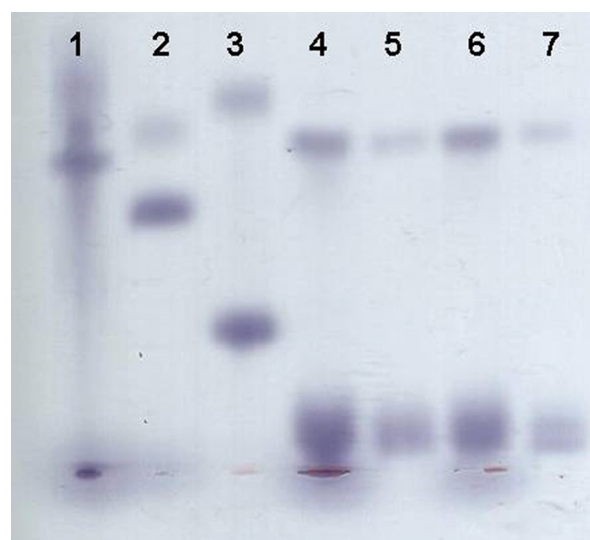


Fig. 3 - Multilocus enzyme electrophoresis representative gel showing the patterns observed for the nucleoside hydrolase (NH) system. Lane 1: *Leishmania (Leishmania) amazonensis* reference strain (IFLA/BR/1967/PH8); Lane 2: *Leishmania (Viannia) guyanensis* reference strain (MHOM/BR/1975/M4147); Lane 3: *Leishmania (Viannia) braziliensis* reference strain (MHOM/BR/1975/M2903); Lanes 4 and 6: *Leishmania (Leishmania) infantum chagasi* reference strain (MHOM/BR/1974/PP75); Lanes 5 and 7: sample isolated from patient's cutaneous lesion that showed similar profiles with *Leishmania (Leishmania) infantum chagasi* reference strain.

braziliensis were previously described in the state of Rio de Janeiro: one in the city of Paraty, in 2007, caused by *Leishmania (L.) amazonensis*¹; and another caused by *L. donovani chagasi* (now known as *Leishmania (L.) infantum chagasi*) in a rural area of the city of Rio de Janeiro in 1986¹⁵. In addition, a case of co-infection in which the patient showed VL caused by *L. donovani* and ATL caused by *L. braziliensis braziliensis* (now known as *L. (V.) braziliensis*) was described¹⁶.

In the case reported here, the identification of the parasite isolated through culture of a cutaneous fragment was performed by multilocus enzyme electrophoresis, considered the gold standard method for the characterization of *Leishmania* species. Moreover, the failure to detect

parasite or *Leishmania* DNA in a bone marrow sample suggests exclusive cutaneous involvement.

In a series of 18 patients with VL in northeastern Brazil, 40% were positive for *L. (L) infantum chagasi* in the culture of fragments of skin lesions or unimpaired skin²⁰. Cases related to *L. (L.) donovani* with dermatological compromise in Africa and in the Indian subcontinent are generally associated with post kala-azar dermal leishmaniasis. In these cases, cutaneous lesions (macules, papules, nodules, or plaques), without a tendency to ulcerate, arise on the skin after the end of the treatment for VL¹⁹. In Brazil, this presentation is rare and is usually related to HIV-coinfection⁴. In Europe, rare cases of cutaneous¹⁰ or mucocutaneous¹¹ leishmaniasis caused by *L. (L.) infantum* have been reported, and these cases seem to be related to specific zymodemes⁹. Alternatively, the exclusively cutaneous involvement by *L. donovani chagasi* is described in Central America. However, no genetic differences between *Leishmania (L.) chagasi* strains causing VL and CL were observed in Honduras¹⁴ and Nicaragua². Cutaneous leishmaniasis caused by *Leishmania (L.) chagasi* in patients from Central America tends to have an atypical presentation: the lesions are papulonodular, surrounded by areas of hypochromia; they predominate in the cephalic segment and do not ulcerate^{2,14}. In these countries, children under five years of age present visceral forms mostly, while the cutaneous forms prevail in older children and young adults.

In Venezuela, patients affected by *L. colombiense* present VL as much as CL¹⁷. The clinical presentation results from a complex interaction among the *Leishmania* species with host immunity.

In Brazil, cases of CL caused by *L. (L) infantum chagasi* are so rare that it is not possible to certify the age range that can influence the clinical expression of the disease. In this report, the benign manifestation of the disease suggests a partially effective immunity that is not related to previous infection with *L. (L) infantum chagasi* in childhood, since our patient was not coming from an LV endemic area and only resided in Caju neighborhood for two years.

The case reported that exclusive cutaneous form caused by *L. (L) infantum chagasi* may not represent an isolated case. Recently, two cases of ATL with cutaneous manifestations arising from a community located in the same region were taken into account by the Brazilian system for notifiable diseases, SINANNET⁶. Although the characterization of the involved *Leishmania* species was not possible in those cases, dermatropic strains of *L. (L) infantum chagasi* could be involved. In this area, no previous ATL cases have been reported, and neither the presence of *Lutzomyia intermedia*, the main vector of *Leishmania (V.) braziliensis* in the state of Rio de Janeiro, was observed. On the other hand, the presence of *Lutzomyia longipalpis*, the principal vector of *L. (L) chagasi infantum* in Brazil, has been demonstrated. Etiologic diagnosis of ATL based upon exclusive clinical criteria may lead to incorrect conclusions. We should be aware of the constant changes in epidemiological patterns related to the leishmaniasis. We therefore suggest that multilocus enzyme electrophoresis of isolated parasites and/or PCR of tissue fragments should be performed in order to identify the involved species in futures suspected cases of ATL in the Caju neighborhood.

RESUMO

Primeiro relato da leishmaniose cutânea causada por *Leishmania (Leishmania) infantum chagasi* em uma área urbana do Rio de Janeiro, Brasil

A leishmaniose tegumentar americana (LTA) é uma doença infecciosa causada por protozoários do gênero *Leishmania*, transmitida por flebotomíneos. No estado do Rio de Janeiro, quase todos os casos de LTA são causados por *Leishmania (Viannia) braziliensis*, enquanto a leishmaniose visceral (LV) é causada por *Leishmania (Leishmania) infantum chagasi*. O ressurgimento de casos autóctones de LV no Rio de Janeiro está relacionado com a expansão geográfica dos vetores *Lutzomyia longipalpis* e à sua capacidade de se adaptar às áreas urbanas. Relatamos o primeiro caso de leishmaniose com manifestações exclusivamente cutâneas causadas por *L. (L.) infantum chagasi* em uma área urbana do Rio de Janeiro. Mulher de 81 anos apresentou três lesões cutâneas pleomórficas não associadas a sintomas sistêmicos ou visceromegalias. A eletroforese de enzimas multilocus obtida a partir da lesão cutânea identificou *L. (L.) infantum chagasi*, por outro lado o exame direto e o PCR da medula óssea foram negativos para *Leishmania* sp. (sugerindo acometimento exclusivamente cutâneo). Discutimos as diferentes apresentações dermatológicas da leishmaniose visceral do Novo e Velho Mundo, assim como a importância clínica e epidemiológica deste caso. O diagnóstico etiológico da LTA com base apenas em critérios clínicos pode levar a conclusões incorretas. Devemos estar conscientes das constantes mudanças nos padrões epidemiológicos relacionados à leishmaniose.

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