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Squamous cell carcinoma arising from chronic cutaneous leishmaniasis: a rare case report

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Abstract

Leishmaniasis is a parasitic disease transmitted by sandflies, commonly manifesting as cutaneous or mucocutaneous lesions. While cutaneous leishmaniasis (CL) is widespread in endemic regions, its link to malignancies like squamous cell carcinoma (SCC) remains uncertain. We report a rare case of SCC developing directly on a CL lesion, contributing to the ongoing debate regarding this potential association. A 75-year-old man from an endemic region presented with a red papule following an insect bite. Despite receiving six sessions of intralesional therapy, the lesion worsened due to a one-year lapse in follow-up and use of alternative therapies. Biopsy confirmed moderately differentiated SCC, leading to surgical removal and recovery without complications. The development of SCC on a previous CL lesion is rare but notable, as chronic infections can trigger malignancy. Although no definitive link has been established between CL and SCC, this case underscores the need for monitoring persistent leishmaniasis lesions, especially in mismanaged cases. It also emphasizes the importance of timely diagnosis and treatment of CL to avoid complications such as SCC. Further research is needed to determine the mechanisms underlying this rare association.

Introduction

Leishmaniasis is a parasitic skin infection transmitted and carried by female sandflies of the genera *Phlebotomus* (Mediterranean, Middle East) and *Lutzomyia* (Central and South America), presenting in three main forms: cutaneous leishmaniasis (CL), mucocutaneous leishmaniasis, and visceral leishmaniasis (the most fatal subtype). CL, the most widespread subtype, causes skin ulcers and can lead to scarring and disfigurement if untreated. Despite its prevalence, with up to a million new cases annually, particularly in the Middle East, South America, and Africa, CL is often underreported, especially in low-income regions where treatment options are limited. Syria is one of the top eight endemic countries that account for over 90% of global CL cases. Early diagnosis and treatment are crucial, but challenges persist due to the variation in disease presentation across species and regions, with diagnostic methods often influenced by available resources rather than accuracy.[1]

SCC is the second most common nonmelanoma skin cancer, arising from the keratinizing layer of the epithelium. Cutaneous squamous cell carcinoma (cSCC) is widespread, with incidence varying based on skin tone and UV exposure. Its development is linked to factors like prolonged UV radiation, chronic inflammation, immunosuppression, ionizing radiation, chemical exposure, and chronic wounds. While cSCC can be invasive, early detection and surgical treatment generally result in a good prognosis. However, delayed diagnosis increases the risk of metastasis, sometimes requiring radiation or chemotherapy.[2,3] Chronic infections caused by viruses, bacteria, and parasites have long been recognized as potential contributors to human malignancy. While certain parasitic infections are

strongly linked to specific cancers, several studies have highlighted a potential association between Leishmania species and the development of malignant lesions, including basal cell carcinoma (BCC), SCC, lymphoma, leukemia, and hemangiosarcoma in both humans and animals.[4,5] We reported a rare case of SCC superimposed on CL, further emphasizing the potential link between these two conditions.

Case Report

A 75-year-old male with a history of hypertension, well-controlled on tribland for the past five years, presented to the leishmaniasis department with a firm, red papule following an insect bite. The initial diagnostic workup involved performing a Giemsa stain on the smear, which confirmed the presence of *Leishmania* amastigotes in the cutaneous lesion specimen. The patient received six sessions of local intralesional pentavalent antimonial salts injections (once a week for 6 weeks), but showed slight improvement. Following this initial treatment course, a one-month pause was implemented to assess the therapeutic response. However, the patient did not return for follow-up and was lost to follow-up for one year. During this period, he pursued traditional herbal therapies for seven months. This resulted in worsening of the lesion, which became larger, more ulcerated, and painful, with new nodules and increased exudate (Figure 1).

The patient returned to the leishmaniasis department due to increased pain and an enlarging lesion on his right thumb. Examination revealed a verrucous, snake-like plaque measuring 7 cm in diameter, surrounded by multiple erythematous papules and nodules, with a central ulceration that was painful and slightly pruritic (Figure 2). The patient was placed on systemic intramuscular glucantime therapy, receiving 10 mL daily for 20 days. However, no significant improvement was noted. A subsequent trial of itraconazole for one month also failed to control the disease. Due to the lesion's progression, a biopsy was performed, revealing moderately differentiated SCC (Grade 2) (Figure 3). Axillary examination reveals no signs of lymphadenopathy. Imaging studies, including chest X-ray and CT scans, were normal, but radiographs showed partial dislocation and increased bone density in the affected thumb. As a result, the patient underwent complete surgical removal of the thumb lesion, including amputation, followed by appropriate wound closure and reconstruction (Figure 4). The patient experienced an uneventful recovery after the surgery, with no complications. At the three-month follow-up, there were no signs of local recurrence or metastasis. The patient reported reduced pain and had resumed daily functions.

