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CASE REPORT

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Two cases of neglected leishmaniasis with marked facial disfigurement: A diagnostic conundrum

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Key Clinical Message

There is a need to pay more attention to cutaneous leishmaniasis in endemic regions which may mimic other dermatoses and treatment should be initiated with a strong clinical suspicion even without any histopathologic or PCR confirmation to avoid disfigurement or development of secondary malignancy.

Abstract

Leishmaniasis is a vector-borne disease with a variety of Clinical manifestations. Cutaneous leishmaniasis (CL) is the most common form of disease and can mimic other dermatoses. We describe two unusual cases of chronic leishmaniasis that remained undiagnosed for many years and led to superimposition of squamous cell carcinoma (SCC) on lesions of one patient. These reports showed that the leishmaniasis should be borne in mind by clinicians when encountering any infiltrated lesion in patients from endemic regions and treatment should be initiated with a strong clinical suspicion even without any histopathologic or PCR confirmation to avoid disfigurement or development of secondary malignancy.

KEYWORDS

chronic lesions, granulomatous dermatitis, leishmaniasis, neglected lesion, SCC

1 | INTRODUCTION

Leishmaniasis is a vector-borne disease with significant morbidity and various clinical manifestations. The three forms of disease consist of visceral, cutaneous, and mucocutaneous types.[1] Cutaneous leishmaniasis (CL) is the most common form of disease and has different types[2,3]: acute or localized CL is considered the most prevalent clinical form of CL in the old world and chronic CL defined when lesions lasting for over 2 years.[4] Chronic CL could be presented by lesions resembling lupus vulgaris and may persist for many years. Nodules usually develop progressively with or without ulceration and might resemble lepromatous leprosy. In fact, chronic CL can mimic many granulomatous dermatoses.[4] Hence, clinical suspicion plays an important role on diagnosing the disease in endemic regions. Since some types of CL such as LR has no amastigotes (lesishman body) in biopsy or smears, it might pose even more diagnostic challenge.

Here, we have reported two unusual cases of chronic neglected leishmaniasis who remained undiagnosed for many years and squamous cell carcinoma (SCC) was superimposed on lesions of one.

2 | CASE DESCRIPTION

2.1 | Case 1

An 87-year-old Iranian gentleman from Isfahan presented to our dermatology clinic with complaint of asymptomatic and progressive facial lesions for past 3 years. The lesions were initiated after one night outdoor camping with his son. Patient did not notice any insect bite, but remembered an unpleasant sensation inside his nose at the morning after that. Moreover, his son developed one nodule on his leg which its smear was positive regarding leishmaniasis. The patient said that facial lesions were gradually extended during these years (Figure 1A, B).

Physical examination revealed bilaterally distributed, confluent, extensive, and erythematous plaques with considerable induration involving nose, cheeks, upper lip, and orbital areas which compromised his vision. Some of lesions had ulceration and crusting with purulent discharge (Figure 1B).

The rest of physical examination was normal. Routine blood tests and CXR were within normal limits. Tuberculin skin test (PPD) was negative.

Over last 3 years, multiple skin biopsies had been obtained and all showed pseudoepitheliomatous hyperplasia and mixed infiltration with occasional noncaseating tuberculoid granulomatous dermatitis. Special stains and cultures for fungi and mycobacteria as well as Giemsa smear and PCR studies for leishmaniasis were negative.

Hence, definite diagnosis had never been established and patient had received many systemic empirical treatments including multiple courses of antibiotics and antifungals, intralesional Glucantime, antituberculous therapy, and even systemic corticosteroid with impression of noninfectious granulomatous disorders. The last biopsy from his upper lip lesion, taken 1 year ago, revealed actinic cheilitis and cryotherapy was performed subsequently.

In our clinic, three punch skin biopsies from different areas of facial lesions were taken, and a tissue sample was sent for PCR evaluation which was negative regarding leishmaniasis. Skin biopsy from left cheek revealed prominent noncaseating tuberculoid granulomatous dermatitis without any leishman body (Figure 2).

