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Case Report

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Leishmaniasis Recidiva Cutis: Intralesional Treatment and Surgical Aproach

Cristiane Comparin Savegnago[1*], Milena Marchini Rodrigues[2], Bruna Costa Santos[3], Günter Hans-Filho[4], Anamaria Paniago[5], CAF de Freitas[6]

[1]Dermatologist, Preceptor of the Medical Residency Program in Dermatology, Federal University of Mato Grosso do Sul, Brazil

[2]Medical resident in Dermatology, São José do Rio Preto Medical School, Brazil

[3]Medica, Campo Grande, Brazil

[4]Department of Dermatology, Federal University of Mato Grosso do Sul, Brazil

[5]Department of Infectious Diseases, Federal University of Mato Grosso do Sul, Brazil

[6]Department of the Head-and-Neck Program, Federal University of Mato Grosso do Sul, Brazil

[*]**Corresponding author:** Cristiane Comparin Savegnago, Dermatologist, Preceptor of the Medical Residency Program in Dermatology, Federal University of Mato Grosso do Sul, Brazil. Tel: +55-6733453662; Email: dermatologia.comparin@gmail.com

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Author Summary

Introduction: Leishmaniasis is parasitic disease caused by different species of *Leishmania spp* and transmitted by bites of phlebotomine sandflies. Tegumentary leishmaniasis affects the skin and may evolve with lesions on mucous membranes. The lesions are often seen in areas of the skin that are most exposed to insect bites, such as the legs, but there are cases described in various places in the body. In endemic areas, its diagnosis can be facilitated when skin lesions are ulcerations features with raised edges (framed) and the medical professional has experience in recognizing the disease. However, rare variants of the disease may hinder its diagnosis, such as Leishmaniasis Recidiva Cutis (LRC). This clinical form should be suspected in view of the appearance of new lesions in regions of previous scars of tegumentary leishmaniasis, or active lesions with poor response to conventional treatment. The gold standard diagnosis is the detection of the parasite in the tissue, however this research may be negative in these cases, and more detailed examinations may be necessary. LRC is often resistant to conventional therapies.

Objective: To describe a case of LRC in which it was necessary to associate the intravenous treatment, intralesional injections and surgical removal of the remaining lesion.

Methods: This article is a case report written from medical records of the patient.

Main finding: This case required three different treatments to achieve remission, including N-methylglucamine antimoniate intravenous and intralesional, besides a surgery to remove the last parasitic focus. None all cases of LRC require this approach, but some patients are very resistant to conventional treatment.

Conclusion: LRC is a rare disease and its treatment can be challenging, since sometimes it is necessary to associate different types of treatments.

Keywords: Cutaneous Leishmaniasis; Leishmaniasis; Parasites; Tropical Medicine

Introduction

Leishmaniasis Recidiva Cutis (LRC) is a rare variant of tegumentary Leishmaniasis (LT). Also known as metaleishmaniosis, lupoid leishmaniasis or chronic tuberculoid leishmaniasis in the old world. It is a peculiar form that denotes refractoriness to the treatment [1,2]. Until the year 1976 there were only reports in the Middle East, currently there are still few reports in America [3]. LRC is characterized by the presence of nodular or verrucous lesions, initially isolated, and then confluent around or within the scar of a previous *Leishmania* lesion, which appears to be late and of long duration [4]. Less commonly, concurrent lesions occur [2].

Case report

A 52-year-old female patient from the center-west of Brazil presented with one year and 6 months of evolution of a lesion who appeared after visiting the rural area. She noticed a papular lesion in the left calf, which evolved centrifugally with central atrophy, without ulceration, with crusty active borders. In the evolution, two more lesions appeared, distal to the previous lesion, in the pre-tibial region and left foot, and another lesion on the right foot (Figure 1), with pain and purulent collection sparse from the lesion's edges.

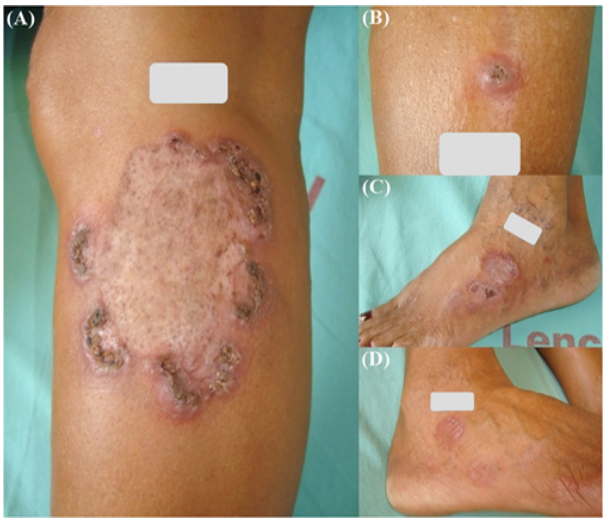

Figure 1: In The primary lesion with cicatricial center and growing verrucous borders is visualized. In B, C and D the three subsequent lesions.