Discussion

Lesions in CL typically appear in exposed areas, starting as nontender, firm, red papules at the site of sand fly bites. These lesions may gradually enlarge, leading to central ulceration, serous crusting, and granuloma formation. While most localized cases resolve spontaneously within six months, some infections can persist longer. In our case, the patient displayed ongoing active leishmaniasis, characterized by a verrucous plaque and painful ulceration, resulting from prior mismanagement, as reliance on traditional herbal treatments allowed the disease to worsen without healing.[3] The development of malignant neoplasms, such as Marjolin's ulcer, at sites of previous scars or chronic wounds is rare, with common causes including traumatic wounds, varicose ulcers, and unhealed burn scars, while leishmaniasis is not typically associated with chronic wound formation. Leishmaniasis has been linked to cancer development in both immunocompromised and immunocompetent patients, though the connection between CL and skin cancer is not well-studied. Four main associations have been identified: i) leishmaniasis mimicking malignant conditions; ii) leishmaniasis occurring in patients already diagnosed with cancer; iii) coexistence of leishmaniasis and cancer in immunocompromised individuals; and iv) cancer developing in tissues or lesions previously affected by leishmaniasis.[3,4]

Chronic infections can trigger various cancers, but there is currently no evidence linking CL to the development of cSCC. Limited reports exist regarding cSCC in immunocompetent patients with a history of CL, typically occurring years later on scarred tissue. However, there are also instances where cSCC has been reported in conjunction with active CL.[2] Most tumors generally arise from leishmaniasis scars, although some cases have been reported where active leishmaniasis infections are associated with skin cancer. Nonetheless, these associations remain uncommon according to current clinical evidence and observations. A previous case demonstrated a rare link between SCC and CL, showing that prolonged lesions can lead to malignancy. This is comparable to our case of a 75-year-old male with a painful verrucous plaque, ultimately diagnosed as SCC. In both cases, mismanagement and delayed treatment contributed to disease progression, highlighting the necessity for timely interventions and vigilant monitoring of leishmaniasis lesions for potential malignant changes. This reinforces the need for further investigation into the relationship between active leishmaniasis and skin cancer risk.[3]

The period between leishmaniasis infection and malignancy development is usually two to five years.[6] In our case, SCC was diagnosed just two years after the leishmaniasis diagnosis, suggesting a potential link between the two. The patient's history of insect bites, residence in an endemic area, and positive leishmaniasis tests affirm the accuracy of the initial diagnosis. These factors indicate that the

SCC may be related to the chronic effects of leishmaniasis, underscoring the need for careful monitoring of patients with leishmaniasis for potential malignancies.

The exact mechanism behind the development of SCC in areas previously affected by leishmaniasis remains unclear. A systematic review also concluded that there is no definitive link between leishmaniasis and malignancy.[7] However, due to the rarity of cases and the complex interactions between chronic infections and cancer, further research is needed to explore this potential relationship in greater detail. More studies would help clarify whether a causal link exists or if the co-occurrence is merely incidental.

Conclusions

In summary, the case of SCC developing after CL underscores the potential for malignant transformation in chronic or inadequately treated leishmaniasis lesions. While no definitive causality has been established, this case reinforces the need for timely diagnosis, proper treatment, and careful monitoring of long-standing lesions in endemic regions. Further research is required to clarify the possible link between chronic leishmaniasis and skin cancer and to improve clinical guidelines for managing such cases.

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Figure 1. The right thumb shows a large, ulcerated, necrotic lesion with verrucous edges. The lesion is consistent with moderately differentiated squamous cell carcinoma (Grade 2) following prolonged leishmaniasis and failed treatments.

Figure 2. The X-ray shows a right hand with increased bone density and partial dislocation in the thumb. These changes likely result from the progression of the lesion affecting the bone structure.

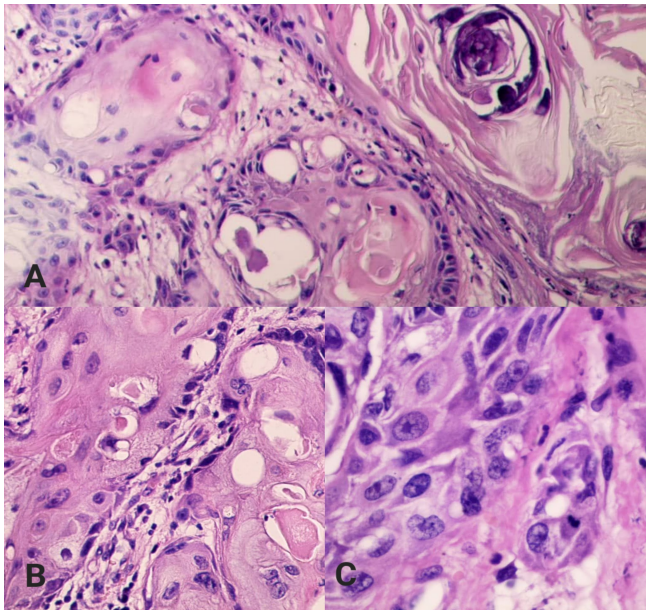

Figure 3. Histopathological examination of the lesion. A) Hematoxylin and Eosin (H&E) stain at x100 magnification showing invasive proliferation within the dermis by islands of non-keratinizing atypical squamous epithelial cells. B) H&E stain at x200 magnification highlights cellular pleomorphism, with evident nuclear hyperchromasia and occasional mitotic figures within the squamous cells. C) H&E stain at x400 magnification, revealing a patchy mixed inflammatory infiltrate within the surrounding stroma. The surgical margins are free of tumor invasion, indicating complete excision.

Figure 4. Post-surgical image of the hand following amputation and reconstruction of the thumb. The skin appears thickened and scaly, indicative of post-treatment changes and healing after the complete removal of the lesion. The patient exhibits no signs of local recurrence or metastasis at this stage, and healing appears uneventful. The surrounding tissue shows mild erythema, but there are no signs of active infection or ulceration.