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Case Report

Leishmaniasis recidivans in Ethiopia: cutaneous and mucocutaneous features

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Abstract

Cutaneous leishmaniasis (CL) is endemic in Ethiopia. An unusual clinical form of this disease is leishmaniasis recidivans (LR), a prolonged, relapsing form of cutaneous leishmaniasis resembling tuberculosis of the skin that may persist for many years with a chronic and relapsing course. This rare variant has been shown to be caused by *Leishmania tropica* species in the Old World and by *Leishmania braziliensis*, *Leishmania amazonensis*, *Leishmania panamensis*, and *Leishmania guyanensis* in the New World, as reported in various studies. To our knowledge, there are no reports from Ethiopia, and mucocutaneous involvement of LR has not been described to date.

This was a retrospective analysis of the patients seen at the Italian Dermatological Center in Mekelle on the Tigrean highlands over a three-year period (2008–2011).

Seven patients with typical clinical features of LR were seen. Two of them presented with signs of mucosal involvement. To date, *Leishmania aethiopica* is shown to be the only species causing CL that is endemic in the Ethiopian highlands. Therefore, it had to be assumed that the lesions in these patients were caused by this species.

The aims of this communication are to report, for the first time, the presence of LR, most likely due to *Leishmania aethiopica*, in Ethiopia, and to report mucosal involvement in this rare clinical form of CL.

Key words: cutaneous leishmaniasis; developing countries; parasitic infections.

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Introduction

Cutaneous leishmaniasis (CL) is a disease caused by several different species of the protozoa *Leishmania* that are transmitted via the bite of an infected female sand-fly. CL is an endemic disease in Ethiopia, particularly in the Tigrean highlands at an altitude > 2,000 meters [1-3].

The disease has a wide clinical spectrum [4,5]. The different clinical presentations depend mostly on the host immune response rather than on the causative species. However, there are some expressions that are more prevalent in one species than in another [6,7]. Unusual clinical variants of CL include mucocutaneous leishmaniasis (MCL), diffuse cutaneous leishmaniasis (DCL), and leishmaniasis recidivans (LR). LR is rare and usually follows a chronic and relapsing course. It recurs typically at the site of an original lesion that had apparently healed after a variable period (months or years) and often within the edge of the scar [8,9]. The recurrent lesions may be notoriously difficult to treat, thus the name chronic relapsing cutaneous leishmaniasis. Clinically, the cutaneous lesions are in the form of plaques simulating discoid lupus erythematosus and lupus vulgaris. One case simulating granulomatous cheilitis has also been reported [10].

LR was described as a clinical variant of CL caused by *Leishmania tropica* in the Old World [8,11]. It is also known as leishmaniasis recidiva cutis (LRC) in the New World. Few patients have been reported from the New World; *L. braziliensis* subspecies, *L. amazonensis*, *L. panamensis*, and *L. guyanensis* have been isolated from patients in Brazil, Colombia, and Guyana [12-15].

To our knowledge, there have been no reports of LR from Ethiopia, and mucosal involvement in this presentation has not yet been described.

Here we report the presence of LR in Ethiopia, where *L. aethiopica* is to date still the only species found in the highlands causing CL [16-20], and describe the mucosal involvement in this uncommon clinical variant.

Case series

Seven patients presenting with the typical features of LR were evaluated at the Italian Dermatological Center (IDC) in Mekelle over a three-year period (2008 to 2011).

Six of them were children 4 to 17 years of age and one was an adult 40 years of age. All the patients were in good general health without other diseases or any other signs of other types of CL.

All patients had already been treated at least once for previous CL. All the lesions were located on the face (head). No lesions were found on the body on further clinical examination. This ruled out a possible relapse of DCL, another uncommon clinical variant, which is also found in northern Ethiopia [21].

The lesions were located on the edge of the previous scars in four patients; inside the edges on the scar in one patient; on and inside the edges in another patient; and on and inside and outside the edges in the last patient. Clinical presentation was similar to discoid lupus erythematosus in three cases and to lupus vulgaris in one case. Skin smears were obtained from the lesions and stained with Giemsa, and *Leishmania* amastigotes were found in samples from all patients. Multiple samples were sometimes needed because of the scarcity of parasites present in the skin smears from the lesions [22].

Two patients showed mucosal involvement of the lesions. Their clinical features are described below.