The diagnosis of the LRC was laborious. The histopathology showed inconclusive, with peseudoepitheliomatous hyperplasia of the epidermis, dermal lymphohistiocytic infiltrate and with giant cells, constituting a loose granulomatous process, but showing no pathogens. Direct research and culture for *Leishmania* also did not contribute to the diagnosis, because both presented negative in two samples. Direct mycological examination and culture for fungi were both negative either. The Montenegro Intradermal Reaction (IDRM) showed strongly positive (62 x 82 mm) and Tuberculin Skin Test (PPD) with strong reactor (14 mm). Lastly, Immunohistochemistry was performed for infectious agents on the biopsy fragment, being negative for fungi and mycobacteria. However, Immunohistochemistry for *Leishmania* was positive, finally concluding the diagnosis (Figure 2).

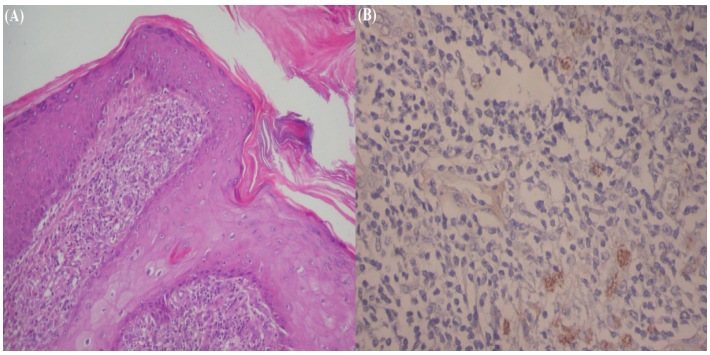

Figure 2: In The granuloma with giant cells and pseudoepitheliomatous hyperplasia. In B, positive immunohistochemistry for *Leishmania*.

The treatment of this case was a challenge, because different therapeutics were required. Firstly, the patient was treated with two cycles of N-methylglucamine antimoniate intravenously (15 mg Sb + 5 / kg / day), with partial resolution of the primary lesion and complete resolution of the others. Remaining active areas of the primary lesion received 5 sessions of intralesional N-methylglucamine antimoniate, each session with direct intradermal injection of 2 ml of the drug without dilution, distributed throughout the lesions, demonstrating good response, but with a single resistant area at the apical edge. Because of the localized remaining lesion, and considering the other areas were in complete remission, the concern regarding the re-exposure of the patient to the toxicity of a new systemic treatment, and due to the known resistance of this clinical form, surgical excision of the persistent site was proposed. Then, excision with a transposition flap was successfully performed (Figure 3). The patient has been under follow-up for 4 years, with no evidence of relapse.

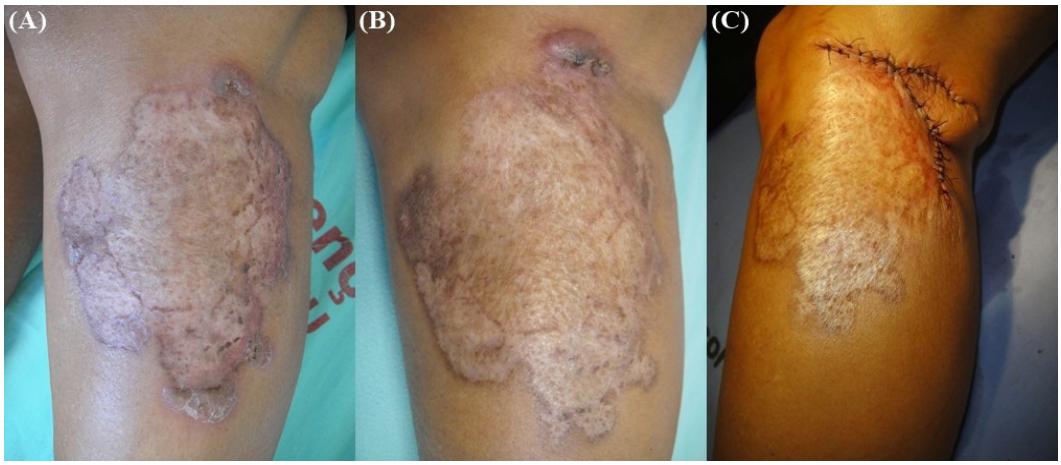

Figure 3: In The lesion after the intravenous treatment with pentavalent antimonial. In B, the reduction of the active areas after the intralesional infiltrations of pentavalent antimonial. In C the postoperative aspect with surgical removal of the remaining upper pole.

