

# Cutaneous Leishmaniasis: An Emerging Infectious Disease in Travelers

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## PRACTICE POINTS

- Cutaneous leishmaniasis is an emerging infectious disease that may be misdiagnosed due to its rarity and varied clinical presentation as well as the limited use of tissue biopsy in general practice.
- United States health care practitioners who evaluate patients with new isolated skin lesions and a history of recent travel to Mexico or South or Central Americas should consider cutaneous leishmaniasis in the differential diagnosis.
- Whenever possible, travelers to rural areas of Mexico and South and Central Americas should be educated about strategies to avoid arthropod bites, such as wearing protective clothing and using insect repellents.

*Leishmaniasis describes any of 3 diseases caused by protozoan parasites of the genus Leishmania, the most common of which is cutaneous leishmaniasis. The majority of cutaneous cases occur in Central and South America, the Mediterranean basin, the Middle East, and Central Asia. Most cases diagnosed among nonmilitary personnel in the United States are acquired in Mexico and Central America. Here, we present the case of an American tourist who developed localized cutaneous leishmaniasis 2 weeks after returning from Costa Rica. After undergoing several unsuccessful rounds of empiric antibiotic treatment for a presumed Staphylococcus aureus skin infection, the patient was referred to our dermatology clinic*

*where cutaneous leishmaniasis was diagnosed by tissue biopsy. This case highlights the importance of cutaneous leishmaniasis as an emerging infectious disease that may be misdiagnosed due to its rarity and varied clinical presentation as well as the limited use of tissue biopsy in general practice. We also provide relevant background information on cutaneous leishmaniasis, a rhyming poem, and an illustration in order to promote greater awareness of this disease and assist clinicians with its diagnosis.*

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**L**eishmaniasis describes any disease caused by protozoan parasites of the genus *Leishmania*<sup>1</sup> and can manifest in 3 different forms: cutaneous (the most common); mucosal, a destructive metastatic sequela of the cutaneous form; and visceral, which is potentially fatal.<sup>2</sup> According to the World Health Organization, the leishmaniasis are endemic in 88 countries.<sup>3</sup> It is estimated that 95% of cutaneous cases occur in the Americas (most notably Central and South America), the Mediterranean basin, the Middle East, and Central Asia.<sup>2</sup> Most cutaneous cases diagnosed among nonmilitary personnel in the United States are acquired in Mexico and Central America.<sup>4</sup> In Central and South America,

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the causative human pathogens include species of the *Leishmania* (*Viannia*) complex (eg, *Leishmania panamensis*, *Leishmania braziliensis*, *Leishmania guyanensis*, *Leishmania peruviana*) and the *Leishmania mexicana* complex (eg, *Leishmania mexicana*, *Leishmania amazonensis*, *Leishmania venezuelensis*). All of these species can cause localized cutaneous lesions, but only *L panamensis*, *L braziliensis*, and *L guyanensis* are associated with metastatic mucosal lesions. In Central and South Americas, only *Leishmaniasis chagasi* (also known as *Leishmaniasis infantum*) is known to cause visceral leishmaniasis.<sup>5</sup>

### Case Report

A 26-year-old man was referred to the dermatology clinic by his primary care provider for evaluation of a nonhealing sore on the left volar forearm of 6 weeks' duration. The patient described the initial lesion as a red bump resembling a mosquito bite. Over 6 weeks the papule evolved into an indurated plaque with painless ulceration. The patient's primary care provider had prescribed antibiotics for a presumed *Staphylococcus aureus* infection of the skin 5 weeks prior to presentation; however, the lesion continued to enlarge in size, resulting in referral to our dermatology clinic.

Skin examination revealed a solitary, 4-cm, painless, ulcerated plaque on the left volar forearm (Figure 1). No lymphadenopathy was noted. The patient reported that he had returned from a mission trip to rural Costa Rica 2 weeks prior to the appearance of the lesion. His medical history was otherwise unremarkable and his vital signs were within normal limits. Our initial differential diagnosis included pyoderma gangrenosum, Sweet syndrome, cutaneous leishmaniasis, and an insect bite.

Histopathologic study of a 5-mm punch biopsy specimen from the lesion showed a dense nodular and diffuse lymphohistiocytic infiltrate containing foci of suppuration. Within these suppurative foci were histiocytes parasitized by intracellular organisms that appeared to be of uniform size and shape on Giemsa staining, all of which are considered to be pathognomonic features of cutaneous leishmaniasis<sup>6</sup> (Figures 2 and 3). The dermatopathologist's diagnosis of cutaneous leishmaniasis was confirmed by the Centers for Disease Control and Prevention. The species was identified by polymerase chain reaction (PCR) as *L panamensis*.

