A pediatric case of disseminated American cutaneous leishmaniasis in Rio de Janeiro, Brazil

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Abstract

American cutaneous leishmaniasis is an infectious disease caused by the protozoa of the genus *Leishmania*. Clinical manifestations vary according to the virulence of the parasite species and the host's immune response. We report a case of a 2-year-old girl vertically exposed to HIV who presented painful and itchy papules throughout her lower limbs with further dissemination of vegetative ulcers all over the body and scalp. The histopathological examination evidenced the amastigote form of *Leishmania* and the polymerase chain reaction was positive for *Leishmania* sp. in the tissue sample. The patient was treated with amphotericin B and demonstrated improvement of lesions. Despite successful treatment for American cutaneous leishmaniasis, she developed osteomyelitis related to a bacterial secondary infection over the site of a previous ulcer on the left ankle and required a 6-week course of intravenous antimicrobial treatment. Children with vertical exposure to HIV, even without seroconversion, are at greater risk of infections if compared to non-exposed children. This is perhaps the reason for such an exuberant and rare case of complicated leishmaniasis.

Keywords: Leishmania, leishmaniasis, HIV

Introduction

American cutaneous leishmaniasis (ACL) is an infectious non-contagious disease caused by *Leishmania* spp. protozoa and transmitted by insects of the *Lutzomyia* genus. The disease is considered a health issue in 85 countries, distributed across five continents (North and South America, Europe, Africa, and Asia), with 0.7 to 1.3 million recorded new cases every year [1]. The World Health Organization (WHO) considers ACL one of the 6 most important infectious diseases around the world due to its high incidence and morbidity. Furthermore, all age groups and genders are at risk of infection [1]. In Brazil, according to the WHO, 16.432 new ACL cases were detected in 2020 alone [2]. Considering age groups, data from 2018 shows that 93.1% of all new ACL cases were reported in subjects aged 10 or older, 3.2% in individuals between 5 and 10 years old, and 2.8% in children under 5 years old [3]. Seven species of *Leishmania* linked to ACL have been identified in Brazil, and *Leishmania braziliensis* is the most frequent species linked to cutaneous disease in the entire country and also in the state of Rio de Janeiro. A recent study demonstrated the prevalence of species of *Leishmania* across the state of Rio de Janeiro: *Leishmania (Viannia) braziliensis* (80.8%), *L. (V.) naiffi* (7.7%), *L. (V.) guyanensis* (6.7%) *L. (Leishmania) amazonensis*, (1%) and genetic subvariants of *L. (V.) braziliensis* (3.8%), [4]. Moreover, a study involving people living with HIV/AIDS identified the presence of an asymptomatic ACL infection in 16% of patients, revealing the need for further investigation of HIV and ACL coinfection [4]. The broad array of clinical manifestations of the ACL may be attributed to both the parasite's virulence

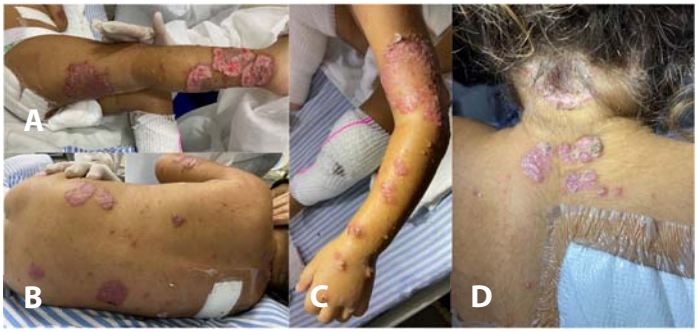

Figure 1. ***A)*** *Disseminated ulcerovegetative lesions before treatment, crusts removed, lower right limb.* ***B)*** *Dorsal region* ***C)*** *Left upper limb* ***D)*** *Vegetative ulcers on the upper dorsal region and on the scalp.*

and the immune status of the host [6]. Children exposed vertically to HIV are also under greater risk of infectious diseases in comparison to children not exposed to the virus during pregnancy [7].