Discussion

LRC is a rare form of LT, with specific clinical and evolution [3]. Differential diagnoses are cutaneous tuberculosis, granuloma annularis, verrucous lupus erythematosus, sarcoidosis and deep mycoses, among others [1]. There are few reports of LRC, and although the pathophysiology is not fully elucidated, there are some hypotheses to explain it: antibodies in residents of endemic areas - where continued exposure would cause antigenic stimulus; the species of *Leishmania* involved; irregular treatments with low doses; and the host immunity profile [3,5,6].

Despite the hypothesis of genetic variability among species as a risk factor, and genetic mutations to explain treatment failure, no specific genetic polymorphism has been related as a risk factor for LRC [7]. Hypersensitivity to Montenegro Intradermal Reaction test (IDRM), histopathology and immunohistochemistry point to LRC to be a late reaction to the persistence of parasites in the previous lesions [8]. Hypersensitivity to IDRM defines LRC as a hyperergic variant, and denotes a considerable degree of sensitization of the host to the parasite, with marked cellular immunity, but insufficient to eradicate the infection [4,9,10]. Histopathology shows granuloma that may be indistinguishable from cutaneous tuberculosis, in addition to pseudoepitheliomatous hyperplasia; the presence of Leishmanias on histopathology were not reported since ancient reports.

The *Leishmania* encounter in the direct examination is the gold standard in LT, and it has become routine for its simplicity and specificity, but it requires an experienced and persistent professional: the chance of finding the parasite is inversely proportional to the evolution time of the injury, being rare after one year, as in this case [11-13]. The detection of amastigotes in formalin-fixed and paraffin-embedded sections has also become routine, but cases such as LRC often do not demonstrate parasites [14-17]. Culture techniques are sensitive; however, they are labor-intensive, require sophisticated laboratory and professional structure, may exhibit variations in efficacy between culture media, and the risk of contamination is a problem [11-13]. The exams such as indirect immunofluorescence reaction and enzyme-linked immunosorbent assay may express the level of circulating antibodies [3]. Immunohistochemistry demonstrates success in the diagnosis of LT and has led to a great advance, which motivates its frequent use for the diagnosis of infectious-parasitic diseases [18-22].

Few cases of LRC have been well documented. Most of the reports present only parasitological evidence, without identification of the agent, which must be done with biochemical and molecular techniques. As LRC occurs predominantly in poor countries, resources are lacking for the realization of these techniques. L (L.) braziliensis, L. Viannia peruviana, *Leishmania* (Viannia) panamensis, L. (L.) mexicana and L. (L.) major-like have already been identified as agents in the new world; L. (L.) tropica and rarely L. (L.) major in the old world [7]. Treatment is a challenge even in endemic areas [3]. The challenge in establishing a correct diagnosis of this clinical form is associated with difficulties in offering therapeutic regimens with alternative injectable medications, such as Amphotericin B or liposomal Amphotericin B, and ends in the lack of skilled manpower in the clinical management of patients who evolve with this evolutionary form [3,7]. LRC is often resistant to conventional therapies. Treatment options include systemic therapy with good response to high doses of meglumine antimoniate (50 mg / kg per day) parenterally, alone or in combination with allopurinol; amphotericin B; intralesional infiltration with antimonials; cryosurgery and exeresis [3,23]. Many studies have shown a good response to multidrug therapy [7].

Conclusion

By this study, it can be concluded that LRC is a rare disease and its treatment can be challenging, since sometimes it is necessary to associate different types of therapeutics. The option for surgical treatment was made by resistance to previous treatments, the desire to avoid the side effects of long systemic treatments and to reduce the source of parasites, which could lead to the spread to other areas in the future. The patient described was diagnosed for one year with a progressive evolution of the condition. Her detailed investigation and the care in carrying out a treatment specifically directed to the disease were successful in achieving the remission, associating clinical and surgical treatment. Then, the main finding of this case-report is that LRC is an old, but rare disease, and its treatment can be arduous, therefore doctors from endemic areas should be aware of this unusual clinical form and have at their disposal combinations of local and systemic treatments, which may be necessary for the cure of the patient.

