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Authors
Oetken, Tara
Hiscox, Bryan
Orengo, Ida
et al.

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Cutaneous leishmaniasis mimicking squamous cell carcinoma

Tara Oetken MD, Bryan Hiscox MD, Ida Orengo MD, Theodore Rosen MD

Affiliations: Department of Dermatology, Baylor College of Medicine, Houston, Texas

Corresponding Author: Ida Orengo MD, Department of Dermatology, Lee and Joe Jamail Specialty Care Center, 1977 Butler Blvd. Suite E6.200, Houston, TX 77030, Email: iorengo@bcm.edu

Abstract

A 41-year-old man from Cuero, Texas with a non-healing lesion on his left cheek was referred to our clinic for removal of a squamous cell carcinoma. The patient first noticed a "pimple" on his left cheek 3-4 months prior to presentation. When the lesion began to grow he presented to his primary care physician and a biopsy was taken, showing "atypical squamous cell proliferation." Mohs surgery was performed and the nodule was removed with no evidence of malignancy seen on histopathology. Upon review of the surgical biopsies by consulting pathologists, the diagnosis of leishmaniasis was established and later confirmed by the Center for Disease Control and Prevention (CDC) as Leishmania mexicana. The patient was referred to infectious disease specialists for further management.

Keywords: leishmaniasis; cutaneous leishmaniasis, Leishmania mexicana

Introduction

Leishmaniasis is a disease with a wide variety of presentations, from fatal systemic disease to self-limited cutaneous forms. The three forms of the disease are: visceral (the most deadly and often referred to as kala-azar), cutaneous (the most common), and mucocutaneous [1]. According to the World Health Organization (WHO), leishmaniasis is endemic in 88 countries with 350 million persons at risk. Approximately 1.5 million new cases of cutaneous leishmaniasis are reported annually, with two thirds of cases in six countries: Afghanistan, Algeria, Brazil, Colombia, Iran, and Syria [1, 2].

We report a patient with cutaneous leishmaniasis misdiagnosed as squamous cell cancer in order to demonstrate the importance of including leishmaniasis in the differential diagnosis of non-healing lesions in regions previously considered free of disease. We discuss the classic clinical course and histological characteristics of the disease as well barriers to diagnosis and suggest changes for improving the recognition of leishmaniasis.

Case Synopsis

A 41 year-old from Cuero, Texas with no travel history to endemic areas and no previous medical history, first noticed a lesion of his left cheek in September 2014. As the nodule began to grow a biopsy was performed and revealed an acanthotic epidermis with areas of atypia, horn pseudocysts, squamous eddies, a fibrotic papillary dermis with dense dermal lymphocytic infiltrate, and atypical cells extending to the biopsy margins. The diagnosis of squamous cell carcinoma was given and complete excision was recommended. The patient was then referred to our center for Mohs surgery.

The patient was seen in clinic for removal of a 1.6 cm by 1.5 cm lesion (**Figure 1**), which appeared clinically consistent with squamous cell carcinoma (SCC). The lesion was removed using the Mohs technique. However, no frank malignancy was observed on frozen section.

The debulked specimen was sent to pathology for review (**Figure 2**). Two cultures were taken at the time of surgery, which were positive for Proteus mirabilis and Klebsiella oxytoca and the patient was started on cefuroximin. Fungal and acid-fast bacillus studies were negative. Sections sent to pathology revealed pseudoepitheliomatous hyperplasia with abundant vacuolated cells with small organisms displaying the "marquee" sign typical of leishmaniasis; the

Figure 1. *Clinical photograph of lesion prior to Mohs procedure showing a hyperkeratotic nodule consistent with cutaneous squamous cell carcinoma.*

diagnosis of cutaneous leishmaniasis was made. Two specimens were sent to the CDC in Atlanta, GA for further identification of species. One specimen was sent in formalin for histologic review, whereas the other was sent in buffered medium for culture and PCR. At the CDC the diagnosis of Leishmania mexicana was confirmed by PCR.

