Clinical Manifestation of Cutaneous Leishmaniasis Following a Mechanical Trauma

Dorothee Busch, MD¹, Christian Bogdan, MD¹,*, and Cornelia Erfurt-Berge, MD¹,*

Abstract
Unusual skin ulcers frequently represent a diagnostic challenge. When the most common disease entities such as arterial, venous or diabetic ulcers have been excluded, the question of further differential diagnoses and procedures arises. Other possible causes include chronic inflammatory diseases, neoplasia, self-inflicted wounds, primary infectious diseases and physical/chemical damage to the skin. To narrow down the differential diagnoses, a detailed history of the patient is essential, which also needs to include events further back in time.

Keywords
leg ulcer, leishmaniasis, delayed diagnosis, trauma

Case
A 43-year-old male patient was hospitalized with a persistent ulcer on his right lower leg. Three months ago, he contracted a deep laceration (diameter ca. 1 cm) at his right lower leg while sawing and cutting trees in the forest. At first, the patient cleaned the wound by himself using water, Band-Aids®, and zinc ointment. When the presumably contaminated wound persisted and increased in size, he consulted his family doctor who recommended the use of hydrocolloids as wound dressings. As the ulcer further progressed, the patient consulted the outpatient clinic of our dermatology department, where a swab was taken from the 5 × 6 cm affected area. Bacterial cultures were positive for Serratia rubidea, Enterococcus faecalis, and Peptoniphilus harei. One week later, a sample of granulation tissue yielded the growth of S. rubidea, E. faecalis, and Actinomyces odontolyticus; an infection with (environmental) mycobacteria was excluded by polymerase chain reaction and culture. Four weeks later, the patient was admitted to our inpatient ward due to the unusual presentation of the ulcer and the recalcitrant course of disease. At this time point, the wound measured 4 × 5 cm and showed small “satellite” lesions in the surrounding (Figure 1). There was no inguinal lymphadenopathy. The patient received intravenous antibiotics (4 g piperacillin plus 0.5 g tazobactam, 3 times a day). The wound was treated topically with an antiseptic solution (polyhexanide 0.04%) and dressed with an absorbent foam. On further questioning, the patient mentioned that he had returned from a 3-week vacation in Peru about 1 month prior to the traumatic leg injury. Except for a stopover in Peru.

Figure 1. Wound at the day of hospitalization. Four months prior to hospitalization, the patient had contracted a deep laceration at the very same site. Five months prior to hospitalization, the patient had returned from a vacation in Peru.

¹Universitätsklinikum Erlangen and Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg, Erlangen, Germany
²Shared senior authorship.

Corresponding Author:
Cornelia Erfurt-Berge, Universitätsklinikum Erlangen, Hautklinik Ulmenweg 18, Erlangen D-91054, Germany.
Email: cornelia.erfurt-berge@uk-erlangen.de
Lima, the patient spent his holiday in the province Tarapoto in Northern Peru. He further reported that he omitted to use an insect repellent while sitting at a riverside on his last day in Peru. Although he did not recall an insect bite on his right lower leg, he noticed around 200 small reddish punctures all over his body on the evening of the very same day and experienced severe discomfort with itching for the following 2 to 3 days. Another tissue biopsy was taken for histological, bacteriological, and parasitological analysis. Culture in modified Schneider’s insect cell medium and 18S rDNA polymerase chain reaction revealed the presence of *Leishmania* parasites, which were identified as *Leishmania (subgenus Viannia) guyanensis* using cytochrome b sequencing.1,2 The patient’s serum was positive for antibodies against viable *L. V. guyanensis* parasites using an indirect immunofluorescence assay (titer 1:200), but negative for antibodies against *L. major.*2

Following the diagnosis of cutaneous leishmaniasis, the antibiotic treatment was stopped and the patient received intravenous liposomal amphotericin B (3 mg/kg body weight/day) in combination with local heat treatment (up to 45°C for 30 minutes per day) for 10 days. Topical wound treatment was continued as described above. Continuous apyrexia, normal differential blood counts, normal size of spleen and liver as determined by abdominal sonography, and absence of otolaryngeal lesions ruled out visceral and mucosal leishmaniasis.

The treatment resulted in a rapid improvement and complete epithelialization of the wound within 2 weeks (Figure 2). A follow-up examination 5 months later showed irritation-free scar tissue, and the patient did not report any symptoms or discomfort related to the infection until today.

