Photo Vignette

A New World disease: Dual diagnostic challenges in travelers returning from Costa Rica

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Abstract

Cutaneous diseases in returning travelers encompass a wide spectrum of etiologies and often pose diagnostic challenges. We present the cases of a 50-year-old man and a 57-year-old woman who presented with a 3-month history of erythematous, ulcerated plaques with well-defined elevated borders and a necrotic center on the lower limbs that began 3 weeks after returning from vacation in Costa Rica. Cutaneous biopsy revealed epidermal ulceration and extensive caseating granulomas throughout the full thickness of the dermis. Giemsa staining revealed no amastigotes. Microbiological examinations identified *Leishmania braziliensis* and excluded mycobacteria and fungi. The diagnosis of cutaneous leishmaniasis was established. Owing to clinical severity and antimonial unavailability, the man was treated with liposomal amphotericin B. The woman underwent surgical excision of the single lesion, along with oral fluconazole. Complete resolution was documented in both patients. These cases, which posed diagnostic and therapeutic challenges, highlight that cutaneous leishmaniasis, in all its versatile and often perplexing presentations, is a parasitic infection that should always be considered in dermatologic patients returning from vacation in endemic countries.

Introduction

Leishmaniasis encompasses a wide spectrum of chronic parasitic infections in humans caused by Leishmania protozoans. It has a worldwide distribution and is endemic in over 90 countries, and its transmission occurs via the bite of infected female sandflies.[1,2] This disease shows important clinical pleomorphism owing to the interaction between host and parasitic factors, and several clinical patterns have been identified, including cutaneous, mucocutaneous, and visceral forms. Depending on its geographical origin, leishmaniasis can be classified as Old World (Asia, Africa, and Southern Europe) or New World (the Americas) disease, which has prognostic implications. Whereas Old World cutaneous leishmaniasis is typically self-limited over several months, New World disease is less likely to spontaneously resolve and active treatment is often necessary.[1-3] Given the increase in travel and migration in recent decades, several dermatologic diseases in returning travelers have emerged, with variable etiologies, including infectious causes. In fact, an increase in cases of imported cutaneous leishmaniasis and mucocutaneous leishmaniasis has been recorded in many countries, and this parasitic infection is considered by the World Health Organization to be one of the most important neglected tropical diseases globally.[2-4]

Case Synopsis

We present the cases of a 50-year-old man and a 57-year-old woman, both with Fitzpatrick phototype III and no relevant past medical history, who presented with a

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3-month history of asymptomatic ulcerated plaques on the lower limbs that began 3 weeks after returning from vacation in Costa Rica, where they reported hiking in the jungle and experiencing unknown insect bites. The patients denied fever, weight loss, diaphoresis, or abdominal pain. Physical examination revealed non-tender, erythematous, firm, ulcerated plaques with well-defined borders and a necrotic center on their lower limbs. The man had multiple bilateral large lesions (**Figure 1**). The woman had a single lesion on her thigh (**Figure 2**). There were no lymphadenopathies or hepatosplenomegaly.

The clinical hypotheses of cutaneous leishmaniasis, cutaneous mycobacterial infection, and subcutaneous mycosis were considered. Laboratory examination revealed peripheral eosinophilia (800 cells/µL) and elevated C-reactive protein (2 mg/dL) in both patients, and was otherwise normal. Abdominal ultrasound was unremarkable. Histopathologic examination revealed ulceration and pseudoepitheliomatous hyperplasia of the epidermis, with a dense nodular inflammatory infiltrate involving the full thickness of the dermis and subcutis, composed of coalescent suppurative caseating granulomas, without visible microorganisms (including amastigotes) on hematoxylin-eosin, Periodic Acid Schiff, Giemsa, and Ziehl-Neelsen stains (**Figure 3** and **Figure 4**). These histopathologic findings were consistent with cutaneous mycobacterial or fungal infection, or cutaneous leishmaniasis, requiring clinicopathologic and microbiological correlation. Mycologic and mycobacterial examinations (direct and cultural studies and polymerase chain reaction [PCR]) were negative. PCR assay of the cutaneous biopsy identified *Leishmania* spp. We established the diagnosis of New World cutaneous leishmaniasis, and further sequencing was initiated to determine the species.