Patient 1

A 16-year-old boy presented with significant scarring on the nose, forehead, cheeks, and upper lip (Figures 1 and 2).

Infiltrated and crusted lesions were visible at the margins of the scar and inside the scar. The patient had previously been treated several times for CL; the first lesions had appeared five years earlier. The last treatment was given two years before with intramuscular meglumine antimoniate (Glucantime, Sanofi, Famar Health Care Services Madrid, Spain) with apparent complete remission. His general health was unremarkable; blood routine tests were within the normal range, and an HIV test was negative.

Lesions continued to increase in size, now affecting the nostrils and the right side of the upper lip (active

Figure 1. Patient 1. Significant scarring on the face, with infiltrated and crusted lesions on the edge of the scars and inside the scars. Swelling of the upper lip and crusts around the nostrils are suggestive of mucosal involvement.

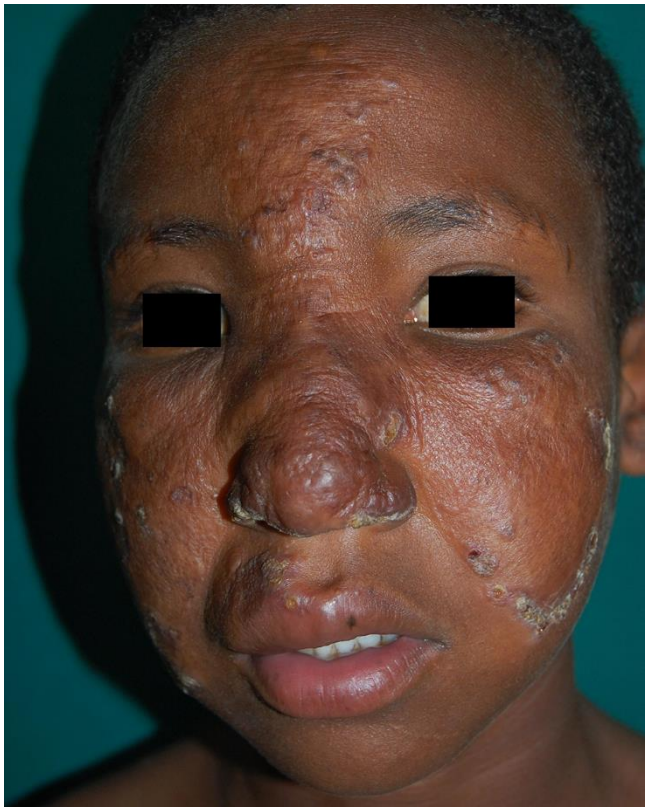
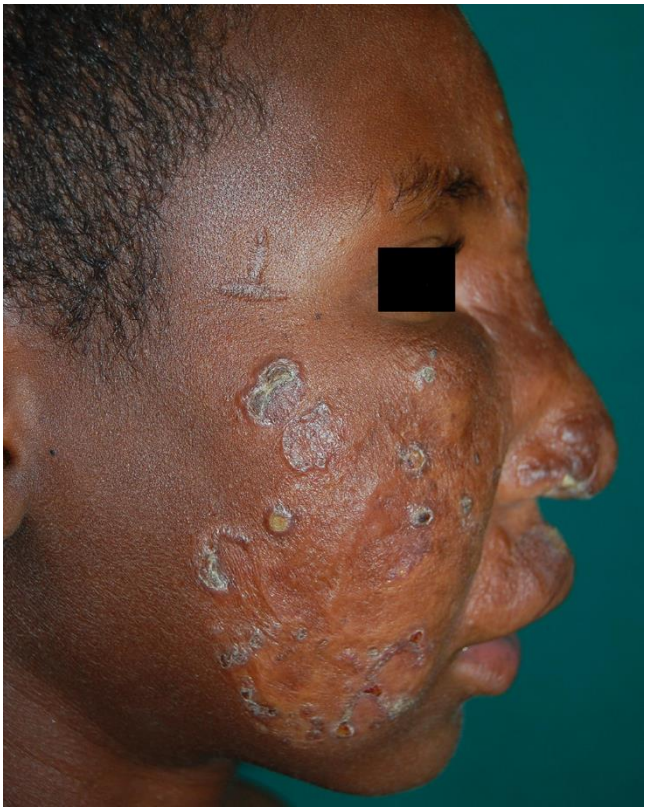


Figure 2. Patient 1. Scarring on the face with crusted infiltrated lesions on the edge of the scars, lateral aspect. Features of leishmaniasis recidivans.



lesions were present on the semimucosa). These features pointed to possible oral and/or nasal mucosal involvement, probably secondary to the increasing size of the lesions over time.