Nasal skin biopsy showed severe epidermal hyperplasia with irregular extension of the dermis by uneven jagged masses and streaks of epidermal cells with cellular

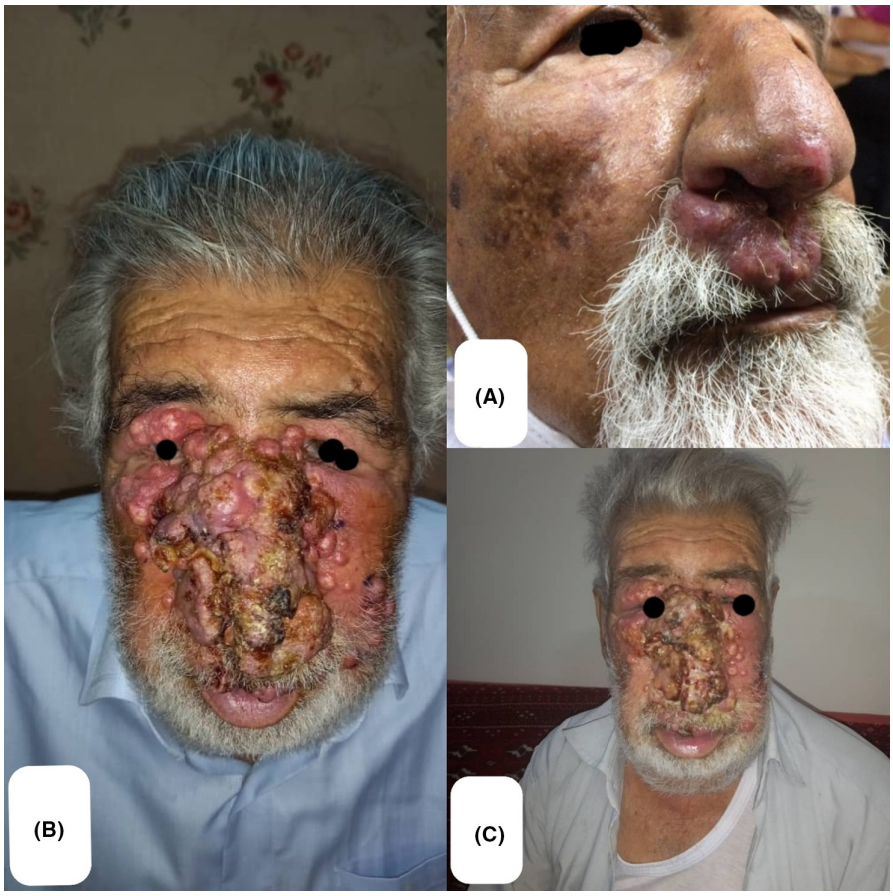

FIGURE 1 (A) Initial lesions about 3 years ago. (B) Multiple nodular lesions with marked facial disfigurement. (C) Some degree of clinical improvement after initiation of Glunantime.

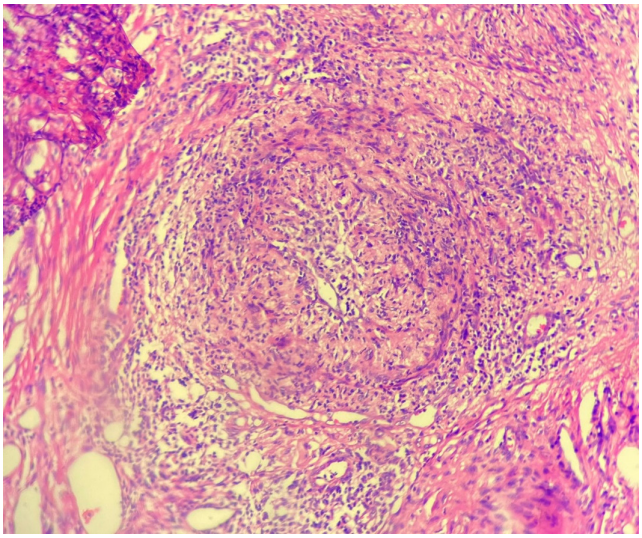

FIGURE 2 Noncaseating tuberculoid granulomatous dermatitis without any leishman body.

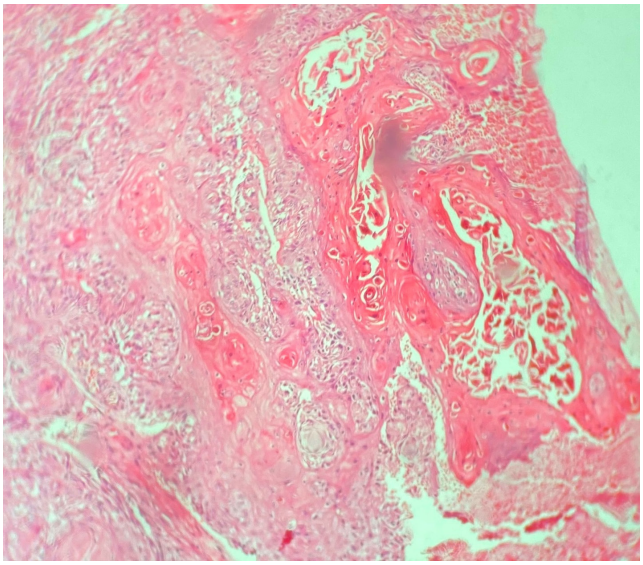

FIGURE 3 Streaks of epidermal cells with cellular atypia and invasion of squamous nests with some keratous pearls.

atypia and increased mitotic features. In the dermis, invasion of squamous nests and some keratinous pearls were seen which were compatible with well-differentiated SCC diagnosis (Figure 3).