Because the man had a severe presentation (multiple long-standing large lesions with progressive worsening) and antimonial drugs and miltefosine were unavailable, he was treated with intravenous liposomal amphotericin B for 10 days (total dose 40 mg/kg), with no complications. The woman had a milder presentation and was concerned about developing a round scar, so we discussed therapeutic options and decided on surgical excision of the lesion along with systemic treatment using oral fluconazole 200 mg daily for 6 weeks. Complete resolution was documented in both patients after 2 months. Sequencing later revealed a 100% match to *Leishmania braziliensis* (Viannia subgenus), which is endemic in Costa Rica, thus confirming the diagnosis.[4] No signs of recurrence or mucocutaneous leishmaniasis were observed at 2 years of ongoing follow-up.

Case Discussion

Leishmaniasis, considered by the World Health Organization a critical neglected tropical disease globally, encompasses a spectrum of chronic vector-borne parasitic infections with a worldwide distribution and several clinical patterns.[1,2,5] The distinctive clinical pleomorphism of leishmaniasis, which depends on geographical origin (Old World versus New World), species, and host factors, is reflected in these patients.[1,2,5] Although they were infected in the same geographical area with the same species, the disease severity and presentation differed.

Diagnosing cutaneous leishmaniasis is challenging and relies on clinical manifestations, epidemiology, histopathology, and microbiology.[5,6] These patients posed a greater challenge because of atypical histopathologic features, specifically caseating granulomas and the absence of amastigotes. In fact, the histopathology of cutaneous leishmaniasis varies with disease duration: early lesions exhibit a macrophage-rich infiltrate with amastigotes, whereas long-standing lesions show granulomatous inflammation without amastigotes and may exhibit caseous necrosis, as observed in the present case.[6] Therefore, microbiological correlation is essential, and PCR is the most sensitive and specific test for *Leishmania* identification.[3,5,6]

Treatment recommendations are variable, with limited evidence and a lack of safe and effective options. Although cutaneous leishmaniasis may be self-limited, New World disease (especially when caused by species of the *Viannia* subgenus) has a worse prognosis and systemic treatment is necessary. Species identification takes time, and in such cases, treatment should be promptly initiated, guided by clinical manifestations and epidemiologic context.[5,6] The pleomorphism of our patients allowed us to choose different treatments, both of which were effective. Although pentavalent parenteral antimonial drugs remain the first-line treatment, liposomal amphotericin B is increasingly used because of availability, safety, and reduced hospital stay.[3,5-8] Fluconazole has also been shown to be safe and effective and may be used in milder cases.[6,7]

Knowledge of leishmaniasis is limited among travelers and physicians, and an increase in cases of imported cutaneous and mucocutaneous leishmaniasis has been recorded in many countries because of increased travel to risk areas.[3] Therefore, it is crucial that physicians are familiar with this parasitic infection, especially in returning travelers, because timely diagnosis and prompt treatment are essential to prevent complications and to limit the development of scars in cosmetically sensitive areas.

Conclusion

These 2 cases of New World cutaneous leishmaniasis in returning travelers demonstrate the clinical heterogeneity of cutaneous leishmaniasis, even among individuals infected in the same endemic region. Despite being infected with the same species, the patients exhibited markedly different clinical presentations, emphasizing the complex interaction between host factors and parasite factors in disease expression. Diagnosis was particularly challenging because of atypical histopathologic features and the absence of detectable organisms on routine staining, highlighting the critical role of PCR in establishing a definitive diagnosis.

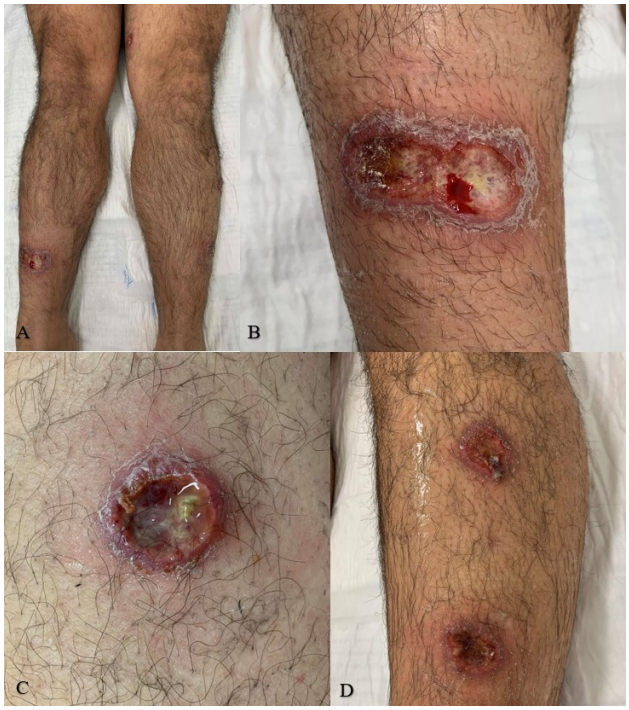

Figure 1. *Clinical images of cutaneous leishmaniasis in 50-year-old man revealing erythematous, asymptomatic, firm ulcerated plaques with well-defined elevated borders and a necrotic center on the lower limbs.* ***(A)*** *Two coalescent lesions on the anterior aspect of the right leg.* ***(B)*** *One lesion on the medial aspect of the left thigh.* ***(C, D)*** *Two lesions on the lateral aspect of the left leg.*