The patient was treated with systemic meglumine antimoniate, the only therapy available, resulting in an apparent complete remission of the lesions. The patient was seen twice in two years with relapse and was not seen thereafter.

Patient 2

A 17-year-old boy in good general health presented at the hospital with scars of previously treated CL lesions on the face (Figure 3). New active lesions had appeared on his cheeks, nose and nostrils, lips, right upper eyelid, and on his right ear. The lesions were infiltrated, crusted, and ulcerated. They were located on and inside the margins of the scars and a few of them were even outside these margins, on the normal skin. The oral mucosae were clearly affected, with ulcerations on and inside the lips in the oral mucosae and inside both nostrils in the nasal mucosae.

Taking his history was difficult. Therefore, the precise duration of the disease could not be determined, although it may have persisted for many years. An HIV test was performed and the result was negative.

These clinical features possibly indicated a mucosal involvement secondary to the increasing size of the previous lesions over time. It was less likely that the lesions had already spread to the mucosae since the first appearance.

This patient too was treated with systemic meglumine antimoniate, resulting in an apparent healing of the active lesions. This presentation resulted in deforming scars after the therapy, with narrowing and impairment of the mouth opening.

The patient was not seen again for follow-up.

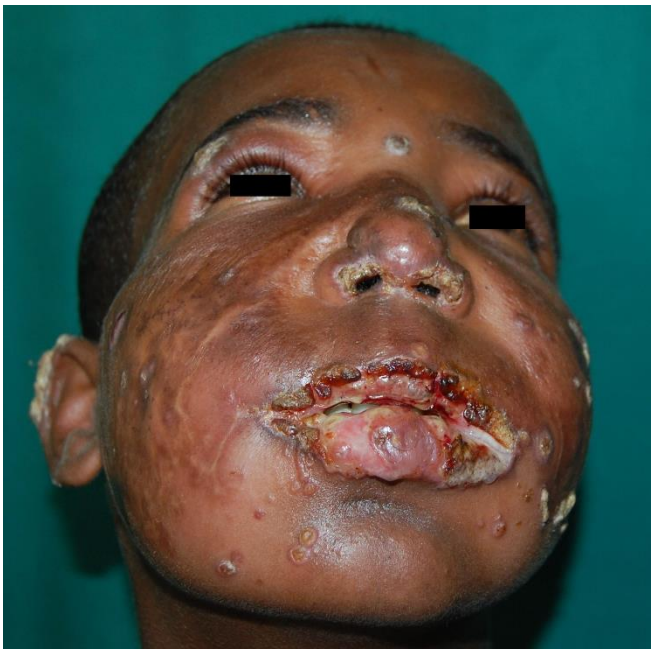
Discussion

LR is an uncommon clinical presentation of CL that occurs in 3%–10% of patients [23,24].

Lesions of LR most likely represent a reactivation of an initial infection, probably due to the persistence of parasites in the scarred tissue [15].

The actual cause of re-activation of the disease is unclear. Reports indicate that local trauma, surgery, or corticosteroids may contribute in the reactivation of leishmaniasis [8,12,25]. The most common mechanism of re-activation hypothesized is a defect in the cellular immunity of the host. A defect in the T-lymphocyte activation by the protozoa would cause the inability of the macrophages to kill all amastigotes [24,9]. Relapses

Figure 3. Patient 2. Scarring on the face left from previous leishmanial lesions; active lesions with ulcers and crusts on the lips and nostrils, indicating mucosal involvement.



may occur after months or up to 30–40 years after the first manifestations of the disease, but more commonly within 2 years [8,11,26].