The patient was seen by an infectious disease specialist who recommended ketoconazole treatment. The patient declined treatment, and at follow up appointments no recurrence of disease was noted.

Case Discussion

Leishmaniasis is a polymorphic parasitic infection caused by the obligate intracellular protozoa of the genus Leishmania, which is transmitted by the bite of the female sandfly and contains approximately 21 species capable of infecting humans. [3, 4]. Leishmaniasis presents in 3 forms: visceral (VL), mucocutaneous (MCL), and cutaneous leishmaniasis (CL). CL is the most common manifestation of leishmaniasis with approximately 1.5-2 million new cases per year [5]. Although not as severe as the MCL or VL, the consequences of disease can be severe, including permanent scarring, disfigurement, possible dissemination of the parasite, and increased risk for skin cancer [6, 7].

Clinically, a typical CL lesion first appears as a small red papule, which is commonly mistaken for an MRSA infection or furuncle. Exposed body areas such as face or extremities are the most common location, which are unfortunately, also common areas where malignant neoplasms such as squamous cell carcinoma can occur. Within 1-3 months, the infection may progress into erythematous nodules, indurated or scaly plaques, or ulcers with raised borders [2, 8]. The lesions are pruritic, generally not painful, and are unresponsive to therapy with antibiotics or corticosteroids. Systemic symptoms are often absent, but have been reported. Typically, lesions heal spontaneously within 6 months to 3 years.

The diagnosis of CL is critical, both to avoid unnecessary treatment such as surgical intervention and for the initiation of proper therapy to reduce the risk of disease complications. [3, 5-8]. However, in non-endemic areas, clinical diagnosis is complicated by physicians' lack of experience with leishmaniasis, a wide clinical differential diagnosis, varying histopathological features, a lack of available screening tests, and the prolonged period from pathogen exposure to disease onset [4, 9, 10].

Classic histopathological findings include dense diffuse infiltrates of lymphocytes, plasma cells, and histiocytes with numerous grey-blue dots of Leishmania in the cytoplasm throughout the reticular dermis [9, 11]. However, leishmaniasis is known to present many atypical histopathological features. The only diagnostic feature on histological exam is the presence of amastigotes, which is highly dependent on the type of T cell response generated by the host [12, 13]. Without visualization of amastigotes, histopathological differentiation between leishmaniasis and other granulomatous skin diseases, malignant processes, cutaneous tuberculosis, and deep mycotic infection can be difficult [12]. Further complicating the diagnosis is the presence of pseudoepitheliomatous squamous hyperplasia, a response to chronic epithelial irritation seen in leishmaniasis, which can simulate SCC [11]. Overall, the sensitivity of histopathologic examination in the diagnosis of leishmaniasis ranges from 16-74% [13]. Whereas PCR offers a specificity of up to 100% and a 20-30% greater sensitivity than conventional methods, it is only available in specialized laboratories such as those of the CDC in

