

Cutaneous Leishmaniasis in Iran

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Citation

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Abstract

Cutaneous Leishmaniasis (CL) is common in Mediterranean countries especially in Iran. It can be seen in many different ages. Two such cases were a housewife with a huge lesion over her shins from Hashtgerd and an army soldier with multiple skin lesions over his arms from south east of Iran. They were treated with Meglumine Antimoniate (Glucantime) with success. A discussion on CL and its management follows.

INTRODUCTION

Leishmaniasis constitutes a diverse collection of human diseases ranging in severity from a spontaneously healing skin ulcer to overwhelming visceral disease. Worldwide, two million new cases occur each year, and a 10th of the world's population is at risk of infection.¹ Although, the disease is highly endemic throughout Northern Africa, the Middle East, parts of Europe, and Central and South America, epidemics are well recognized. When considering a cutaneous lesion of possible infective source, history of living in or traveling to an endemic place of CL should be sought.

CASE 1

A previously well 30 years old woman from Hashtgerd (city of Iran) presented with a non-healing ulcer over her shins in Jan 2002. She was a housewife with no history of traveling abroad or keeping pets, but she had a positive history of allergic rhinitis. The lesion started as an itchy red papule which slowly enlarged into an ulcerated plaque. There was negative history of insect or fly bite. The ulcer failed to heal despite several courses of systemic antibiotics, including Cloxacillin and Cefalexin. There was a history of Traditional Herbal medical use over the lesions that exacerbated the inflammation.

When she was seen at our center in July 2002, she was noted to have an 8x8 cm crusted, ulcerated plaque with exudation, on the middle anterior of her left shins (Fig.1). There was no regional lymphadenopathy, no muco-cutaneous changes and no systemic symptoms. A clinical diagnosis of Cutaneous Leishmaniasis was made. A skin biopsy showed chronic inflammation, and lots of macrophages with intracellular

amastigotes (Leshman Bodies). She was treated with Meglumine Antimoniate (Glucantime) (40 mg/km/day) intramuscular and intra lesional for a month. The ulcer healed after the course of treatment.

Figure 1

Figure 1: Ulcerated lesion of Cutaneous Leishmaniasis over the knee of a young woman is shown. Super infection with streptococcus is noted.



CASE 2

A previously well, 21 years old males of the Iranian military force attended a combat course in the South west of Iran in March 2002. The patient recalled being bitten by sand flies during his duty. Four weeks after returning home, he noticed

multiple asymptomatic purple nodules and plaques after 5 days on his arms and shoulders. They began to slowly enlarge but the patient did not experience any systematic symptoms. He sought medical advice and was told that he had CL.

On examination, the patient had eight 2×2 cm erythematous plaque with central ulceration all over his arms and shoulders (Fig.2). There was neither regional lymphadenopathy nor muco-cutaneous changes. Systemic examination was unremarkable. A clinical diagnosis of CL was made. Biopsy showed epidermal hyperplasia with foci of necrosis and a dense infiltration of lymphocytes and plasma cells in the dermis. There was multiple epithelial granulomas and intra-cellular amastigotes (Leshman Bodies). This was compatible with a diagnosis of Cutaneous Leishmaniasis.

Figure 2

Figure 2: Purple plaque of Cutaneous Leishmaniasis over the elbow (right) and arm (left) of a 21 years old soldier.



The patient was given intramuscular Meglumine Antimoniate (Glucantime) 40 (mg/kg/day) for 3 weeks with slow but definite improvement of the lesion, and remains on follow up.

DISCUSSION

Leishmaniasis is a group of parasitic diseases caused by several species of the genus *Leishmania*. Each species tends to occupy a particular geographical zone. They are transmitted by the bites of female sand flies, which are of the genus *Phlebotomus* in the old World and *Lutzomyia* in the New World. ²

Humans are usually accidental hosts of these 2 mm long flies; natural hosts include a variety of rodents, small

mammals, and dogs. The disease is geographically and ecologically widespread, occurring in tropical and subtropical regions on all continents except Australia. The incidence of Leishmaniasis is increasing, with many endemic areas reporting a 500% increase over the past seven years. ¹ The geographical distribution of Leishmaniasis is extremely wide; it is prevalent on four continents and considered to be endemic in 88 countries, including Bangladesh, Brazil, Afghanistan, Iran, Saudi Arabia, Peru, Sudan and India. ³ The incidence increased in Iran over the last 20 years ⁴ and also has been reported in many countries where CL is not endemic like Costa Rica, Russia and Croatia ^{5, 6, 7} Leishmaniasis remains an important problem for military personnel operating in endemic regions.⁸ CL has been a recurrent problem for troops training in the Middle East ⁹ and in Latin America. ¹⁰