References

1. Oliveira-Neto MP, Mattos MS, Perez MA, Da Cruz AM, Fernandes O, et al (2000) American tegumentary leishmaniasis (ATL) in Rio de Janeiro State, Brazil: main clinical and epidemiological characteristics. Int J Dermatol 39: 506-514.
2. Murray HW, Berman JD, Davies CR, Saravia NG (2005) Advances in leishmaniasis. Lancet 366: 1561-1577.
3. Stefanidou MP, Antoniou M, Koutsopoulos AV, Neofytou YT, Krasagakis K, et al. (2008) A rare case of leishmaniasis recidiva cut is evolving for 31 years caused by Leishmania tropica. Int J Dermatol 47: 588-589.
4. Costa JML, Lago EL, Magalhães AV, Marsden PD (1996) Leishmaniose recidiva cútis causada por Leishmania Viannia braziliensis. An Bras Derm 71: 329-333.
5. Strick RA, Borok M, Gasiorowski HC (1983) Recurrent cutaneous leishmaniasis. J Am Acad Dermatol 9: 437–443.
6. Dostrovsky A (1934) Leishmaniasis recidiva of the skin. Harefuah 8: 118.
7. Gomes CM, Cesetti MV, de Morais OO, Mendes MS, Roselino AM, et al. (2015) The influence of treatment on the development of leishmaniasis recidiva cutis: a 17-year case-control study in Midwestern Brazil. J Eur Acad Dermatol Venereol 29: 109-14.
8. Gangneux JP, Sauzet S, Donnard S, Meyer N, Cornillet A, et al (2007) Recurrent American cutaneous leishmaniasis. Emerg Infect Dis 13: 1436–1438.
9. Sagher F (1947) Leishmania vaccine test in leishmaniasis of the skin. Arch Derm Syph 55: 658-663.
10. Petit JHS (1962) Leishmaniasis Relapse. Br J Derm 74: 127-132.
11. Melo MN (1982) Culture of Leishmania in defined medium. Study of your nutritional requirements 133f.
12. Marfurt J, Nasereddin A, Niederwieser I, Jaffe C.L, Beck HP, et al. (2003) Identification and Differentiation of Leishmania Species in Clinical Samples by PCR Amplification of the Miniexon Sequence and Subsequent Restriction Fragment Length Polymorphism Analysis. J Clin Microbiol 41: 3147-3153.
13. Gomes AH, Armelin IM, Menon SZ, Pereira-Chioccola VL (2008) Leishmania (V.) braziliensis: detection by PCR in biopsies from patients with cutaneous leishmaniasis. Exp Parasitol 119: 319-324.
14. Livni N, Abranowitz A, Londner M, Okon E, Morag A (1983) Immunoperoxidase method of identification of Leishmania in routinely prepared histological sections. Virchows Arch A Pathol Anat Histopathol 401: 147-151.
15. Ferrer L, Rabanal RM, Domingo M, Ramos JA, Fondevila D (1998) Identification of Leishmania donovani amastigotes in canine tissues by immunoperoxidase staining. Res Vet Sci 4: 194-196.
16. Bourdoiseau G, Marchal T, Magnol JP (1997) Immunohistochemical detection of Leishmania infantum in formalin-fixed, paraffin-embedded sections of canine skin and lymph nodes. J Vet Diagn Invest 9: 439-440.
17. Tafuri WL, Santos RL, Arantes RM, Gonçalvez R, De Melo MN, et al. (2004) An alternative immunohistochemical method for detecting Leishmania amastigotes in paraffin-embedded canine tissues. J Immunol Methods 292: 17-23.
18. Weigle KA, de Dávalos M, Heredia P, Molineros R, Saravia NG, et al. (1987) Diagnosis of cutaneous and mucocutaneous Leishmaniasis in Colombia: a comparison of seven methods. Am J Trop Med Hyg 36: 489-496.
19. Salinas G, Valderrama L, Palma G, Montes G, Saravia NG (1989) Detección de amastigotas en leishmaniasis cutanea y mucocutanea por el metodo de inmunoperoxidasa, usando anticuerpo policlonal: sensibilidad y especificidad comparadas con metodos convencionales de diagnotico. Mem Inst Oswaldo Cruz 84: 53-60.
20. Kenner JR, Aronson NE, Bratthauer GL, Turnocky RP, Jackson JE, et al. (1999) Immunohistochemistry to identify Leishmania parasites in fixed tissues. J Cutan Pathol 26: 130-136.
21. Schubach A, Cuzzi-maya T, Oliveira AV, Sartori A, de Oliveira-Neto MP, et al. (2001) Leishmanial Antigens in the Diagnosis of Active Lesions and Ancient Scars of American Tegumentary Leishmaniasis Patients. Mem Inst Oswaldo Cruz 96: 987-996.
22. Quintella LP, Cuzzi T, Madeira MF, Okamoto T, Schubach AO (2009) Immunoperoxidase technique using an anti-Leishmania (L.) chagasi hyperimmune serum in the diagnosis of culture-confirmed American tegumentary leishmaniasis. Rev Inst Med Trop São Paulo 51: 83-86.
23. Machado PRL, Araújo MIAS, Carvalho L, Carvalho EM (2004) Mechanisms of immune response to infections. An Bras Dermatol 79: 647-664.