Case Synopsis

A 2-year-old girl, from Niterói, Rio de Janeiro, Brazil, presented with a two-month history of growing erythematous and pruritic papules throughout the lower limbs that disseminated throughout the child's skin, sparing mucosae. Notably, the patient had no record of previous trips to other regions of the country during her lifetime. Throughout pregnancy, the child had been vertically exposed to HIV without seroconversion. Antibiotic therapy with cephalexin and benzathine penicillin followed by intravenous oxacillin was prescribed without improvement due to a presumptive diagnosis of pyoderma, In spite of that the lesions worsened and became disseminated ulcerative-vegetative plaques (**Figure 1**). Serology for HIV, hepatitis B and C, syphilis, coccidioidomycosis, aspergillosis, histoplasmosis, and paracoccidioidomycosis were negative and a chest radiograph was normal.

A biopsy of one of the lesions on the abdomen was performed and showed a chronic inflammatory process associated with necrosis and acute inflammation. Abscesses with countless microorganisms were identified as the amastigote form of *Leishmania* (**Figure 2**). A fragment of an ulcer was sent for parasite identification, and also to perform a polymerase chain reaction test that

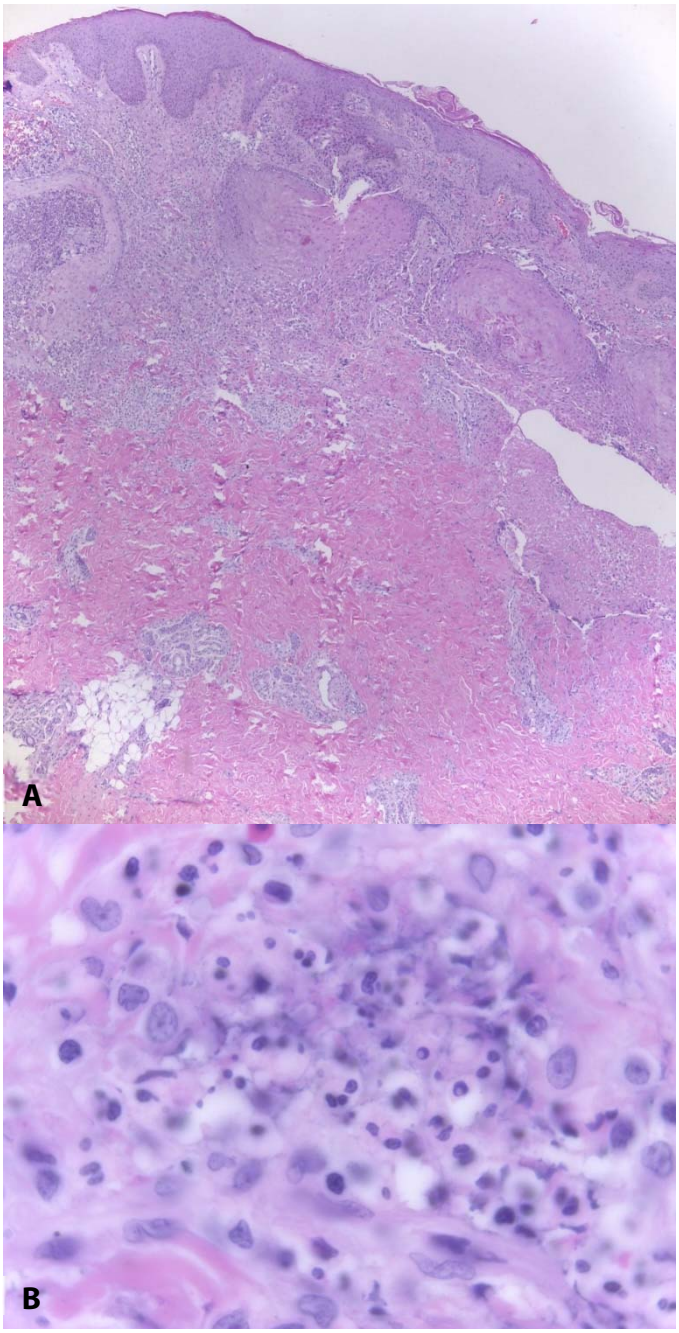

Figure 2. ***A)*** *H&E histopathology. Chronic inflammatory process, suppurative granuloma with pseudoepitheliomatous acanthosis, 40×.* ***B)*** *Many amastigote Leishmania bodies within the cytoplasm of histiocytes. Oil immersion, 1000×.*

revealed the presence of *Leishmania braziliensis* DNA. Another biopsy fragment was sent for culture for fungi and mycobacteria, with negative results. Considering the diagnosis of disseminated American cutaneous Leishmaniasis, treatment with amphotericin B deoxycholate (5mg/kg/day) was employed for 5 days, followed by a change to liposomal amphotericin B (3mg/kg/day) for an

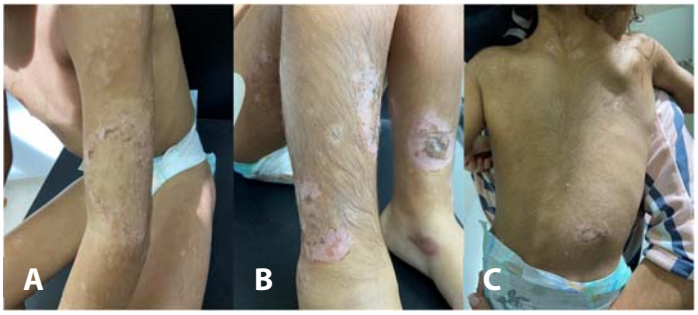

Figure 3. *50 days after treatment.* ***A)*** *Upper left arm. Scars with mild infiltration and a few crusts. Fifty days after treatment with amphotericin B.* ***B)*** *Lower limbs with remaining crusts.* ***C)*** *Residual lesions on the back.*

