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CASE REPORT

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Disseminated cutaneous leishmaniasis caused by *Leishmania braziliensis* in Southern Brazil

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ABSTRACT

The authors report a case of disseminated cutaneous leishmaniasis caused by *Leishmania (Viannia) braziliensis*, in a 55 years old patient with 1,119 lesions distributed throughout the body. The patient resides in *Sabáudia* municipality, North of *Paraná* State, Southern Brazil, where there was no previous report of this form of leishmaniasis. Treatment with meglumine antimoniate was successful, although the diagnosis was made only five months later.

KEYWORDS: *Leishmania (Viannia) braziliensis.* Disseminated cutaneous leishmaniasis. *Paraná State, Brazil.*

INTRODUCTION

Leishmaniases are infectious diseases caused by protozoa of the genus *Leishmania*, with a wide spectrum of clinical manifestations, depending on the species of *Leishmania* involved[1]. Originally, leishmaniases were considered wild zoonoses, but have been reported in rural and urban areas where domestic animals, especially dogs, have been often diagnosed with *Leishmania* infection[2].

Disseminated cutaneous leishmaniasis (DL) caused by *Leishmania (Viannia) braziliensis* and *Leishmania (Leishmania) amazonensis* is a rare form of clinical manifestation and accounts for approximately 2% of the reported cases of cutaneous leishmaniasis (CL) in Brazil[2]. Torres[3] reported the first case of DL caused by *L. (V.) braziliensis* in the State of Bahia, Brazil. In 1986, Costa *et al.*[4] published the first case of CL. Since then, just a few cases[5] of DL, with additional research on the parasites characteristics, their immunological behavior and response of patients to treatment[2,5] have been reported. DL is characterized by expressing multiple papular acneiform lesions, compromising exposed areas, such as limbs, and frequently face and trunk[2,4,5]. The number of lesions can reach hundreds, according to the Ministry of Health[2].

Another atypical form of CL, known as difuse cutaneous leishmaniasis (DCL) or anergic-DCL, caused by *L. (L.) amazonensis*[2], was first reported by Silva[6], in Brazil, and Convit[7], in Venezuela. DCL is characterized by the presence of multiple non-ulcerated nodular lesions, weak response of T-cells to antigens of *Leishmania* parasites (amastigotes) and a large number of *Leishmania* inside macrophages[8]. DCL is also rare, with 1 or 2 cases diagnosed per year and the number of lesions can, as well, reach the hundreds[2,8]. These two clinical forms, DL and DCL, were precisely compared and differentiated based on reported cases by Hashiguchi *et al.*[9].

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This report deals with a case of DL in an inhabitant of Vila dos Crentes, a rural town in the municipality of *Sabáudia*, North of *Paraná State*, Southern Brazil, showing an extraordinary number of cutaneous lesions.

CASE REPORT

At the beginning of March 2015, the patient, a 55 years old driver, observed a lesion on the anterior surface of his leg, with a granular bottom and raised edges. After approximately three months of development of the primary lesion, small lesions appeared on the face and thereafter throughout the body (scalp, all the face, neck, arms, hands, including the palms, legs and the dorsal part of the foot), except in the palms surface and genital organ, totaling 1,119 lesions, counted with the a manual counter (Hand Held). The disease was identified five months after the onset. During this period, the patient had lost about 15 kg. When the first lesion appeared, the patient initially received an unsuccessful treatment for allergy. Thereafter, he was treated with six ampoules of penicillin G benzathine 1,200,000 IU, and had unsuccessful results once again. It is noteworthy that the municipality of *Sabaúdia* is located in the important center of *Ivai-Pirapó* from the circuit *Paraná-Paranapanema* of CL incidence, in the North-Central mesoregion of *Paraná State*[10].