Few cases of LR, caused mainly by *L. tropica* in the Old World and by *L. braziliensis* and other species in the New World, have been reported previously [11,14,15,23,27,28]. These lesions may have variable clinical appearance. Differential diagnoses include lupus vulgaris, discoid lupus, bacterial infections, squamous cell carcinoma, and, when the lesions are found on the lips, syphilitic chancre and granulomatous cheilitis [9,10,23]. The disease follows a chronic and relapsing course. The treatment of LR is notoriously difficult. According to the literature, it includes systemic therapy with pentavalent antimony, alone or in combination with allopurinol or pentoxifylline [26], amphotericin B, and local therapy with intralesional antimonials, cryosurgery, or excision. In children, fluconazole may represent an effective and well-tolerated therapy [29,30], although we think that for *L. aethiopica*, pentamidine, which is hardly available in the country, is the treatment of choice [31].

To our knowledge, no cases of LR have yet been reported from Ethiopia, where CL is an endemic disease. Our patients all came from the Ethiopian highlands around Mekelle. It has been demonstrated that CL on the Ethiopian highlands (> 2,000 meters) is caused by *L. aethiopica*, which was the only species

isolated from patients living in the highlands of different regions including Tigray in several studies [16-21].

Therefore, although we unfortunately did not have the facilities to identify the species, it seems highly likely that the cases reported here were caused by *L. aethiopica*. To our knowledge, this species has not yet been reported as a possible cause of LR.

We also reported here the possible mucosal involvement in this rare form of CL, which has not been described elsewhere. The mucosal lesions in our patients were probably due to the progression of the previous lesions, leading to increased size over time.

Conclusions

Leishmaniasis recidivans is seen in northern Ethiopia, and it is most likely caused by the most common causative species, *L. aethiopica*. Mucosal involvement of this rare clinical presentation has been described. Further studies are imperative to confirm the possible mucosal involvement of this clinical form of CL and to confirm the causative species.

References

1. Padovese V, Terranova M, Toma L, Barnabas GA, Morrone A (2009) Cutaneous and mucocutaneous leishmaniasis in Tigray, northern Ethiopia: clinical aspects and therapeutic concerns. Trans R Soc Trop Med Hyg 103: 707-711.
2. Morrone A, Pitidis A, Pajno MC, Dassoni F, Latino O, Barnabas GA, Padovese V (2011) Epidemiological and geographical aspects of leishmaniasis in Tigray, northern Ethiopia: a retrospective analysis of medical records, 2005-2008. Trans R Soc Trop Med Hyg 105: 273-280.
3. World Health Organization (2014) Country profiles: Ethiopia. Available: http://www.who.int/leishmaniasis/resources/Leishmaniasis_cp_Ethiopia_2014_updated.pdf?ua=1. Accessed 26 October 2016.
4. Akilov OE, Khachemoune A, Hasan T (2007) Clinical manifestations and classification of Old World cutaneous leishmaniasis. Int J Dermatol 46: 132-142.
5. Bari A, Rahman SB (2008) Many faces of cutaneous leishmaniasis. Indian J Dermatol Venereol Leprol 74: 23-27.
6. Ul Bari A, Raza N (2010) Lupoid cutaneous leishmaniasis: a report of 16 cases. Indian J Dermatol Venereol Leprol 76: 85.
7. Hepburn NC (2003) Cutaneous Leishmaniasis: an overview. J Postgrad Med 49: 50.
8. Marovich MA, Rosalia L, Marc S, Fuchs GH, Kruetzer R, Nutman TB, Franklin AN (2001) Leishmaniasis recidivans recurrence after 43 years: a clinical and immunologic report after successful treatment. Clin Infect Dis 33: 1076-1079.
9. Ekiz O, Rifaioglu EN, Sen BB, Culha G, Ozgur T, Dogramaci AC (2015) Leishmaniasis recidiva cutis of the lips mimicking granulomatous cheilitis. Indian J Dermatol 60: 216.
10. Masood S, Naveed S, Alvi RU (2012) Infiltrated Leishmaniasis Recidivans Cutis on the face: a rare clinical presentation. Trop Doc 42: 120-121.
11. Stefanidou MP, Antoniou M, Koutsopoulos AV, Neofytou YT, Krasagakis K, Kruger-Kragasakis S, Tselentis Y, Tosca AD (2008) A rare case of Leishmaniasis Recidiva Cutis evolving for 31 years caused by Leishmania tropica. Int J Dermatol 47: 588-589.
12. Gangneux JP, Sauzet S, Donnard S, Meyer N, Cornillet A, Pratlong F, Guiguen C (2007) Recurrent american cutaneous Leishmaniasis. Emerg Infect Dis 13: 1436-1438.
13. Paes-Oliveira M (1977) Leishmaniasis Recidiva Cutis. An Bras Dermatol 52: 353-359.
14. Calvopina M, Uezato H, Gomez EA, Korenaga M, Nonaka S, Hashiguchi Y (2006) Leishmaniasis recidiva cutis due to Leishmania (Viannia) panamensis in subtropical Ecuador: Isoenzymatic characterization. Int J Dermatol 45: 116-120
15. Oliveira-Neto MP, Mattos M, Souza CS, Fernandes O, Pirmez C (1998) Leishmaniasis Recidiva Cutis in New World cutaneous leishmaniasis. Int J Dermatol 37*:* 846-849.
16. Ashford RW (1977) The comparative ecology of leishmania aethiopica. Colloques Internat CNRS 239: 233-240.
17. Lemma W (2008) Hyraxes and Leishmaniasis in Ethiopia. Ethiop J Health Biomed Sci 1: 63-69.
18. Bsrat A, Berhe N, Balkew M, Yohannes M, Teklu T, Gadisa E, Medhin G, Abera A (2015) Epidemiological study of cutaneous leishmaniasis in Saesie Tsaeda-emba district, eastern Tigray, northern Ethiopia. Parasit Vectors 8: 149.
19. Gadisa E, Genetu A, Kuru T, Jirata D, Dagne K, Aseffa A, Gedamu L (2007) *Leishmania* (Kinetoplastida): Species typing with isoenzyme and PCR RFLP from cutaneous leishmaniasis patients in Ethiopia. Experim Parasitol 115: 339-343.

