

Cutaneous Leishmaniasis with Unusual Clinical and Histological Presentation: Report of Four Cases

Hamideh Moravvej¹, Mohammadreza Barzegar¹, Soheila Nasiri¹, Ehsan Abolhasani¹, and Mehdi Mohebal²

¹ Skin Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

² Department of Medical Parasitology and Mycology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

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Abstract- Old world cutaneous leishmaniasis (OWCL) usually causes a single, self-healing and uncomplicated lesion mainly on the exposed area of body. This report presents four cases of OWCL from Iran that misdiagnosed with sarcoidosis, lymphoma, and acne agminata. Two out of four patients showed a history of purplish red plaques for at least 5 years who misdiagnosed as sarcoidosis because of histological and clinical characteristics. The other one presented with flesh-colored nodules disseminated all over his skin that was misdiagnosed as lymphoma for ten years. The last patient was misdiagnosed as acne agminata due to tuberculoid reactions in examination of the lesion biopsy. All the patients responded to the treatment with meglumine antimonate.

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Introduction

Old world cutaneous leishmaniasis (OWCL) is endemic in some parts of Iran where it is caused by *Leishmania major* and *Leishmania tropica*; the transmission is by the bite of infected female sandflies (1-3). The virulence of microorganisms, the host defense mechanisms, and some environmental factors determine the clinical features and the course of the infection (4). True cutaneous leishmaniasis (CL) can take typical or atypical clinical pictures; It can also be acquired endogenously (i.e. lupoid leishmaniasis and post kala-azar dermal leishmaniasis). HIV infection, renal transplantation, and drug-induced immunosuppression can change the clinical picture of CL (5,6). We report four cases of unusual clinical and histological presentation of CL from Iran.

Case Reports

Case 1

A 30-year-old woman presented with a five-year history of plaques all over her face, which were atrophic at center and surrounded by minute papules (Figure 1). The lesions were misdiagnosed histopathologically as

discoid lupus erythematosus and received hydroxychloroquine without any response. A few months later, she was biopsied again and sarcoidal granuloma (SG) was suggested for which she received methotrexate (MTX) plus prednisolone for the next four years. During this period, her face was covered with purplish-brown papules healing at the expense of atrophy.



Figure 1. Case 1; a 30-year-old woman with plaques on her face, misdiagnosed as sarcoidal granuloma

Corresponding Author: Hamideh Moravvej

Skin Research Center, Shahid Beheshti University of Medical Sciences, Shohada-e-Tajrish Hospital, Shahr-dari Street, Tajrish square, Tehran, Iran
Tel: +98 21 22741507, Fax: +98 21 22244020, E-mail: Hamideh_Moravvej@yahoo.com

We performed another biopsy and granuloma was seen around the nerve. PCR was performed for *M.leprae*, *M.tuberculosis*, *L.major*, and *L.tropica* by Kinetoplast PCR which revealed an amplification band of 620-bp, compared to reference stocks (Iranian strain of *L.major* = MRHO/IR/75/ER). Meglumine antimonate was administered intramuscularly for 28 days as well as tretinoin to vanish the atrophic scars. The patients responded to the treatment regime, however, the lesions relapsed four years later. At this time, she presented with panniculitis; the lesions vanished completely with fluconazole and intralesional meglumine antimonate.

Case 2

A 40-year-old diabetic man presented with a five-year history of purplish-red plaques over his chest and back (Figure 2). He had also pulmonary involvement. His lesions were biopsied twice and were diagnosed as SG, for which he had received MTX plus prednisolone without any response. We performed another biopsy that showed SG (Figure 3).



Figure 2. Case 2; a 40-year-old man purplish-red plaques over his chest, back, and arms, misdiagnosed as sarcoidal granuloma.

The PCR on both skin and bronchoalveolar lavage was positive for *L.major*. Meglumine antimonate was administered intramuscularly for 28 days. Seven days after treatment, a Jarisch-Herxheimer reaction was seen for which prednisolone was added for five days. All the lesions disappeared within a few weeks and no relapse was observed three years after treatment.

Case 3

A 54-year-old man presented with a 10-year-history of flesh-colored nodules all over his body. The patient had been treated with MTX and chemotherapeutic drugs for lymphoma. We performed another biopsy and numerous intra- and extracellular leishmania were seen. PCR was performed for *L.major* and *L.tropica*, and the analysis revealed an amplification band of 620-bp compatible with *L.major*. Meglumine antimonate was administered intramuscularly for 28 days. All the lesions vanished within one month. No relapse was observed during next year.

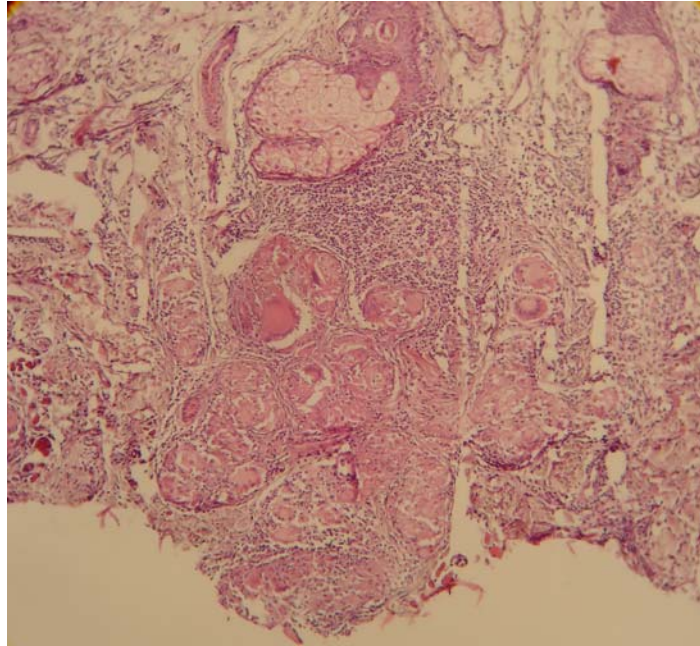


Figure 3. Case 2. Sarcoidal granulomas with demarcated islands of epithelioid cells, few giant cells and sparse lymphocytic (H&E; magnification $\times 4$).

