

Case presentation

Pink plaque on the arm of a man after a trip to Mexico: cutaneous leishmaniasis

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Abstract

Cutaneous leishmaniasis is a parasitic infection caused by protozoa of the *Leishmania* genus that presents as asymptomatic pink papules that may ulcerate. There are several species of *Leishmania* found in 98 endemic countries and whereas all are associated with cutaneous disease, only specific species can cause mucocutaneous or visceral disease. Although the diagnosis of cutaneous leishmaniasis can be confirmed with Giemsa staining of a biopsy or "touch prep" specimen, only speciation at specialized centers such as the Centers for Disease Control (CDC) can determine the risk of mucocutaneous or visceral disease. Treatment of cutaneous leishmaniasis is varied and depends on the extent of cutaneous disease and the risk of mucocutaneous or visceral disease.

Keywords: leishmaniasis, parasitic infection, Yucatan peninsula, topical therapy

Case synopsis

A 64-year-old man presented with an asymptomatic erosion on his left arm that appeared at the end of a trip to Mexico. During the trip, he stayed in Cancun and traveled inland on the Yucatan Peninsula. The patient was in good health and took no regular medications. He denied fevers, chills, or night sweats.

Physical examination showed a 2 cm pink plaque with slight erosion and hemorrhagic crust at the center on his left lateral proximal arm (Figure 1). The remainder of the physical examination was unremarkable.

Figure 1. Two centimeter pink plaque with slight erosion and hemorrhagic crust on the left lateral proximal arm



Histopathologic analysis of a skin biopsy of the plaque showed *Leishmania* amastigotes parasitizing macrophages and also located in the extracellular space (Figure 2). The organisms were highlighted with Giemsa staining (Figure 3). These findings were consistent with cutaneous leishmaniasis.

A sample was sent to the Centers for Disease Control (CDC) on Novy-MacNeal-Nicolle (NNN) medium for speciation by culture and polymerase chain reaction (PCR) to determine the risk of mucocutaneous disease. The culture and PCR results from the CDC showed infection with *L. mexicana*.

Given that *L. mexicana*, the causal organism in our patient's case, is not associated with mucocutaneous or visceral disease, the lesion was initially observed. Two months later, the patient developed a second ulcer several centimeters away in a lymphatic distribution and requested therapy at that time. Both lesions resolved completely within several weeks of combined cryotherapy, thermotherapy, and imiquimod.

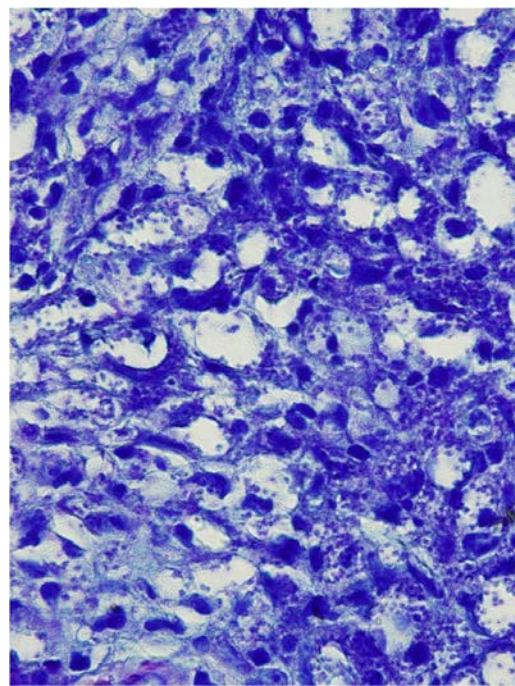
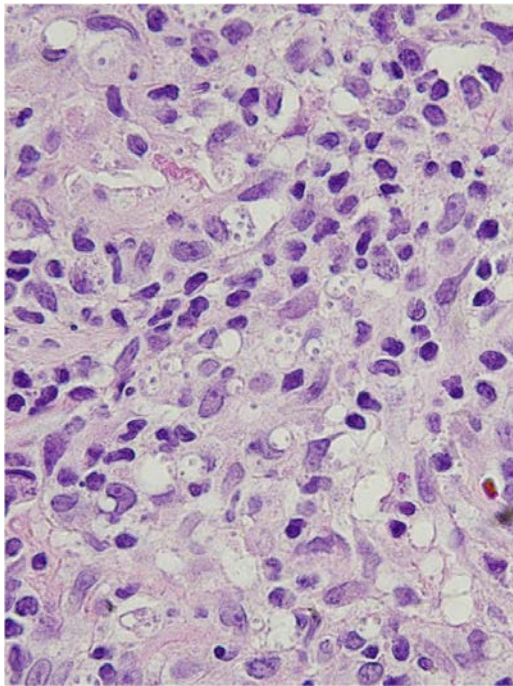


Figure 2. Hematoxylin and Eosin (1000x) staining of left lateral proximal arm skin biopsy shows parasitized macrophages and amastigotes in the extracellular space, consistent with cutaneous leishmaniasis. **Figure 3.** Giemsa staining (1000x) of left lateral proximal arm skin biopsy highlights the *Leishmania* organisms.