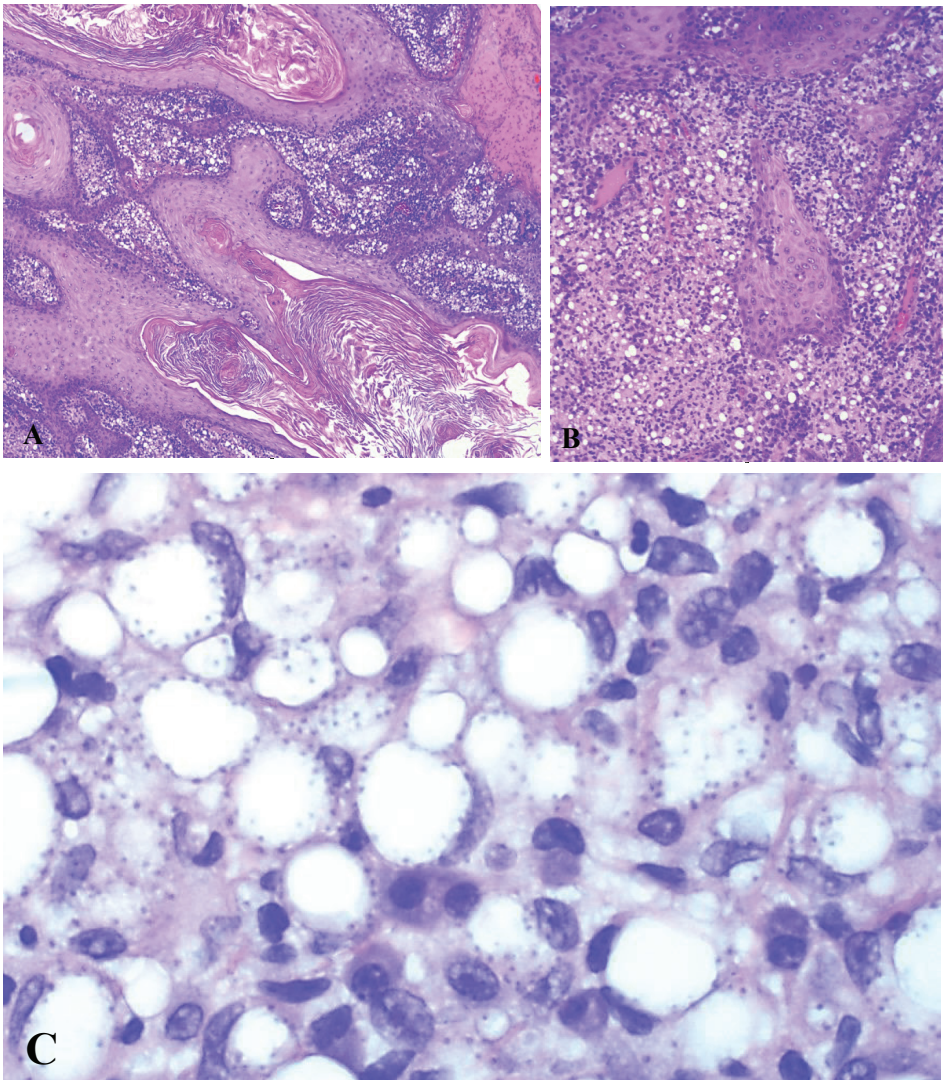

Figure 2. *Histology of the surgical specimen at 40X (A), 100X (B), and 400x (C) with hematoxylin-eosin. At high power, the amastigotes of Leishmania can be readily seen along the periphery of parasitized histiocytes.*

Atlanta [5].

Although the United States is not currently considered an endemic region, evidence suggests an increase in the incidence of Leishmania infections may be expected. Increased travel of civilians and military personnel to endemic areas means more exposure to vectors and thus, more disease. Clarke et al. note an increase in autochthonous CL in northeastern Texas and southeastern Oklahoma with 13 reported cases in an 8 year span from 2000-2007, when only 29 cases had been reported in a 93 year span from 1903-1996. The authors cite many factors for this increase including climate change providing a more hospitable environment for vector and reserved species, and increased human intrusion into previously unoccupied areas [4, 9, 10].

Conclusion

In conclusion, cutaneous leishmaniasis may present as many clinical entities. We report one of the first known cases of leishmaniasis mimicking SCC in the United States [9, 14]. The consequences of missed or delayed diagnosis include unnecessary clinical procedures, exposure to toxic therapies, scarring and disfiguration, risk of disseminated disease, and increased risk of skin cancer. Relying on histopathological examination alone may lead to under diagnosis of the disease as leishmaniasis shares many features with other granulomatous processes and can commonly mimic SCC. Owing to the lack of sensitivity of standard examination methods and leishmaniasis' wide spectrum of clinical presentation, we agree with our colleagues Boer et al. who recommend that PCR for Leishmania-specific DNA be performed during diagnosis in any unusual granulomatous dermatitis [9]. PCR provides the additional benefit of correlation of clinical and histopathological presentation with species for more reliable epidemiological data and studies. Additionally, we recommend leishmaniasis be added to the list of nationally reportable conditions [10].

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