

Cutaneous leishmaniasis mimicking sarcoidosis in Libyan patient: A case report

Abstract

Leishmaniasis is vector-borne disease caused by parasitic protozoans belonging to the genus *Leishmania* and is transmitted by infected phlebotomine sand flies. Sarcoidosis is a multisystemic disorder of unknown cause characterized by the formation of immune granulomas in affected organs. Clinical symptoms, severity and evolution of sarcoidosis are highly heterogeneous and can lead to other diseases with similar clinical and pathologic presentations. In this report we present a case of 77 years-old diabetic Libyan male, with chronic erythematous indurated plaques, and nodules on the face. The patients were treated by multiple physicians with topical and systemic corticosteroids for 25 years without improvement. Microscopic examination of Giemsa stained smears from all lesions showed numerous *Leishmania* amastigotes in and outside monocytes. *Leishmania tropica* was identified as causative species. The patient was treated with combination of oral rifampicin (600 mg/day) and isoniazide (300 mg/day) and followed up for 9 months until skin-slit smears and PCR turned negative. In conclusion, CL can be misdiagnosed clinically with any granulomatous skin lesions which are compatible with sarcoidal type granuloma. Molecular diagnosis of CL by implementing *Leishmania*-specific PCR approaches should be performed routinely in any granulomatous skin lesion.

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Introduction

Leishmaniasis is a vector-borne disease caused by parasitic protozoans belonging to the genus *Leishmania* and is transmitted by infected phlebotomine sand flies. The clinical manifestations is polymorphic and range from cutaneous (CL) and muco-cutaneous leishmaniasis which is characterized by localized lesions on the skin and in mucous membranes, to visceral leishmaniasis which is the most severe form and mostly fatal in many developing countries if left untreated.¹ These manifestations (dermotropic and viscerotropic) depend on the causative *Leishmania* species,²⁻⁴ and the immunological response of the infected host.⁵ CL may appear as unusual clinical and histopathological forms and mimic other co-morbidities that causes diagnostic challenge and may lead to misdiagnosis.

Sarcoidosis is a multi-systemic disorder of unknown cause characterized by the formation of immune granulomas in affected organs. The most affected organs are the lungs and lymph nodes. However, it can affect every organ of the body from the skin and eyes to be most common extra pulmonary organs that develop serious clinical manifestations.⁶⁻⁸ Estimated mortality attributable to sarcoidosis is between 0.5% and 5%. Most of these deaths result from pulmonary, cardiac and central nervous system.^{9,10} Clinical symptoms, severity and evolution of sarcoidosis are highly heterogeneous and is affiliated to other diseases with similar clinical and pathologic presentations. The majority of cases are time limiting and may show spontaneous resolution within 1-3 years. However, serious and prolonged course

may be experienced in some patients.⁹ Sarcoidal granuloma in this study, we reported for the first time in Libya a patient with CL symptoms mimicking sarcoidosis.

Case report

In this report we present a case of 77 years-old diabetic Libyan male, with chronic erythematous indurated plaques, and nodules on the face and ears for more than 25 years duration. According to his clinical and histological characteristics, the patient was misdiagnosed with sarcoidosis and was treated by multiple physicians with topical and systemic corticosteroids for 25 years without improvement. The patient was admitted to our department in March 2015. On examination there were several small painless popular lesions with indurations. The lesions showed central ulceration with erythematous borders over the forehead and cheek (Figure 1A). Skin smears and biopsies were taken under local anesthesia and sent for Lab analysis. Microscopic examination of Giemsa stained smears from all lesions showed numerous *Leishmania* amastigotes in and outside monocytes (Figure 2). *Leishmania tropica* was identified as causative species by amplification of the Internal transcribed spacer 1 (ITS1) PCR followed by RFLP with *HaeIII* restriction enzyme. The patient was treated with combination of oral rifampicin (600 mg/day) and isoniazide (300 mg/day) and followed up for 9 months until skin-slit smears and PCR turned negative (Figure 1B). The cutaneous lesions of the face disappeared and there has been no evidence of recurrence after three years (Figure 1C).



Figure 1 (A) the patient was admitted on March 2015 with small painless lesions with central ulcerations and erythematous borders over the forehead and cheek. (B) after 9 months of treatment with oral rifampicin and isoniazide. (C) the patient was completely recovered after 3 years of follow up.