The patient was treated with intravenous sodium stibogluconate 20 mg/kg for 20 consecutive days as recommended by expert consensus. The decision to treat a frequently self-limited cutaneous lesion with a highly toxic systemic drug was based on the small but real risk of metastatic mucosal lesions,

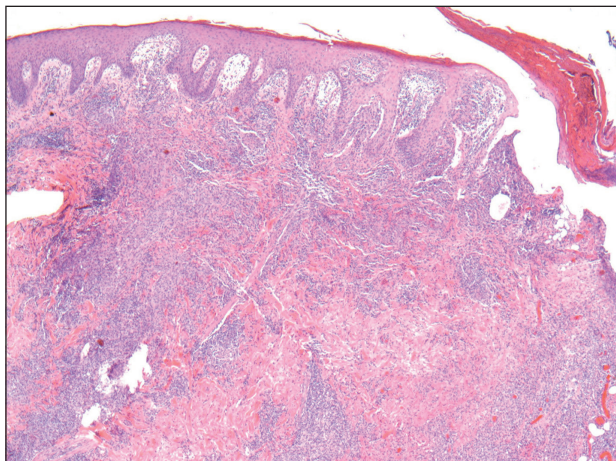


**Figure 1.** Nonhealing, pink, crusted plaque with central ulceration on the left volar forearm.

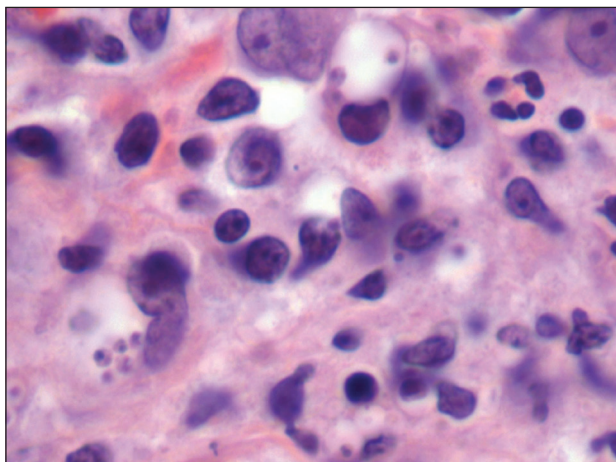
which is caused by the *Viannia* subgenus, including *L panamensis*. Of note, sodium stibogluconate and other antimony drugs are not sold in the United States. Sodium stibogluconate is approved by the US Food and Drug Administration to be distributed by the Centers for Disease Control and Prevention under a protocol requiring baseline and weekly electrocardiograms and monitoring of patients' creatinine, transaminase, lipase, amylase, and complete blood count levels.<sup>7</sup> Our patient tolerated treatment but experienced mild to moderate flulike symptoms. The patient experienced no remarkable sequelae other than scarring in the affected area. He was warned to notify his health care providers of any persistent nasal symptoms, including nasal stuffiness, mucosal bleeding, and increased secretions, heralding the possibility of mucosal metastasis.

### Comment

The true incidence of cutaneous leishmaniasis in American travelers returning from Mexico and South and Central Americas is not known. The best incidence estimates are based on the number of



**Figure 2.** Dense nodular and diffuse lymphohistiocytic infiltrate containing foci of suppuration (H&E, original magnification  $\times 10$ ).



**Figure 3.** Histiocytes parasitized by intracellular organisms of uniform shape and size on Giemsa staining (original magnification  $\times 1000$ ).

physician requests for sodium stibogluconate and travel surveillance data collected by the Centers for Disease Control and Prevention. One study estimated the incidence of cutaneous leishmaniasis in Americans to be 1 case per every 100,000 travelers to Mexico.<sup>9</sup> Data on the incidence of cutaneous leishmaniasis in American travelers seen in travel clinics for skin lesions gives a different perspective.<sup>10</sup> Leishmaniasis is one of the most common dermatologic diseases seen in patients (European, North American, and other) returning from South America, accounting for 143 of every 1000 patients diagnosed with a skin disease acquired in South America.

Although males are thought to be at higher risk for cutaneous leishmaniasis infection than females, other demographic and behavioral risk factors are not well defined. In a case series of US travelers diagnosed with cutaneous leishmaniasis between January 1985 and April 1990, Herwaldt et al<sup>9</sup> found that 46% (27/59) were conducting field studies, while 39% (23/59) were tourists, visitors, or tour guides. At least 15 of the 58 travelers interviewed (26%) were in forested areas for 1 week or less, and of these 15 respondents, at least 6 had a maximum exposure of 2 days.<sup>9</sup>

