Cutaneous and mucocutaneous leishmaniasis

Differential diagnosis, diagnosis, histopathology, and management

Marc Z. Handler, MD,[a] Parimal A. Patel, MD,[a] Rajendra Kapila, MD,[b,c,d] Yasin Al-Qubati, MD,[e] and Robert A. Schwartz, MD, MPH, FRCP (Edin)[a,c,d,f]
Newark, New Jersey, and Taiz, Yemen

Learning objectives
After completing this learning activity, participants should be able to describe the complexities in the management of cutaneous lesions of leishmaniasis and identify appropriate treatment plans for patients with cutaneous leishmaniasis.

Disclosures
Editors
The editors involved with this CME activity and all content validation/peer reviewers of the journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Authors
The authors involved with this journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Planners
The planners involved with this journal-based CME activity have reported no relevant financial relationships with commercial interest(s). The editorial and education staff involved with this journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

The diagnosis of leishmaniasis can be challenging because it mimics both infectious and malignant conditions. A misdiagnosis may lead to an unfavorable outcome. Using culture, histologic, and/or polymerase chain reaction study results, a diagnosis of leishmaniasis can be established and treatment initiated. Appropriate management requires an accurate diagnosis, which often includes identification of the specific etiologic species. Different endemic areas have varying sensitivities to the same medication, even within individual species. Species identification may be of practical value, because infections with select species have a substantial risk of visceral involvement. In addition, HIV and otherwise immunocompromised patients with leishmaniasis have a propensity for diffuse cutaneous leishmaniasis. For most New World Leishmania species, parenteral antimonial drugs remain the first line of therapy, while Old World species are easily treated with physical modalities. Historically, live organism vaccination has been used and is effective in preventing leishmaniasis, but results in an inoculation scar and an incubation period that may last for years. A more effective method of vaccination would be welcome. (J Am Acad Dermatol 2015;73:911-26.)

Key words: antimony; carbon dioxide slush; CDC; HIV; Leishmaniasis; ketoconazole; miltefosine; protozoa; sodium stibogluconate; tropical disease; vaccination; vaccine.

DIFFERENTIAL DIAGNOSIS

Key points

- **Leishmaniasis may mimic other infectious diseases and a variety of malignancies**
- **A second or third infection may coexist with cutaneous leishmaniasis**

Leishmaniasis has many clinical manifestations and may appear similar to a wide variety of other conditions[1-3] (Table I; Fig 1). Differentiation between conditions that mimic cutaneous leishmaniasis may require microbiologic, cytologic, and/or histologic evaluation.[4] These include disorders that

From Dermatology,[a] Infectious Diseases,[b] Medicine,[c] and Preventive Medicine and Community Health,[d] Rutgers New Jersey Medical School; Dermatology,[e] Taiz University School of Medicine, Yemen; and the Rutgers School of Public Affairs and Administration, Newark.[f]
Funding sources: None.
Conflicts of interest: None declared.
Accepted for publication September 5, 2014.
Reprint requests: Robert A. Schwartz, MD, MPH, FRCP (Edin), Professor and Head, Dermatology, Rutgers University New Jersey Medical School, 185 S Orange Ave, Newark, NJ 07103-2714. E-mail: roschwar@cal.berkeley.edu.
0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2014.09.014
Date of release: December 2015
Expiration date: December 2018

Abbreviations used:

CDC:	Centers for Disease Control and Prevention
HLA:	human leukocyte antigen
NADPH:	nicotinamide adenine dinucleotide phosphate
PCR:	polymerase chain reaction
RFHT:	radiofrequency-induced heat therapy
RPMI:	Roswell Park Memorial Institute (medium)

are infectious, malignant, or other disorders such as pyoderma gangrenosum.[5]

In patients with a travel history to regions where leishmaniasis is endemic, leishmaniasis must be considered in the differential diagnosis of those having nonspecific systemic symptoms, such as fever, or examination findings, such as splenomegaly. A major obstacle to diagnosis is unfamiliarity with leishmaniasis. In 48% of American cases, it was the patient or patient's family who first considered the possibility of leishmaniasis.[6] Patients with a history of malignancy that may clinically appear similar to cutaneous or visceral leishmaniasis should have the diagnosis of cutaneous or visceral leishmaniasis entertained (Table II). A delay in diagnosis, especially in visceral leishmaniasis, may prove fatal. In addition, leishmaniasis in immunosuppressed patients, such as those with leukemia or AIDS, may be aggressive, with visceral leishmaniasis refractory to treatment.[7] Because of chronic inflammation from a Leishmania infection, a primary skin cancer may develop at the site of an old leishmanial scar.[7] Chronic relapsing cutaneous leishmaniasis may also clinically resemble lupus vulgaris, a type of cutaneous tuberculosis, and tuberculoid leprosy.[8,9] Cancer patients may not have an immune system that is able to produce a fever or splenomegaly, and therefore a clinical suspicion for leishmaniasis should be maintained in appropriate settings.[7] In addition, those with immunodeficiencies may develop cryptic forms of infection with Leishmania. *Leishmania infantum* has been found in bone marrow aspirates in 11% of patients with HIV in the Mediterranean basin.[10] The initiation of antiretroviral therapy has been shown to decrease the prevalence of clinical signs of visceral leishmaniasis in those with HIV.[11]

Diffuse cutaneous leishmaniasis can be clinically indistinguishable from other infectious diseases[12] (Table III). Diffuse cutaneous leishmaniasis may mimic post–kala-azar dermal leishmaniasis (PKDL), but only the latter condition will have visceral disease.

When diagnosing cutaneous leishmaniasis, dual and triple infections should also be considered. Diffuse cutaneous leishmaniasis may mask another disease, such as leprosy or HIV disease.[13]

Table I. Differential diagnosis of cutaneous leishmaniasis

Infectious
Ecthyma
Furuncle
Carbuncle
Sporotrichosis
North American blastomycosis
Paracoccidiomycosis
Tuberculosis cutis
Syphilitic gumma
Yaws
Prototheca infection
Condyloma acuminata
Lupus vulgaris (similar to leishmania recidivans)
Tuberculoid leprosy
Cutaneous furuncular myiasis
Tungiasis
Neoplastic
Basal cell carcinoma
Squamous cell carcinoma
Lymphoma
Other
Insect bite
Xanthoma tuberosum
Sarcoidosis
Pyoderma gangrenosum

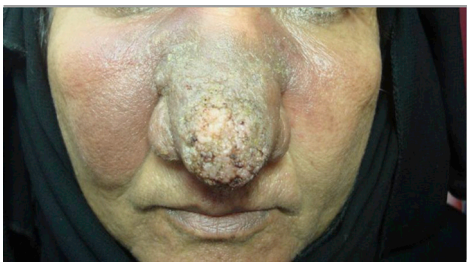

Fig 1. Lupoid plaque of the nose in a woman with Old World leishmaniasis.

Mucocutaneous leishmaniasis causes destructive changes suggestive of syphilis, yaws, rhinoscleroma, and oral squamous cell carcinoma[4] (Table IV). Unlike syphilis and yaws, mucocutaneous leishmaniasis does not cause destruction of cartilage and, unlike rhinoscleroma, does not produce nasal septum perforation.[4,14]

DIAGNOSIS

Key points

- **World travel has brought leishmaniasis to nonendemic regions**
- **The US Centers for Disease Control and Prevention accepts submissions for leishmaniasis testing worldwide**