During staging, no systemic involvement of SCC was found.

Culture from purulent discharge grew Staphylococcus aureus with sensitivity to cloxacillin, but treatment with cloxacillin 500 mg/TDS for10 days did not lead to a considerable improvement. Botryomycosis, a rare microbial condition, was excluded among our differential diagnosis based on the fact that patient's lesions were not responsive to cloxacillin, as well as multiple previous antibiotic courses. Hence, existing Staphylococcus aureus considered as a secondary infection. Consultations with otolaryngology and oncology departments were asked for choosing the best therapeutic approach regarding his SCC and surgical plan was scheduled for him.

Although the results of histopathologic and PCR studies were nonrevealing again, considering the fact that patient's living region, Isfahan distinct, is one of the foci of leishmaniasis in Iran along with a confirmed diagnosis of leishmaniasis in his son and the history of an outdoor sleep and presence of an unpleasant sensation inside his nose before initiation of lesions, an empiric course of systemic meglumine antimoniate (Glucantime, 1500 mg/ BD, intramuscular) was initiated. After 20 days of treatment, lesions were markedly improved (Figure 1C), but unfortunately, patient could not finish his course of treatment due to his unexpected death in a car accident.

2.2 | Case 2

A 34-year-old lady visited our outpatient clinic from Kurdistan distinct, another endemic area for leishmaniasis in Iran, complaining from multiple long-lasting nodular lesions on her face, leg, and forearm which were a little pruritic and painful (Figure 4A, C). She told us that the lesions were initiated from her left leg about 14 years ago and her facial and forearm lesions were added about 10 and 5 years ago, respectively. On physical examination, multiple erythematous plaques and nodules in abovementioned areas were noted leading to a saddle nose deformity.

Similar to previous case, multiple smears and biopsies during these years were obtained with negative results regarding tuberculosis and leishmaniasis. A 6-month empiric anti-TB treatment was also prescribed which was not effective.

In our clinic, a PPD and nasal discharge smear for leprosy was performed which both were negative. Two punch skin biopsies from facial and forearm lesions were taken which revealed inflammatory granulomatous reaction with multinucleated giant cells and central necrosis of granuloma. Special staining for fungi, Leishman body, and acid-fast bacilli were also negative.

Empiric therapy with systemic meglumine antimoniate (Glucantime, 1.5 gr/BD, intramuscular) was initiated based on strong clinical suspicion and after 1 month of treatment, lesions were dramatically improved (Figure 4B, D).

3 | DISCUSSION

Leishmaniasis is a serious disorder with severe morbidity and potentially life-threatening features due to some