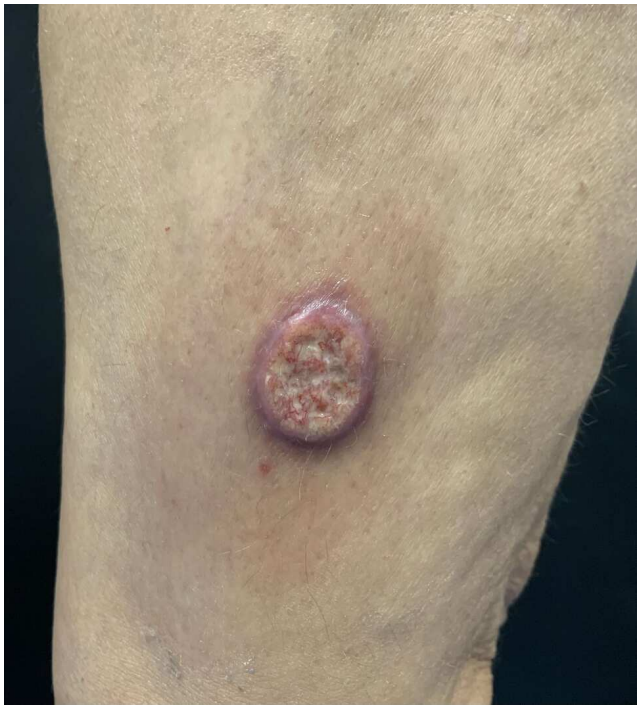

Figure 2. *Clinical image of cutaneous leishmaniasis in 57-year-old woman revealing a single erythematous, asymptomatic, firm ulcerated plaque with well-defined elevated borders and a necrotic center on the lateral aspect of the right thigh.*

Therapeutic approaches were individualized for each patient based on disease severity, lesion burden, and patient preferences. Both patients achieved complete resolution within 2 months and remained disease free with no evidence of recurrence or mucosal involvement at 2 years of follow-up. These cases highlight that cutaneous leishmaniasis, in all its versatile and challenging presentations, is a parasitic infection that should always be considered in dermatologic patients returning from vacation in endemic countries. They further demonstrate that prompt and tailored treatment can lead to good outcomes while minimizing complications and long-term sequelae.

Authors' note

The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. All authors have seen and approved the manuscript for submission and publication. The authors certify that they have obtained all appropriate patient consent forms. There are no funding sources or conflicts of interest to declare.

Potential conflicts of interest

The authors declare no conflicts of interest.