Evidence suggests that cutaneous leishmaniasis is inefficiently diagnosed in the United States. One study showed that some patients may consult up to 7 physicians before a definitive diagnosis is made, and the median time from noticing eruption of the lesions to definitive treatment was 112 days.<sup>9</sup> Several factors may contribute to delays and inefficiencies in diagnosis. First, the lesions of cutaneous leishmaniasis are varied in morphology, and although ulcers are thought to be the most commonly presenting lesions,<sup>11</sup> there are no specific morphologic features that are pathognomonic for cutaneous leishmaniasis. Second, the temporal association with travel to endemic countries is not necessarily apparent, with lesions developing gradually or weeks after the patient returns home. In the one study, 17% (10/58) of patients were home for more than 1 month before they noticed skin lesions.<sup>9</sup> Finally, definitive diagnosis requires biopsy or scraping of the lesion followed by PCR, special histopathological staining (Giemsa), or culture. Polymerase chain reaction is currently the best means of identifying the causative *Leishmania* species.<sup>12-14</sup> However, since skin biopsies are not routine in primary care settings and few practitioners are familiar with PCR for identification of leishmaniasis, diagnosis is typically made only after referral to a specialist.

Leishmaniasis transmission occurs in diverse geographical settings though a variety of mechanisms (Figure 4). The morphology of cutaneous leishmaniasis varies and may include papules, nodules, psoriasiform plaques, or ulcers. The differential diagnosis may include staphylococcal skin infection, insect bite, cutaneous neoplasm, pyoderma gangrenosum, sporotrichosis, blastomycosis, chromomycosis, lobomycosis, cutaneous tuberculosis, atypical mycobacterial infection, syphilis, yaws, leprosy, Hansen disease, and sarcoidosis. A definitive diagnosis can be made only after identifying the causative parasite. A scraping or punch biopsy taken from a cleaned lesion provides an adequate sample. Identification can then be accomplished by histopathology, tissue culture, or PCR.<sup>5</sup>



**Figure 4.** *Leishmania* species can infect humans in diverse geographical scenarios. In Costa Rica (left), *Leishmania panamensis* and *Leishmania braziliensis* infection is common in locals and tourists. Forest rodents serve as the reservoir hosts and transmission is by the bite of the sand fly (center). In Iraq (top right), *Leishmania major* infection has been reported in soldiers. Reservoir hosts include desert rodents, and transmission occurs through the bite of the sand fly. *Leishmania tropica* infection is common in Kabul (bottom right) and occurs in humans, dogs, and rodents with transmission by the bite of the sand fly. Illustration by Elizabeth Noble Ergen, MD, Vanderbilt University Medical Center (Nashville, Tennessee).

We present a rhyme that can be used to promote greater awareness of cutaneous leishmaniasis among US health care practitioners:

A global traveler begins to unpack  
And on his leg finds an ulcerated plaque.  
The possibilities are many,  
Numbering far more than 20.  
Leishmaniasis is a lurking issue,  
So the savvy physician tests the tissue.

Although clinical resolution of cutaneous leishmaniasis usually occurs over months to years, the unsightly appearance of the lesions as well as the potential for scarring and mucosal metastasis (associated with some species) drives medical treatment.<sup>15</sup> Pentavalent antimonial drugs, which have been the mainstay of treatment for more than 50 years,

remain the most popular treatment for cutaneous leishmaniasis. Two antimony compounds, sodium stibogluconate and meglumine antimoniate, often lead to clinical cure in less than 1 month<sup>7</sup>; however, these drugs are far from ideal because of the inconvenience of obtaining them, emerging parasite resistance, long treatment course, parenteral route of administration, and serious side effects including infusion reactions, arrhythmias, pancreatitis, and liver toxicity. Moreover, the subclinical persistence of cutaneous leishmaniasis years after treatment and clinical cure is common. There have been reports of spontaneous disease reactivation in immunocompromised individuals, and *Leishmania* has been detected in old cutaneous leishmaniasis scars on PCR testing.<sup>16-18</sup> Other therapies that have been used to treat cutaneous leishmaniasis include allopurinol, aminosidine sulphate, amphotericin B, the Bacillus Calmette–Guérin vaccine, cotrimoxazole, cryotherapy, dapsone, fluconazole, itraconazole, ketoconazole, laser therapy, metronidazole, miltefosine, paromomycin, pentamidine, pentoxifylline, photodynamic therapy, rifampicin, and surgical excision of the entire lesion.<sup>8</sup> A 2009 Cochrane review of the various treatments for cutaneous leishmaniasis concluded that “no general consensus on optimal treatment has been achieved” and suggested “the creation of an international platform to improve the quality and standardization of future trials in order to develop a better evidence-based approach.”<sup>8</sup>

## Conclusion

Cutaneous leishmaniasis should be included in the differential diagnosis for travelers returning from endemic areas who present with new skin lesions. Since no specific lesion types are pathognomonic for cutaneous leishmaniasis, tissue biopsy for histopathology and PCR are essential for diagnosis. Prevention of cutaneous leishmaniasis hinges on appropriate counseling of travelers to endemic regions.

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