Leishmania Recidiva Cutis in Morocco: About Two Cases

Awatif El Hakkouni¹, & Nabil Mansouri²
¹Avenzoar hospital Laboratory, Marrakech, Morocco.
²CHU Mohamed VI Pathology Laboratory, Marrakech, Morocco.
Corresponding Author: Dr. Awatif El Hakkouni
awatif.elhakkouni@hotmail.fr

ABSTRACT

In Morocco, leishmaniases are endemic diseases. Two forms of cutaneous leishmaniases are described: CL caused by Leishmania major and CL due to Leishmania tropica. These parasites are transmitted to humans by the bites of the infected female phlebotomine sand fly, a tiny, only 2–3 mm long insect vector. L. major is transmitted by Phlebotomus papatasii from the animal reservoir to humans. L. tropica is transmitted by P. sergenti from person to person. The World Health Organization considers CL a severely neglected disease and a category 1 emerging and uncontrolled disease. Leishmaniasis recidiva cutis LRC is an unusual complication of acute CL. It consists of active lesions around or inside the scar of classical CL that apparently clinically healed. It appears after a variable period of time. Its prevalence increasing especially in immunocompromised subjects. Diagnosis of LRC is often complicated by the scarcity of the microorganism in direct smear and tissue specimens. Actually, the management of CL and LRC is different from region to region and is mainly based on local expertise. In this paper, we report two cases of recurrent CL in two women, two years after the complete healing of the primary lesions. On the basis of the available anamnestic data, the possible pathogenesis of LRC in these particular cases is also discussed.

Keywords: Leishmania recidiva; amastigotes; pentavalent antimonial

1. INTRODUCTION

The leishmaniases are a group of diseases caused by protozoan parasites from more than 20 Leishmania species. These parasites are transmitted to humans by the bites of the infected female phlebotomine sand fly, a tiny 2–3 mm long insect vector. There are three main forms of leishmaniiasis: cutaneous (CL), visceral (VL) or kala-azar, and mucocutaneous (MCL). Over one billion people live in endemic areas at risk of infection, 300 000 estimated cases annually with over 20 000 deaths for VL and one million CL cases reported from 2009 to 2014 according to the WHO [1].

Cutaneous leishmaniasis (CL) is endemic in Morocco. Its prevalence is increasing especially in immunocompromised subjects [2].

Leishmania recidiva cutis (LRC), which also denominates leishmaniasis, leishmania recidiva of the skin, lupoid leishmania, and late cutaneous leishmaniasis, is an unusual complication of acute CL. It consists of active lesions around or inside the scar of classical CL that apparently clinically healed. It appears after many months or years and can last for years without treatment [1,3].
Diagnosis of LRC is often complicated by the scarcity of the microorganism in direct smear and tissue specimens. Furthermore, most patients may be resistant to regular treatment for CL [4]. In this paper, we report two cases of recurrent CL in two women, two years after the complete healing of the primary lesions.

2. CASE REPORT

Case report one
A 62-years old woman from Errachidia (Morocco), presented with painless crusted and ulcerative infiltrated lesions of the left peri-orbital region and the border of the upper lip, expanding slowly within the edge of an old scar. General physical examination and anamnesis found treated type II diabetes diagnosed 6 months ago and iron deficiency anemia. A smear prepared from material obtained by puncture of indurated edge with May Grunwald Giemsa stain showed abundant intra and extra cellular Leishmania amastigotes. The medical history revealed that approximately two years earlier, she had observed papules on the same site of her face. The papules became confluent and begun to ulcerate. After therapeutic failure with local antibiotic treatments, CL was diagnosed on the basis of clinical findings and epidemiological data, and a positive smear prepared from the new lesion. The first lesion completely healed after intralesional meglumine antimoniate [Glucantime®] treatment. The LRC was treated with intralesional antimonial plus cryotherapy.

Case report two
A 57-years old woman from Tinghir (Morocco), presented with a single painless, 1cm erythematous infiltrative plaque of the left cheek, within the edge of an old scar. General physical examination and biological tests did not show any pathological findings except untreated iron deficiency anemia. A smear prepared from the active part of the lesion with May Grunwald Giemsa stain showed intra and extra cellular Leishmania amastigotes. The medical history revealed that approximately 2 years earlier, the patient was diagnosed with CL and treated by intralesional pentavalent antimonial [Glucantime®]. The original ulcer completely healed leaving a scar, and after two years, the disease reactivated in the border of healed lesion and continued spreading. This case of LRC was treated with intralesional antimonial plus cryotherapy.

Figure 1: Clinical image of patient 1

Figure 2: Clinical image of patient 2

Figure 3: Numerous organisms, which appear as round to oval structures 2–4 µm in size, were present inside and outside the macrophages [original magnification ×100], May-Grunwald-Giemsa stain.
3. DISCUSSION

In Morocco, leishmaniasis are endemic diseases. Two forms of cutaneous leishmaniasis are described: CL caused by Leishmania major and CL due to Leishmania tropica. Leishmania infantum, a common parasite inducing visceral leishmaniasis, was thereafter observed in cutaneous lesions. These parasites are transmitted to humans by the bites of the infected female phlebotomine sand fly, a tiny, only 2–3 mm long insect vector. L. major is transmitted by Phlebotomus papatasi from the animal reservoir to humans. L. tropica is transmitted by P. sergenti from person to person [1].