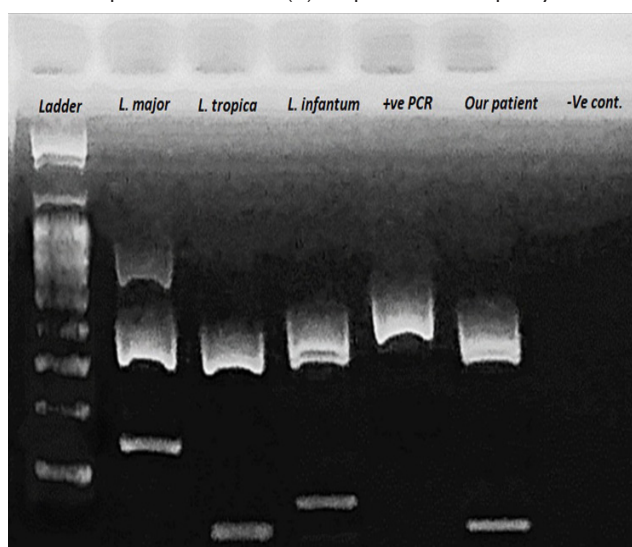


Figure 2 Restriction fragment length polymorphism (RFLP) profile of amplified ITS1 region with the *Hae III* restriction enzyme. From the left: Lane 1 is 100 bp marker, lane 2, 3 and 4 are digested positive controls of *L. major*, *L. tropica* and *L. infantum* respectively. Lane 5 is an undigested PCR product of the ITS1 region showed the characteristic band of about 300 bp, and lane 6 is the digested PCR product from our patient identified as *L. tropica*.

Discussion

Sarcoidal granuloma may appear with heterogeneous presentations that mimic several infectious diseases such as tuberculoid leprosy, lupus vulgaris, lupoid rosacea, granuloma annulare and coetaneous leishmaniasis.¹⁰⁻¹² This appearance is challenging in deferential diagnosis between these infectious diseases and sarcoidosis which should be always remembered as diagnosis of exclusion. The emergence and development of modern diagnostic techniques has led to better discrimination of these cases. Patients who were previously diagnosed with sarcoidosis were tested positive for different coinfections.¹³⁻¹⁶ However, few cases of CL associated with sarcoidosis have been described previously.¹⁷⁻¹⁹ *Leishmania* parasites were isolated from significant number of patients with single and/or multiple nodular lesions of the skin. Chronic forms of nodular skin lesions represent a diagnostic dilemma in clinical settings and from a histological aspect.^{17,20} In case of unusual CL forms and coinfections, *Leishmania* amastigotes are either difficult to trace in these chronic skin lesions or is altogether absent. In clinical practice, these forms may be misinterpreted as sarcoidosis, particularly in cases where microscopic screening for *Leishmania* amastigotes from skin-slit smears from these lesions reported negative. This misdiagnosis of CL with other mimicking diseases such as sarcoidosis has led to implementation of treatment strategy which is in complete contradiction to CL treatment. Our patient received a long-term therapy of corticosteroids which significantly modulated the immune response and increasing the patient's susceptibility to parasitic infections such as CL.²¹ Administration of immunosuppressive therapies such as corticosteroids has been described as a risk factor associated with CL reactivation.²¹ Previous experimental studies have shown that CL is usually being controlled predominately by T-cell mediated immunity with a preferential Th1 pattern.²² Hence, the incidence of CL in these immune-compromised patients may be due to inadequate cellular immune response. Moreover, the causative agent of CL in our patient belonged to *L. tropica* species. To the best of our knowledge, the phenomenon of CL mimicking sarcoidosis due to *L. tropica* has not been reported before in Libya. The advancement of molecular diagnostic techniques for CL in Libya has led to an accurate and rapid detection of *Leishmania* amastigotes where microscopic and histological diagnosis failed to identify them. Moreover, it has enabled a precise identification of the causative species, better deferential diagnosis from comorbidities, and consequently better treatment and recovery of patients.²³⁻²⁵ The sensitivity of molecular diagnostic methods for CL including kDNA and ITS1 PCR was higher compared to other diagnostic approaches. These differences in sensitivity become more significant in patients with chronic forms of nodular skin lesions.^{17,22}

In conclusion, CL can be misdiagnosed clinically with any granulomatous skin lesions which are compatible with sarcoidal type granuloma. From Histopathological point of view, CL may be misinterpreted as sarcoidosis especially when *Leishmania* amastigotes are not seen microscopically. Considering their epidemiological features, endemicity, and geographical distribution, molecular diagnosis of CL by implementing *Leishmania*-specific PCR approaches should be performed routinely in any granulomatous skin lesion.

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None.

Conflicts of interest

Authors declare that there is no conflict of interest.

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