additional 14 days, resulting in an accumulated total dose of 67mg/kg of amphotericin B. The patient showed a slow and progressive improvement of the lesions (**Figure 3**). One month after hospital discharge, the patient presented with fever and edema of the left ankle. Magnetic resonance imaging (MRI) revealed osteomyelitis in the distal tibial epiphysis, plus an infectious/inflammatory process extending to the surrounding soft tissues and cuboid-calcaneus joint. Initially intravenous oxacillin and cefepime were utilized. The culture from a bone fragment biopsied identified *Staphylococcus warneri* and exudate culture revealed oxacillin-resistant *Klebsiella pneumoniae*. The antimicrobial therapy was then changed to intravenous vancomycin and sulbactam-ampicillin for the following 8 weeks, resulting in reduction of the ankle edema; the patient was discharged on oral amoxicillin-clavulanate. Eleven months after amphotericin B treatment, all ulcers resolved with hypochromic scarring (**Figure 4**) and the child's symptoms have improved.

Case Discussion

Traditionally, leishmaniasis has been known to affect mainly men performing outdoor activities and was considered an occupational disease [8]. Nevertheless, in Latin America, there has been an increase in the number of ACL cases in the last decades with involvement among all age ranges and both males and females. Cases of involvement of whole families suggest an intra- and peridomiciliary pattern of transmission, thus exposing infants to a greater risk of infection [8]. A high frequency of American cutaneous leishmaniasis was shown in young age groups and cases clustered in urban neighborhoods of Manaus [8]. Disseminated cutaneous leishmaniasis (DCL) is characterized as more than 10 lesions in at least two parts of the body and is a rare clinical form of leishmaniasis [9]. Less than 2% of total cases affected with ACL develop DCL [10]. Multiple clones of *Leishmania braziliensis* species are involved in the pathogenesis of different clinical forms of leishmaniasis and cases are frequently described in immunocompetent patients [11]. Leishmaniasis can also present with atypical features such as vegetative, verrucous, crusted, and lupoid lesions. In a cohort study among 1396 patients diagnosed with ACL in 2005–2006 in Bahia Brazil, 35 (2.5%) patients presented with atypical manifestations of the disease. Among these patients, 14 were pregnant women, two were co-infected with HIV, and 19 had no comorbidity or other apparent risk factors for the development of atypical ACL. These 19 patients were predominantly adult males, frequently presenting with facial lesions and had higher rates of treatment failure with antimonial therapy when compared with patients with classic ACL [12]. In children and teenagers, the number of lesions tend to be greater, and head and face lesions are far more frequent. Younger age, larger lesions, and greater number of lesions have been linked to higher therapy failure rates [9].