Human Leishmaniasis is usually classified as cutaneous, visceral and mucosal. ⁸ Visceral Leishmaniasis (VL) or 'Kala-Azar' is caused by *L. donovani*, *L. infantum* and *L. chagasi*. But on occasion, other *Leishmania* species such as *L. amazonensis* in Latin America ¹¹ or *L. tropica* in the Middle East ¹² or Africa ¹³ are isolated from patients with Visceral Leishmaniasis. These species, in contrast with the other species of *Leishmania* that infect man, are normally viscerotropic, and cause a severe systemic infection, often accompanied by gross splenomegaly, anemia, diarrhea, hepatomegaly, lymphadenopathy and signs of malnutrition like weight loss. ^{14, 15} It is also known as Kala-Azar, Dumdum fever, Assam fever or infantile splenomegaly in different areas of the world. ⁸ Visceral Leishmaniasis has gained notoriety as an important opportunistic infection in persons with AIDS in Spain, southern France and Italy. ^{16, 17, 18} Before the introduction of HIV, it was encountered primarily in children (infantile splenomegaly) and adults immunocompromised by cancer or immunosuppressive therapy in the Mediterranean region. ¹⁹

Cutaneous Leishmaniasis (CL) is caused mainly by *L. tropica*, *L. major* and *L. aetiopica* but *L. donovani* and *L. infantum* have been implicated. It also produces simple cutaneous Leishmaniasis on occasions. ²⁰ The incubation period in CL is usually measured in months but ranges from a few days to over a year. In our second patient, the lesions appeared 4 weeks after he began combat course in south east of Iran. The face, neck and arms are the commonest targets, although the location of the lesion in a covered area such as the shins, like in the first case, is not unusual in Iran. There are four clinical types of CL, reflecting the different natural

history caused by the different organisms as well as variety in host response.²¹

(1) Acute CL: This is the most common clinical form of cutaneous Leishmaniasis. It can be caused by any species that causes CL. It is defined as a lesion that does not last beyond 1 year, and can present in a variety of morphologies, including an ulcerated nodule, eczematoid or verrucoid plaques and a zosteriform pattern.²² Our cases belongs to this category.

(2) Chronic CL: An infection that lasts for more than one year, is considered to be chronic CL, and is more likely to be due to *L. tropica*. It usually presents as a boggy erythematous plaque surrounded by distinct coalescing papules.

(3) Leishmaniasis recidivans: In this form, a new papule develops around the apparently healed lesion. There is clinical overlap with chronic CL. This is very chronic and lasts 20 to 30 years in some cases; it is not uncommon in Iran.⁸

(4) Diffuse CL: In this form, the initial nodule does not ulcerate, and new nodules develop on the face and trunk, resembling lepromatous leprosy clinically. The disease progress slowly and may persist for 20 years or more. The leishman skin test is negative.

A definite diagnosis depends on the identification of amastigotes in stained smears of scraping from the base of the ulcer or from biopsy specimens or aspirate of its border. Antileishmanial antibodies may be present in the serum of some patients with cutaneous Leishmaniasis as detected by ELISA, IFA, or other assay. Differential diagnoses include infective granulomas such as lupus vulgaris, deep fungal infections such as blastomycosis, yaws, syphilis, cutaneous tuberculosis and leprosy. A high index of suspicion is required, and histology is necessary.⁸

Treatment of CL is often difficult. Even though most sores will heal spontaneously, their duration cannot be predicted in an individual case. Ketoconazole has been shown to have some clinical utility in Central America, where 16 out of 21 patients (76%) treated were cured,²³ but results from South America were not encouraging.²⁴ A randomized double-blind study using Itraconazole to treat CL caused by *L. tropica* in Iran showed a poor response rate.²⁵

Antimonials are still the first line drug in the treatment of CL. Sodium Stibogluconate (Pentostam) and Meglumine

Antimonite (Glucantime) are essentially similar drugs which contain pentavalent antimony (Sb). Sodium Stibogluconate can be administered intravenously or intramuscularly, while Meglumine Antimoniate should only be given via the intramuscular route. The recommended dose is 20 mg/ kg/ day for 15 - 20 days.²⁶ Treatment with Antimonials is associated with some side effects such as myalgia, as well as possible liver or cardiovascular toxicity, which fortunately is rare. A recent study using intralesional sodium Stibogluconate showed that alternate day or weekly administration of intralesional sodium Stibogluconate was effective in the treatment of CL.²⁷ Dapsone and Allopurinol have also been used for the treatment of CL.

The mechanism of action is not known, although basic biochemical studies have shown that *Leishmania* cannot make all of their own nucleic acids and use the host's purines through the purine salvage pathway. Other systemic options include Amphotericin B and Pentamidine, which are second line drugs used only when treatment fails with Antimonials. Besides systemic treatment, local measures such as cryotherapy, local excision of a small focus and topical treatment using 15% Paromomycin ointment has also been shown to be effective in some cases.²⁸ Vaccines for prophylaxis and immunotherapy have been developed, and are currently undergoing trials in many countries, including Venezuela, Brazil and Iran. The development of molecular biology techniques is also improving knowledge on the structure, evolution and expression of the *Leishmania* genome, and the study and definition of the mechanisms that regulate the parasite biochemical and molecular features will certainly contribute to the development of new and more effective strategies for Leishmaniasis treatment.⁸

These cases emphasize the point that when assessing lesions of possible infective etiology, a detailed travel history and knowledge of the common infective agents in the location concerned are of great importance in arriving at a diagnosis and appropriate treatment.

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