Unusual Presentations of Cutaneous Leishmaniasis in Two Iranian Patients

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Abstract
Leishmaniasis affects 1.5-2 million new cases in the world annually. Two major complications of cutaneous leishmaniasis include diffuse cutaneous leishmaniasis (DCL) occurring in the setting of deficient cell mediated immunity, typically with HIV infection, and chronic cutaneous leishmaniasis (CCL) developing in approximately 4% of L. tropica infections in Iran and Afghanistan which also may complicate vaccination with a live strain of leishmania (leishmanization). The Iran–Iraq war took place in a hyper endemic area of Old-World cutaneous leishmaniasis. We report two Iranian soldiers who were both infected in the battle field and presented several years after the war; one was an HIV positive patient with DCL and the other was a previously leishmanized patient with CCL. (Iran J Dermatol 2010;13: 99-102)

Key words: chronic cutaneous leishmaniasis, diffuse cutaneous leishmaniasis, HIV, leishmanization

Introduction
The leishmaniases are a group of diseases caused by several species of the genus *leishmania*. The disease can be classified mainly into three forms: cutaneous (CL), visceral, and mucocutaneous. Two major types of CL are identified: dry (urban) CL, due to *L. tropica* and wet (rural) CL, due to *L. major*. However, there are two major complications of CL including diffuse CL (DCL) and chronic CL (CCL). In "diffuse CL", from an initial lesion, the nodules that do not ulcerate disseminate locally to other parts of the skin, often involving large areas. In the Old World, this form of the disease is due to *L. aethiopica*. It is a rare anergic form of CL occurring in the setting of deficient cell mediated immunity. Immune suppression, typically with HIV infection, can be an important factor for the atypical presentation and widespread progression of the disease with no species-specific relationship.

"Chronic CL" (*Leishmaniasis recidivans, lupoid leishmaniasis*) presents with brown-red or brown-yellow papules which are usually close to or even in the scar of an old lesion of CL. It has been estimated that approximately 4% of *L. tropica* infections in Iran and Afghanistan develop this chronic form of the disease. Reactivation of a dormant infection (after up to 15 years) causes most of the cases. It may complicate vaccination with a live strain of *leishmania* and usually occurs in the setting of hyperactive T cell immunity and low antibody titers.

Afghanistan and Iran are located in the hyper endemic area of Old-World cutaneous leishmaniasis (CL). The Iran–Iraq war took place in an actually hyper endemic region. Hence, in the first years of the war, the number of infected soldiers notably increased. In this extraordinary situation, "leishmanization" of the military soldiers started and during the war, about 2 million soldiers were leishmanized. Follow-up studies demonstrated a leishmanization coverage of 89.6 % among these soldiers.

We would like to report two cases: one HIV positive patient with DCL and one previously leishmanized patient with CCL. They were two Iranian soldiers who presented several years after the Iran-Iraq war. Both were infected in the battle...
field and initially misdiagnosed as cutaneous lymphoma.

Case report

Patient 1

A 40-year-old man presented with asymptomatic grouped lesions on his left arm since 20 months ago. On careful examination, there were multiple reddish-brown papules and nodules around a scar and some of them were excoriated (Figure 1). Clinical examination was otherwise normal. There was neither lymphadenopathy nor organomegaly. Skin biopsy had been performed with the differential diagnosis of cutaneous lymphoma and sarcoidosis. Histopathological examination showed focal epidermal ulceration, mild irregular acanthosis, minimal epidermal spongiosis and scattered exocytosis of lymphocytes. In the underlying superficial and deep dermis, there was a heavily dense infiltration of mixed inflammatory cells composed of lymphocytes, plasma cells and histiocytes producing large dense aggregates mostly around blood vessels. There were numerous intracellular round to oval Leishman bodies within the cytoplasm of histiocytes or free in the dermis between inflammatory cells (Figure 2).

He was previously vaccinated with live leishmania parasites in this area of his arm when he was in the war. In laboratory studies, the tuberculin and HIV serology tests were negative. Chest X-ray and routine laboratory tests were reported normal.

Patient 2

A 41-year-old man was referred to our ward with a 12-month history of generalized, pruritic but painless lesions. He was a military soldier in the Iran-Iraq war and still worked as a mine sweeper in the war zone and during this period. He has progressively developed these lesions throughout his body without any herald lesions he could remember.