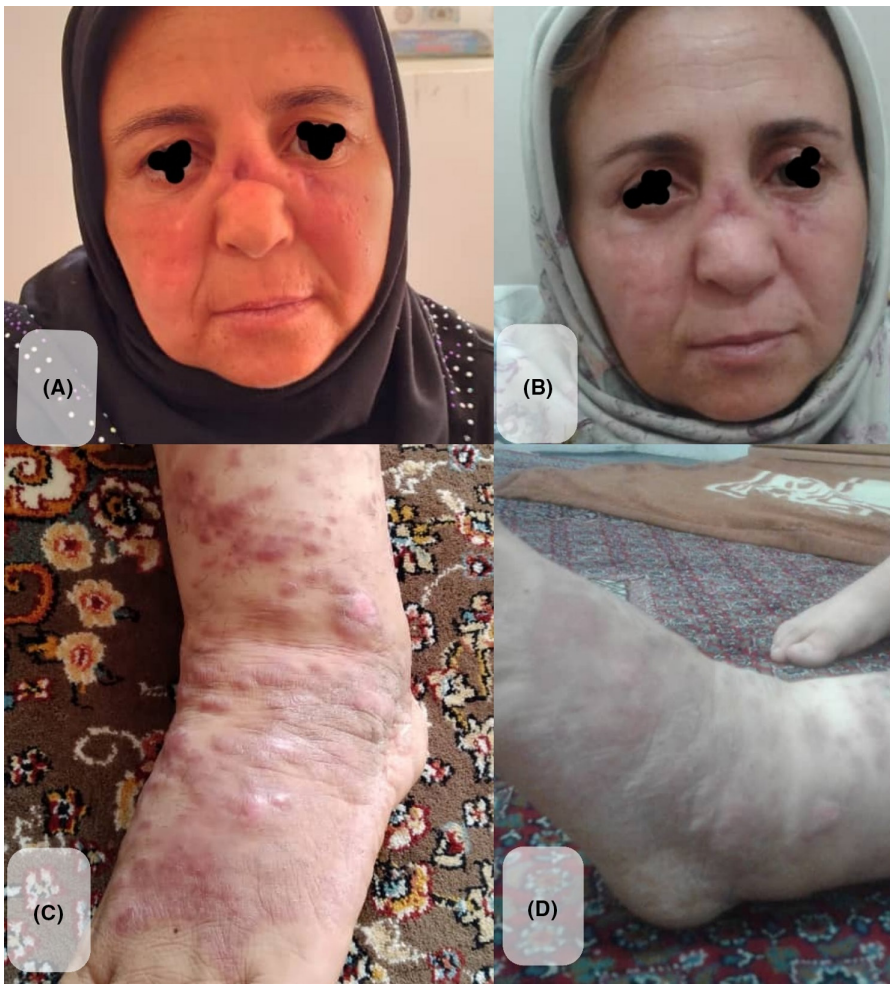

FIGURE 4 Initial lesions on face and extremity (A, C) and considerable clinical improvement (B, D) after initiation of Glunantime.

clinical form of disease such as visceral type as well as development of superimposed malignancy on chronic undiagnosed lesions.[5]

Moreover, dramatic disfigurement caused by chronic lesions, as in our cases, may pose considerable psychologic pressure on patients.[6,7] The diagnosis of CL is critical both to reduce disease complications and to initiate appropriate treatment.

However, clinical diagnosis could be challenging due to existing a wide range of clinical differential diagnosis, nonspecific histopathological features in some cases, and lack of parasite in some tissue samples, especially in chronic lesions.[4]

In fact, histopathologic evaluation in chronic lesions might be confusing due to the presence of pseudoepitheliomatous hyperplasia as a response to chronic irritation of epithelium which can mimic SCC.[8] However, it is worthy to note that actual SCC can also develop over chronic CL lesions as happened to our first case and after multiple tissue samples with only pseudoepitheliomatous hyperplasia, SCC was noted in the last one.

Hence, the possibility of SCC development should always be borne in mind by clinicians in dealing with any chronic inflammatory condition.

Overall, diagnosis of leishmaniasis based on histopathological evaluation occurs in 16%–74%.[9] Dar et al. revealed that skin biopsy showed Leishman bodies (LB) in 89.74% of patients, saline aspirate smears and skin slit smears in 30.76% and 32.05% of patients, respectively. They suggested that sensitivity of diagnosis by smear could be increased by testing various skin smears.[10] Even molecular techniques such as PCR could have false negative results in 53% of chronic lesions.[11] Indeed, a considerable number of clinically diagnosed CL cases in endemic countries such as Iran cannot be confirmed by various diagnostic techniques of smear, culture, skin biopsy specimens, and even PCR testing.[12] We could not confirm the diagnosis in our patients, but their improvement via systemic Glucantime might be inferred as a confirmation of our clinical suspicion. These interesting cases showed the diagnosis of leishmaniasis might be extremely challenging even in a patient from an endemic region and might take as much as 15 years to be made!

Considering routine BCG vaccination in Iran, the negative PPD in our patients could be inferred as a sign of defective host defense mechanisms, along with previous corticosteroid therapy in our first case, might contribute to extension of lesions.

In conclusion, we reported two cases of leishmaniasis with an unusual presentation to emphasize the need to pay more attention to this serious condition in endemic regions which may mimic other dermatoses and treatment should be initiated with a strong clinical suspicion even without any histopathologic or PCR confirmation to avoid disfigurement or development of secondary malignancy. However, further studies are needed to shed more light on the matter of hard-to-diagnosis chronic granulomatous disorders.

AUTHOR CONTRIBUTIONS

Zeinab Aryanian: Conceptualization; visualization. **Kamran Balighi:** Data curation; methodology. **Fatameh Mohaghegh:** Resources; software; supervision. **Ifa Etesami:** Visualization; writing – review and editing. **Zahra Razavi:** Investigation; methodology. **Parvaneh Hatami:** Conceptualization; methodology; writing – original draft.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest regarding the publication of this article.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The patients provided written informed consent to publication of this case report and accompanying images.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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