Regarding the clinical aspect, cutaneous leishmaniasis with L. tropica is described as a single lesion starting as a nodule at the site of inoculation. A crust develops centrally which may fall away exposing an ulcer which heals gradually. The second cutaneous form is that caused by Leishmania major. It was known in villages located in the southern slopes of the Atlas Mountains. Clinically, the lesion is often severely inflamed and ulcerated and heals in 4–6 months. The epidemiologic cycle of this rural form includes Phlebotomus papatasi as the proven vector and a commensally rodent, Meriones shawi grandis as the reservoir [5].

Because of the rarity of the atypical clinical forms of CL reported here, even physicians working in such an endemic area can misdiagnose them and treat them inappropriately as seen in case 1.

The differential diagnosis of “classical” ulcers of CL includes infected insect bites, traumatic ulcers, fungal, myco-bacterial and spirochete infections, and squamous cell carcinoma.

LRC is commonly misdiagnosed as lupus vulgaris, but blastomycosis, sarcoidosis, and tinea incognita must be also considered [6].

Variation in the clinical forms of CL is thought to be associated with the parasite species, host immune response, and the saliva of the sandflies, yet the mechanisms are poorly understood. In the Old World, LRC is mostly linked with L. tropica and rarely with L. major.

The diagnosis of CL is based on clinical features, epidemiologic data and laboratory testing. Diagnostic methods include direct parasitological examination (microscopy, histopathology, and parasite culture) and/or indirect testing with serology and molecular diagnostics. The selection of the diagnostic test employed in the endemic areas of infection depends on the available local infrastructure and resources [7].

Parasitological diagnosis is still considered the gold standard in leishmaniasis diagnosis because of its high specificity. Microscopical diagnosis is performed by the direct identification of amastigotes in Giemsa-stained lesion smears. Amastigotes appear as round or oval bodies, about 2–4 μm in diameter, with characteristic nuclei and kinetoplasts, (figure 3).

Histology of the nodule biopsies is tuberculoid in nature, with tubercles of epithelioid cells and giant cells surrounded by lymphocytes and histiocytes all residing in the dermis. Areas of necrosis are few or absent, and there are few plasma cells. The epidermis is usually atrophic or rarely shows pseudocarcinomatous hyperplasia. In essence the histology and clinical appearance are nearly identical to lupus [8].

A simplified collection method is the press-imprint-smear (PIS). When compared with histopathology for the diagnosis of CL, PIS was positive in 85.3 % in study cases suspected of CL, and histopathology was only positive in 44 %. PIS is considered a rapid and relatively sensitive method for the diagnosis of CL. Parasite culture in Novy-MacNeal-Nicolle medium from suspected lesions is difficult, requires significant technical expertise, is prone to contamination, and is time consuming [7].

Serologic diagnosis tests include Indirect immunofluorescence assay (IIFA) and enzyme-linked immunosorbent assay (ELISA). These formats are not widely employed for the diagnosis of CL, because of their low sensitivity [7].

Isoenzyme analysis of Leishmania has been used for strain typing and even the differentiation between antroponotic and zoonotic variants within a single species. This methodology is based on variation in the electrophoretic mobility of enzymes isolated from Leishmania parasites. Strains are consigned to various zymodesms. This highly specialized method is performed in a few reference laboratories only, but now the Leishmania species identification is relatively easier with new DNA techniques that enable a more rational therapy choice. Current treatment guidelines for CL are based on poorly de-signed and reported trials [7].

According to the WHO recommendations, the treatment of CL should be based on the grade of evidence, of geographic distribution, clinical manifestation, and Leishmania species.

In the Old World CL, the following criteria to recommend local treatment were set: proven or strongly suggested L. major as the infecting agent; up to 4 lesions; the diameter of the lesions less than 5 cm;
no potentially disfiguring or disabling lesion; no immunosuppression; and the possibility for follow-up. Options for local therapy include the use of 15% paromomycin plus 12% methylbenzethonium chloride ointment or intralesional antimonial plus cryotherapy or thermotherapy [7].

There is some debate as to whether the recurrent lesions are due to relapse or reinfection. In our patients, reinfection is unlikely, although the highly endemic area in which they both live, because the lesions recurred at the border of the old scar of a previous ulcer that was due to CL. The persistence of living parasites around or in "cured" leishmaniasis has been demonstrated in several studies, suggesting that reactivation is the most likely mechanism. Clinical data also support reactivation. Intracellular leishmania may be more likely to persist if therapy is insufficient or incomplete or if the infection has healed without treatment. It must be presumed that, in LRC, dormant parasites persist in the healed lesion and are reactivated by a certain stimulus. The nature of this stimulus is unknown. Saravia et al. have demonstrated a relatively weak cutaneous delayed type hypersensitivity response to leishmanin skin test antigens in patients with recurrent leishmaniasis and have suggested that it may be a risk factor for relapse in Colombia [9]. Other reports have suggested that local trauma and topical corticoids might reactivate lesions after many years. The cases reported here both presented iron deficiency anemia. Nutritional status, low dietary iron intake, and reduced mean hemoglobin values have been shown to be risk factors for acquiring CL in the population studied, but we don’t know if they are also risk factors for reactivation [10].

REFERENCES