Discussion

Leishmaniasis manifests with cutaneous, mucocutaneous, or visceral disease [1]. All species can cause cutaneous disease, which generally resolves spontaneously [2]. However, certain *Leishmania* species in Latin America, including in the inland Yucatan peninsula, can cause highly destructive mucocutaneous disease [3-5]. The diagnosis of leishmaniasis can be confirmed with Giemsa staining of a biopsy specimen or "touch prep" from the ulcer surface showing *Leishmania* amastigotes parasitizing macrophages and invading the extracellular space [2, 4]. However, different *Leishmania* species appear the same on Giemsa stain and so histology alone is not helpful in speciating the specific pathogen. When inoculation occurs in a geographic region endemic to strains that may cause mucocutaneous or visceral disease, further speciation should be attempted using polymerase chain reaction (PCR) or culture on Novy-MacNeal-Nicolle (NNN) medium, both of which can be obtained from specialized facilities such as the CDC in the United States [1, 2, 5, 6].

In the United States, the CDC can perform histologic and microbiologic analysis of skin biopsies, aspirates, and scrapings, as well as perform serologic testing when *L. donovani* species complex is the pathogen. When specimen collection can be planned in

advance, it is best to contact the CDC Division of Parasitic Diseases and Malaria (Phone, 404-718-4175; email, DPDx@cdc.gov) to have a collection kit sent to the practitioner with all necessary forms and supplies, including NNN medium; if collection must be performed without prior notice, specimens for culture or PCR can be placed in a sterile vile with sterile buffered medium at a neutral pH, such as Roswell Park Memorial Institute (RPMI) medium. CDC form 50.34 can be obtained at the CDC website here: <http://www.cdc.gov/laboratory/specimen-submission/form.html>. In either scenario, specimens should be collected on Monday through Thursday to ensure prompt handling at the CDC laboratories with overnight delivery at room temperature (*not* on ice).

At a minimum, 2 full thickness biopsy specimens (e.g. two 3mm punch biopsies or 1 larger punch biopsy split into 2 full thickness sections) should be obtained from the edge of the newest and most active lesion, after removing superficial debris, sterilizing with 70% alcohol only, and anesthetizing with low concentration local anesthetic (e.g. 1% lidocaine). Place the first specimen in the sterile culture medium for culture and PCR and the second into 10% formalin for histologic review. A third specimen for impression smears ("touch prep") is highly recommended if possible; briefly and gently dab the specimen on gauze to remove excess blood, file it with a blade, and roll it with gentle pressure onto several sites on a glass slide to be fixed and Giemsa stained locally or at the CDC.

When possible, the CDC recommends that similar samples be obtained from adjacent, clinically non-involved skin. A variety of other samples can and should be obtained when possible to increase the sensitivity of the testing, including aspirates and dermal scrapings for Giemsa staining locally or at the CDC, and culture/PCR at the CDC. Detailed descriptions of all of these techniques and procedures can be obtained from the CDC's "Practical Guide for Specimen Collection and Reference Diagnosis of Leishmaniasis" at http://www.cdc.gov/parasites/leishmaniasis/resources/pdf/cdc_diagnosis_guide_leishmaniasis.pdf [6]. Further information can be obtained by consulting the CDC website (http://www.cdc.gov/parasites/leishmaniasis/health_professionals/index.html) or laboratory personnel.

Leishmaniasis is a parasitic infection of increasing global incidence caused by protozoal species of the *Leishmania* genus. The disease is divided into "Old World" and "New World" variants based on endemic area, which spans 98 countries [1]. Old World species are carried by the *Phlebotomus* sand fly and are endemic to Africa, Asia, and southern Europe; New World species are endemic in Latin America, where the *Lutzomyia* sand fly is the vector [1, 2].

Several weeks to months after a sand fly bite, the inoculation site develops a pink papule that enlarges and painlessly ulcerates. The ulcer often has an indurated border and may have fibrinous exudate or dry crust [1, 2, 5]. Initially localized cutaneous leishmaniasis may spread along lymphatics or disseminate to distant cutaneous surfaces [1, 2]. Mucocutaneous disease most commonly arises from *L. braziliensis* infection and features ulceration of mucous membranes (mouth and nose) with eventual severe tissue destruction [1, 2, 7]. Visceral leishmaniasis involves internal organs and can be life threatening; it is particularly severe in immunocompromised hosts [1, 2, 7, 8].

Therapy for cutaneous leishmaniasis is varied and depends on both clinical and microbiologic features [1, 7, 9-24]. Local therapies include cryotherapy, thermotherapy, intralesional pentavalent antimonials, paromomycin, and imiquimod. Oral medications include ketoconazole, fluconazole, and miltefosin. Parenteral therapies include pentamidine, and pentavalent antimonials.

Some of these systemic therapies—notably pentamidine and pentavalent antimonials—are highly toxic. Hence, although no universal therapeutic guidelines have been defined, two recent systematic reviews of treatment both emphasized the need for individualized management, based in part on each patient's presentation and potential for future morbidity [7, 9]. Cutaneous leishmaniasis, when caused by a species incapable of producing mucocutaneous or visceral disease, may be observed until resolution over 6-24 months [3]. However, local and sometimes systemic therapies may accelerate healing and reduce scarring [7, 9, 25]. Mucocutaneous and visceral leishmaniasis are treated systemically. Additionally, systemic therapy should be strongly considered in any patient with a cutaneous infection caused by a *Leishmania* species with potential for causing mucocutaneous disease [1, 2, 4, 5, 7, 9, 25, 26].

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