Evolution of the case and laboratory examination

The patient fail to respond to treatment within three months of the disease onset, then he sought medical resources in the municipality of Arapongas, *Paraná*, where he was subjected to the following tests: V.D.R.L., negative; FTA-Abs IgG and IgM, negative; Herpes simplex Virus anti-IgG, positive (23.8 U/mL); Herpes simplex Virus anti-IgM, negative; Rubella anti-IgG, positive (73.7 IU/mL); Rubella anti-IgM, negative; Aspartate Aminotransferase (AST), normal; Alanine Aminotransferase (ALT), normal; Lactic dehydrogenase (LDH), normal; Gamma Glutamyl Transferase, normal; Alpha 1-Acid Glycoprotein, increased 164 mg/dL; Hepatitis B, negative; Hepatitis C, negative; Brucella anti-IgG and IgM, negative; Chlamydia trachomatis anti-IgG, reagent (1/80); Chlamydia trachomatis anti-IgM, negative; Complete blood count, normal; Anti-HIV, negative. The biopsy, performed in a private laboratory, showed the absence of viral infection, a favorable morphologic pattern in the diagnosis of a staphylococci and screening for fungi negative. The indirect immunofluorescence test (IIF) for *Leishmania*, held in another laboratory was negative. This examination was performed with a kit containing *L. (L.) infantum*, for diagnosis of visceral

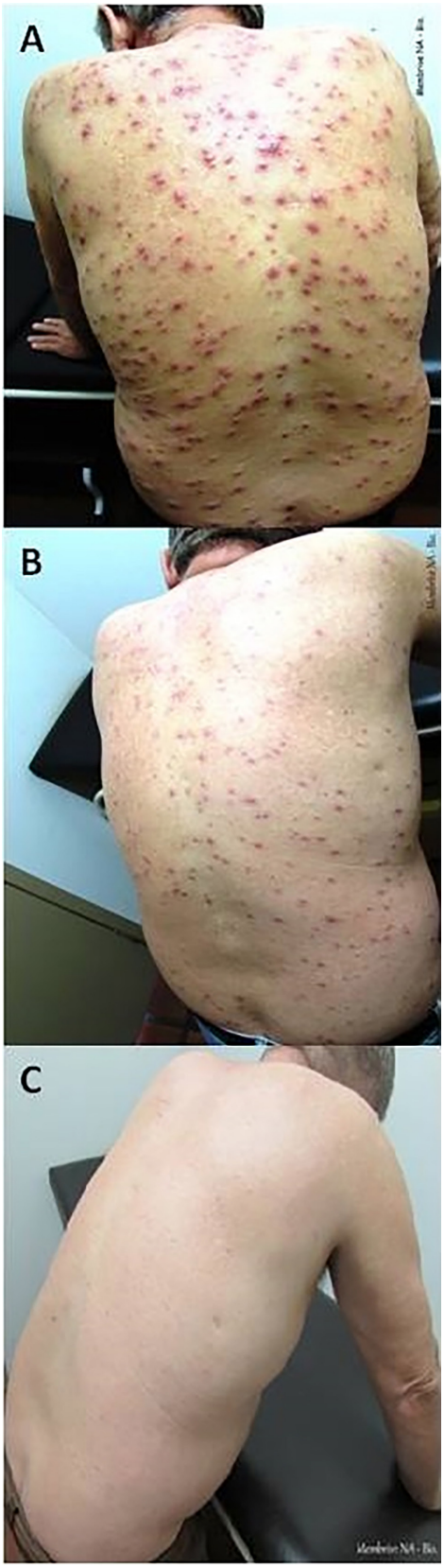

Figure 1 - Patient with disseminated leishmaniasis. (A) Disseminated lesions before treatment; (B) After treatment with 60 ampoules of Glucantime®; (C) After treatment with 120 ampoules of Glucantime®