Vertical exposure to HIV is still a prevalent situation in developing countries, despite efforts towards its reduction. Even without seroconversion, this increases susceptibility to infections. For this reason, research interest in the health needs of HIV-exposed, uninfected (HEU) infants emerged. This population remains challenging to study because of the confounding effects of anti-retroviral therapy (ART)

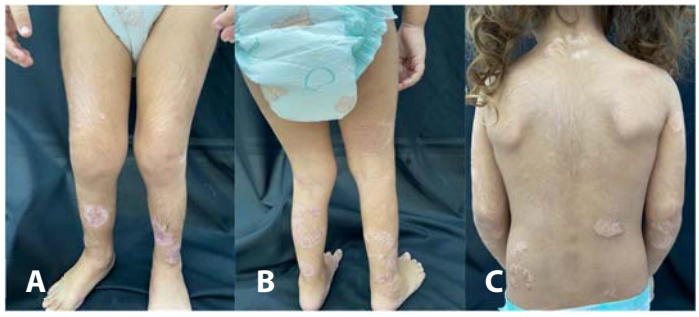

Figure 4. *Eleven months after treatment. Hypochromic scars showing no inflammation or infiltration.*

exposure, feeding modality differences, difficulties in confirming HIV status, and a scarcity of comparable, contemporaneous control groups. Immunological abnormalities have been reported in HIV-exposed, uninfected infants from both developing and developed countries. The maternal HIV disease possibly interferes with infant's immunity to infectious pathogens as some studies have demonstrated a reduced transplacental transfer of antibodies from HIV-infected mothers and reduced thymopoiesis and functional defects of antigen-presenting cells in HEU infants [13]. Early cessation of breastfeeding reduces HIV transmission but may also contribute to a reduction of an infant's immune defenses because absence of breastfeeding is associated with higher susceptibility to infections in early life. Moreover, maternal immunodeficiency may increase bacterial carriage [14]. Disseminated cutaneous forms, relapse, reinfection (especially one year or more after clinical cure), and failure of therapy may suggest an opportunistic behavior of leishmaniasis [1]. This is likely the reason for the rapid onset of the severe manifestations and the secondary bacterial osteomyelitis in the presented case. Leishmaniasis remains an important neglected and underreported disease and delay in diagnosis can result in severe complications.

Conclusion

We present a rare case of a pediatric patient with disseminated cutaneous leishmaniasis and her successful therapy, despite complications. Our case combines two relevant issues in public health—HIV and leishmaniasis—emphasizing that immune deficiency directly relates to worse prognosis in infectious diseases. The diagnosis of ACL is challenging due to the numerous clinical manifestations and complications that can mimic several diseases. Although some areas of the state of Rio de Janeiro are endemic for ACL, this difficult differential diagnosis may be overlooked, leading to incorrect medical treatment. Early clinical suspicion may lead to prompt diagnosis and treatment, preventing complications. Therefore, it is essential that pediatricians, dermatologists, and other health professionals are provided with proper training to enhance diagnosis of cutaneous leishmaniasis in children, with special attention to those at risk for immunosuppression.

Potential conflicts of interest

The authors declare no conflicts of interest.

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