He had numerous infiltrated nodules and plaques which were reddish-brown in color and distributed on the head and neck, trunk and extremities. His face was diffusely infiltrated, giving him a coarse leonine-like appearance (Figure 3,4).

His medical history revealed a single lesion on his great toe, diagnosed as an infective process, for which he had undergone surgery and received multiple antibiotics. After developing generalized lesions, drug eruptions were proposed and since pancytopenia was also presented in his laboratory examinations, lymphoma was suggested, too. Chest X-ray and abdominopelvic cavity spiral CT-Scan were reported normal. There was no lymphadenopathy or organomegaly. Bone marrow aspiration and fluocytometry did not show any abnormalities.

The diagnosis of diffuse cutaneous leishmaniasis was established based on the skin biopsy which revealed moderately dense infiltrations of mixed inflammatory cells including lymphocytes, many plasma cells and histiocytes containing numerous Leishmania organisms. Aggregates of both intracytoplasmic and extracellular Leishman bodies and inflammatory infiltrate were extending from the subepidermal portion down to mid reticular dermis and even in the upper border of the subcutaneous fat (Figure 5).

He declined any previous history of leishmaniasis but stated that many co-workers in the mine sweeping team had leishmaniasis.

In laboratory studies, the tuberculin test was negative but HIV serology test was positive.
Detailed history revealed that he was an IV drug abuser.

**Discussion**

Leishmaniasis, which affects 1.5-2 million new cases annually and threats over 350 million people living in active areas of parasite transmission, is one of the top five diseases targeted for research and training in tropical diseases by World Health Organization special program.

In the Iran-Iraq war period (seven years), 36441 persons were infected in the war zone which demonstrates a high prevalence rate and constitutes approximately 30% of all leishmaniasis patients in Iran during this period of time. Due to the absence of an effective vaccine and progressive infestation of soldiers causing many problems during the war, leishmanization of military soldiers was performed and reported to be effective since it decreased leishmaniasis infection to one-sixth.

Leishmanization is done by intradermal inoculation of live and active *L. major* promastigots into the unexposed parts of the body, particularly arms, which causes an active ulcer that heals spontaneously resulting in long-term immunization against urban and rural leishmaniasis. Although leishmanization was reported to be successful in controlling leishmaniasis burden in the Iran-Iraq war, this procedure discontinued after termination of the urgent situation due to its multiple side effects. During the post-war period, numerous cases of leishmanization complications were recorded including long-lasting or non-healing lesions.

Our first case had a completely healed lesion after leishmanization in the war, leaving an atrophic scar on his arm. It is assumed that re-infection did not occur in this site. Therefore, reactivation of
dormant leishmaniasis in the form of CCL without existence of any apparent immunosuppression ensued after about 20 years as a rare phenomenon, proposing that Leishmania parasites have remained alive during this period without exhibiting any activation. Even if we assume that the patient was not immunized after the first exposure, there is no apparent reason for its reactivation after these years. Therefore, measuring anti-Leishmania antibody titer does not seem to help in this regard, which was the reason why we did not evaluate it. Although CCL is usually seen after infection by L. tropica in our country, occurrence of this form after leishmanization with L. major is also notable. Furthermore, existence of numerous parasites in the lesion was also unexpected since finding parasites in this form of CL is difficult.

Diffuse CL without visceral involvement can be the first manifestation of an HIV infection, as in our second case. On the other hand, visceral leishmaniasis with cutaneous involvement has been reported to be more common in HIV infection. Immune suppression caused by HIV infection leads to cumulative deficiency in cell-mediated immunity and produces atypical presentation or diffuse spread of cutaneous leishmaniasis. It occurs via dissemination after either a new infection (resulting from a new sand fly bite or a possible parasite transmission through sharing of contaminated syringes by intravenous drug users) or the reactivation of a latent infection; however, we could not determine which one occurred in our case. It is possible that his toe lesion was the undiagnosed primary leishmaniasis which became disseminated due to concurrent HIV infection although it was limited to the skin and no extracutaneous involvement was detected in his workup.

There are few reports on the association of HIV and DCL and in all of them, clinical manifestations are similar to our case with generalized cutaneous involvement. Coarsening of facial appearance has been demonstrated in some, similar to the present case.

These cases emphasize that when patients present with clinical features resembling lymphoma, atypical and unusual forms of leishmaniasis should be considered, especially in hyperendemic areas.

References