**Discussion**

In patients with atypical ulcers and a history of travel to an endemic area cutaneous leishmaniasis is a relevant differential diagnosis. Leishmaniasis is a disease in Mediterranean, subtropical, and tropical countries that is caused by intracellular parasites of the genus *Leishmania* and occurs in a cutaneous, mucocutaneous, or visceral form. It is transmitted by bites of sand flies.3,4 The clinical manifestation of leishmaniasis is determined by the species, strain, virulence, and dose of the infecting parasite, the site of intradermal inoculation, as well as by the genetic background, age, health, and immune status of the host.3,5 Consequently, there is a broad spectrum of manifestations of the disease, and a single species of *Leishmania* can cause lesions with diverse characteristics in different individuals and geographic regions.3,6-8 In general, there is a range from asymptomatic infection to potentially lethal visceral leishmaniasis.9 Whereas visceral leishmaniasis, also known as “kala-azar,” is a life-threatening infection with symptoms such as fever, cachexia, hepatosplenomegaly, pancytopenia, and hypergammaglobulinemia,10 cutaneous leishmaniasis usually manifests itself in the form of localized albeit chronic skin lesions, which are highly pleomorphic in their appearance. At first, an asymptomatic erythematous papule develops at the site of the sand fly bite, which later can turn into a vesicle, pustule, plaque, or an ulcer.11 The incubation period after the insect bite averages at several weeks, but can vary from days to many months or even years, which is highly relevant when taking the patients’ histories.10,12 Ulcerated lesions in Central and South America are typically painless (if not superinfected) and characterized by a raised, indurated, and erythematous border, a central depression, and granulation tissue.7,11 If untreated, the lesions ultimately heal over months to years and evolve into atrophic, initially hyperemic and later hypopigmented scars.10,13

Systemic treatment for cutaneous leishmaniasis caused by species of the *Leishmania Viannia* subgenus consists of amphotericin B,2,4 usually applied in a lipid-based formulation to reduce toxicity.14 Another treatment option is oral miltifosine, although the success rate is variable depending on the geographic region.15 In endemic areas, pentavalent antimony, either injected perilesionally or systemically, is still used for the treatment of American cutaneous leishmaniasis.11,12

Mechanical trauma and injuries have been sporadically described as triggers for the cutaneous manifestation of a so far asymptomatic *Leishmania* infection (reviewed in Wortmann et al12 and Mulvaney et al16). For example, Martins et al reported on a patient in whom cutaneous leishmaniasis was triggered by electrocoagulation.17 In other cases, minor traumas, like manipulating a pimple, a bee sting, or a submucosal nasal resection, were also sufficient to elicit the development of a *Leishmania* ulcer.12,18 Long19 reported a case of a 24-year-old North American Veteran, who was admitted with an enlarging *Leishmania* sore at the
forehead, after having been to the Panama Canal Zone on duty with the US army. He remembered a mechanical trauma at the site of the ulcer. Ten to 12 days after the trauma, the bump, which had only appeared red at first, enlarged and ulcerated. Importantly, in patients with already preexisting cutaneous leishmaniasis mechanical trauma at other body sites can trigger the appearance of additional Leishmania skin lesions, an observation known as (pseudo-) Koebner phenomenon.16,20 Both the trauma-induced primary manifestation of cutaneous leishmaniasis as well as the distant metastasis are thought to be due to the presence of Leishmania parasites in the blood and at extraneous skin sites.21,22 Based on the medical history of our patient, we assume that he had latent parasitemia following the insect bites in Peru when he contracted the laceration at his lower leg.

Taking detailed medical history including traveling to disease-endemic areas should always be the first step in diagnostics when approaching chronic wounds.23 Especially in cases of refractory ulcers, it is very important to consider the rarer causes for chronic wounds such as cutaneous leishmaniasis. As the incubation period for cutaneous leishmaniasis may last from weeks to several months,11 the ulcer may appear unrelated to the travel history for the treating physician and cause delays in diagnosis and treatment.

Acknowledgements
The authors wish to thank Heidi Sebald, Andrea Debus and Walter Geißdörfer (Microbiology Institute, University Hospital Erlangen) for carrying out the Leishmania cultures and the sequencing.

Declaration of Conflicting Interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD
Cornelia Erfurt-Berge https://orcid.org/0000-0002-3722-6383

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