20. Lemma W, Erenso G, Gadisa E, Balkew M, Gebre-Michael T, Hailu A (2009) A zoonotic focus of cutaneous leishmaniasis in Addis Ababa, Ethiopia. Parasit Vectors 2: 60.
21. Dassoni F, Abebe Z, Naafs B, Morrone A (2013) Cutaneous and mucocutaneous leishmaniasis resembling borderline tubercoloid leprosy: a new clinical presentation? Acta Derm Venereol 93: 74-77.
22. Srebrenik A, Brenner S (1996) Leishmaniasis recidivans mimicking lupus vulgaris. Int J Dermatol 35: 572-573.
23. Cannavò SP, Vaccaro M, Guarneri F (2000) Leishmaniasis Recidiva Cutis. Int J Dermatol 39: 205-217.
24. Momeni AZ, Aminjavaheri M (1995) Treatment of recurrent cutaneous leishmaniasis. Int J Dermatol 34: 129-133.
25. Mavilia L, Rossi R, Massi D, Difonzo EM, Campolmi P, Cappuggi P (2002) Leishmaniasis Recidiva Cutis: an unusual two step recurrence. Int J Dermatol 41: 506-407.
26. Gomes CM, Damasco FDS, Oliveira de Morais O, Ribeiro de Paula CD, Sampaio RN (2013) Recurrent cutaneous leishmaniasis. An Bras Dermatol 88: 462-464.
27. Calvopina M, Gomez EA, Uezato H, Kato H, Nonaka S, Hashiguchi Y (2005) Atypical clinical variants in New World cutaneous leishmaniasis: Disseminated, erysipeloid, and recidiva cutis due to Leishmania (V.) panamensis. Am J Trop Med Hyg 73: 281-284.
28. Bittencourt AL, Costa JM, Carvalho EM, Barral A (1993) Leishmaniasis Recidiva Cutis in American cutaneous leishmaniasis. Int J Dermatol. 32: 802-805.
29. Esfandiarpour I, Dabiri SH (2007) Treatment of cutaneous leishmaniasis recidivans with a combination of allopurinol and meglumine antimoniate: a clinical and histologic study. Int J Dermatol 46: 848-852.
30. Sklavos AV, Walls T, Webber MT, Watson AB (2010) Cutaneous leishmaniasis in a child treated with oral fluconazole. Australas J Dermatol 51: 195-197.
31. Zaar K, Wunderlich F, Belehu A (1982) Electron microscopical studies on cutaneous leishmaniasis in Ethiopia. I. The diffuse form and its treatment with pentamidine. Ann Trop Med Parasitol. 76: 595-605.

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