leishmaniasis. Finally, after 5 months, the patient was sent to an infectious disease specialist of the Laboratory of Medical Entomology from the city of Arapongas, and amastigote forms of *Leishmania* were detected via direct search (DS) of material collected from the primary lesion of the right leg and three other lesions (face, abdomen, and back). Lesion aspirates were mixed with a saline solution containing penicillin G potassium (Sigma) (25,000 IU/mL), and streptomycin (Sigma) (2 mg/mL), at 4 ºC for 24 h; later they were incubated in 199 medium, containing 10% of inactivated fetal bovine serum at 25 °C and the presence of the parasite was detected after five days. It was isolated in the Laboratory of Leishmaniasis from *Universidade Estadual de Maringá* (UEM) and was sent to *Coleção de Leishmania do Instituto Oswaldo Cruz* (CLIOC), Rio de Janeiro, Brazil, for identification. The parasite was identified as *L. (V.) braziliensis* (IOC-L 3636).

After the diagnosis, the patient was treated with intravenous Glucantime® (Sanofi-Aventis Farmacêutica Ltda.), 20 mg/kg /day for 20 days (August 7, 2015, to August 26, 2015). The patient showed a great improvement, with partial healing of lesions, requiring more 20 days of treatment (August 27, 2015, to September 9, 2015), according to the above described procedure. In total, 120 ampoules of glucantime were used. The patient was discharged and showed clinical cure one month after the end of treatment.

DISCUSSION

The extraordinary number of 1,119 lesions observed in the patient is the most important fact in this case. The parasite was identified in the CLIOC as *L. (V.) braziliensis*, confirming that most of the DL cases described in Brazil are associated with this species of *Leishmania*[4,11]. In *Paraná* State, the occurrence of human and canine-CL cases is mainly attributed to infection by *L. (V.) braziliensis*[12].

The current case draws attention to the number of lesions compared to other cases described in Brazil and in the Southern region, given that the cases of CL have been reported almost exclusively in the North and Northeast of Brazil[4,5,11]. In *Maranhão State*, Galvão *et al.*[5] reported a patient with 58 lesions; Carvalho *et al.*[8], in the State of Bahia, found in eight patients, a number of lesions ranging from 75 to 800. Turetz *et al.*[11], also in Bahia, described 42 cases of DL, with the number of lesions ranging from 10 to 300. They drew attention to the increase in the number of patients with DL, classifying it as an emerging form of leishmaniasis, with distinct clinical forms, associated with agricultural activities and the immune response of the host[11,13]. Nevertheless, there is evidence that isolates of *L. (V.) braziliensis*- from DL patients differ genotypically from the ones isolated from patients with cutaneous and mucosal leishmaniasis[14,15], and DL isolates also induce higher inflammatory responses than isolates from CL patients[16].

The dissemination of the lesions in the studied patient occurred in the third month, starting from the beginning of the first lesion. However, there was no impairment of mucous tissue. DL presents numerous acneiform, papular and ulcerated lesions that may arise abruptly, suggesting the hematogenous or lymphatic dissemination of the parasite[11]. Usually, the finding of amastigote forms of *Leishmania* on DS for the diagnosis of DL is low[2,13], but in this case, the number of amastigote forms of *Leishmania* detected on DS was abundant, although the disease had appeared 150 days before being confirmed. The patient's weight loss (15 kg) is not something new, given that fever, general malaise, muscle pain and especially weight loss-are reported among the various systemic manifestations of DL[2,5,11].

Despite biopsy and IIF negative results, the abundant amastigote forms found in the sample collected from lesions and the rapid development in culture medium were decisive factors for the fast and accurate diagnosis of the current DL case. Treatment with meglumine antimoniate was successful, and the response to the medication was quick, given that the patient had the DL diagnosis after five months from the onset of the first lesion. It is noteworthy that the patient did not exhibit any signs of recurrence of -disease until June 2016, nine months after the end of the treatment.

In addition to the extraordinary number of cutaneous lesions, which motivated this case report, the difficult path search for treatment by the patient, who lived in an important endemic area of TL should be pointed. It shows clearly the lack of preparation of the staff working in the Brazilian health system, mainly concerning vector-borne diseases like leishmaniasis.

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