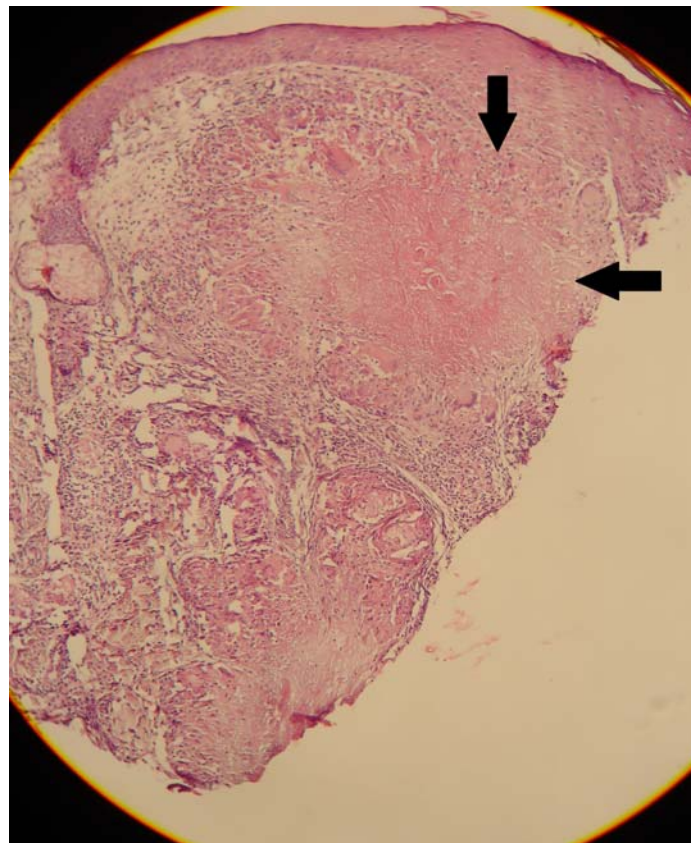


Figure 4. Case 4. A granuloma in dermis (black arrows) with central acellular necrosis and histiocytes and lymphocytes aggregation. (H&E, magnification $\times 4$).

Case 4

A 50-year-old man with several nodules in his face presented to our clinic due to persistence of the nodules despite treatment. His lesions were multiple, symmetric, reddish-brown papules around his eyes, cheeks, chin, and around his upper lip. One of his lesions was biopsied with suspicion of granulomatous diseases. In his pathology, granuloma in the dermis with central acellular necrosis and histiocytes and lymphocytes aggregation in adjacent dermis was seen (Figure 4); in addition, no acid-fast organism was detected by Ziehl-Neelsen stain. His condition was diagnosed pathologically as acne agminata and he was treated with doxycycline, minocycline, and isotretinoin for over a year. We performed PCR with respect to endemic prevalence of atypical mycobacterium and leishmania (*L.major* and *L.tropica*) species. The PCR revealed leishmania in the sample; patient was treated with intramuscular and intralesional meglumine antimonate for 28 days and lesions resolved.

Discussion

The four cases we have described confirm that clinical presentation of OWCL can change because of immunosuppression. As mentioned before, one of the key elements that determine the clinical picture and the course of the infectious disease is the host defense mechanism; in the other words, HIV infection, renal transplantation (5) and drug induced immunosuppression for instance by MTX (6) can alter the clinical picture of CL. The unusual presentation of leishmaniasis is reported previously; Vardy *et al.* reported a case of CL caused by *L.major* in a patient with Rheumatoid arthritis receiving MTX plus prednisolone who had numerous nodules concomitant with CL, mimicking sporotrichoid spread of the disease (7). When examined by electron microscopy, *leishmania* parasites were observed at intracellular and extracellular locations in the nodules (7).

Sarcoidosis is a multisystem inflammatory disease of unknown etiology that predominantly affects the lungs and intrathoracic lymph nodes. Sarcoidosis is manifested by the presence of noncaseating granulomas in affected organ tissues. T-lymphocytes play a central role in the development of sarcoidosis, as they likely propagate an excessive cellular immune reaction. There is an accumulation of CD4⁺ cells accompanied by the release of interleukin-2 at sites of disease activity. The cellular mediated mechanisms of sarcoidosis are the same as CL but prednisolone and MTX-induced

immunosuppression may cause the extension of CL lesions (3).

Re-emergence of CL in immunosuppressed individuals after initial successful treatment has also been reported (7,8). Saha *et al.* reported CL in two patients who were taking MTX at the time of exposure and at development of clinical disease (9). They concluded that the T-cell mediated response to leishmaniasis infection could be modulated by MTX and may render an immunosuppressed individual more susceptible to develop clinical disease (9). The three out of four cases we reported here had been treated inappropriately with MTX and other chemotherapeutic drug. All the cases had a history of trip to endemic areas; in addition, they had atypical clinical and histological picture that could not fit into any of clinical and histological pictures of CL. It can be concluded that MTX can change the clinical and histological picture of CL and lead to disseminated disease due to alteration in host defense mechanisms. Based on this experience, PCR is recommended to be used to determine the presence of leishmania in endemic area when immunosuppression is used in treatment of the primary diagnosed disease and no improvement is seen.

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