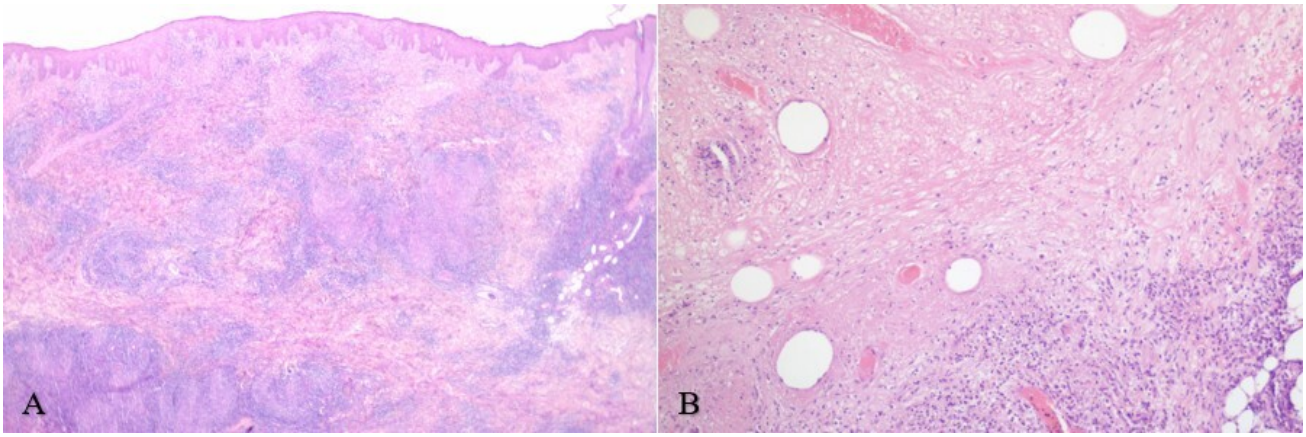

Figure 3. *Histopathologic examination of cutaneous leishmaniasis in 50-year-old man.* ***(A)*** *Pseudoepitheliomatous hyperplasia of the epidermis with a dense nodular inflammatory infiltrate in the full thickness of the dermis (hematoxylin-eosin, original magnification ×25).* ***(B)*** *Infiltrate composed of coalescent suppurative caseating granulomas, with numerous plasma cells, neutrophils, lymphocytes, and histiocytes (hematoxylin-eosin, original magnification ×100). No microorganisms (including amastigotes) were visible on hematoxylin-eosin, Periodic Acid Schiff, Giemsa, or Ziehl-Neelsen stains.*

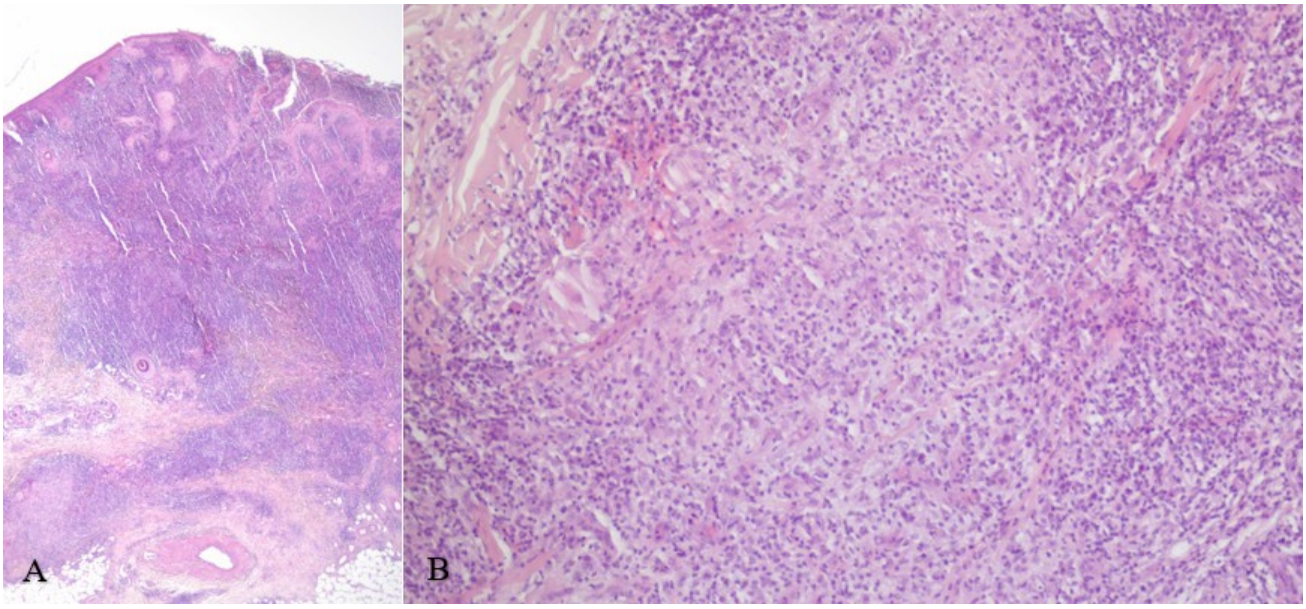

Figure 4. *Histopathologic examination of cutaneous leishmaniasis in 57-year-old woman.* ***(A)*** *Pseudoepitheliomatous hyperplasia of the epidermis with a dense nodular inflammatory infiltrate in the full thickness of the dermis (hematoxylin-eosin, original magnification ×16).* ***(B)*** *Infiltrate composed of coalescent suppurative caseating granulomas, with numerous plasma cells, neutrophils, lymphocytes, and histiocytes (hematoxylin-eosin, original magnification ×100). No microorganisms (including amastigotes) were visible on hematoxylin-eosin, Periodic Acid Schiff, Giemsa, or Ziehl-Neelsen stains.*

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