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CASE REPORT Open Access

Squamous cell carcinoma associated with an active cutaneous leishmaniasis in immunocompetent patient: case presentation of an unlikely association and literature—review

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Abstract

Background: Association between leishmaniasis and malignancy can be classified into four categories: leishmaniasis mimicking malignancy, leishmaniasis co-existing with malignancy, malignancy developing in patients with leishmaniasis scar, and leishmaniasis developing in patients with malignancy. In immunocompetent patients, the main form of association is cutaneous squamous cell carcinoma (cSCC) developing within cutaneous leishmaniasis scar years after cutaneous leishmaniasis is cured. Association of active cutaneous leishmaniasis and cSCC is exceptional, we are aware of two more cases.

Case presentation: A 30-year-old man presented with 2 years history of an unhealed wound on the dorsum nasi. As there still exist few sites of leishmaniasis in Morocco, systematic screening for leishmania was performed. Leishmania bodies were identified on slit skin smear by Giemsa staining. The patient received local antibiotic and on-site injections of 4 cc of meglumine antimonate for 2 months without any improvement. The lesion volume has increased significantly, a biopsy revealed an invasive squamous cell carcinoma. After staging assessment, the patient underwent a complete removal of the nasal tumor with a 1-cm margin, associated with right modified radical neck dissection. Histopathological examination confirmed the diagnosis of SCC with no lymph nodes metastasis. Nasal reconstruction was performed 2 weeks later using a frontal flap. Oncology meeting board advised adjuvant radiation on the tumor. The patient is followed up regularly and remains free of disease for a year now.

Conclusion: Although many cancers are related to infection (viral or parasitic), there is no proven link between leishmaniasis and malignancy. However, there are many etiopathogenic theories based on pathology finding that involve chronic inflammation inducing dysplasia, mitotic abnormalities, and expression of p53.

Keywords: Squamous cell carcinoma, Cutaneous leishmaniasis, Skin cancer, Chronic infection

Background

Cutaneous squamous cell carcinoma (cSCC) is a widely spread cancer, its incidence varies depending on the skin tone of population and the level of sun ultraviolet radiations unprotected exposure. The main risk factor is unprotected prolonged sun exposer especially

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for non-dark skinned persons. However, many cases of cSCC were related to viral infection such as human papilloma virus, burn scares, unhealed wounds. Coexisting cSCC and active cutaneous leishmaniasis in the same lesion in immunocompetent patient is exceptional, we are aware of two more cases [1, 2]. Many authors argue that cutaneous leishmaniasis could trigger the development of cSCC and bring out some pathology modifications induced by leishmaniasis that can trigger carcinogenesis [3–5]. We report the case of an association of active cutaneous leishmaniasis and cSCC in an immunocompetent patient. Also, we discuss different types of association found and the founding etiopathogenic theories of causality.

Case presentation

A 30-year-old man with no significant medical history was admitted to dermatology department because of 2 years history of an unhealed wound on the dorsum nasi. That lesion was reluctant to all medications that the patient received. The patient reported a history of first appearing nodule on the dorsum nasi followed spontaneously by a central ulceration that kept enlarging**.** As there still exist few sites of leishmaniasis in Morocco, systematic screening for leishmania was performed. Leishmania bodies were identified on slit skin smear by Giemsa staining. The patient received local antibiotic therapy based on chlortetracycline hydrochloride and on-site injections of 4 cc of meglumine antimonate for 2 months without any improvement. Before the progression of the lesion volume (Fig. 1), the patient underwent a biopsy which revealed an invasive squamous cell carcinoma. Staging assessment was then carried out identifying 22 × 46 mm tumor with poorly defined borders and irregular outlines involving nasal septum and the dorsum nasi associated with several right lymphadenopathies predominantly in the IInd, IIIrd, Vth lymph node groups, the largest measuring 7 mm (Figs. 2 and 3). The patient was referred to the ENT department for further treatment. He underwent a complete removal of the nasal tumor with a 1-cm margin, associated with right modified radical neck dissection. Histopathological examination confirmed the diagnosis of SCC with no lymph nodes metastasis. Nasal reconstruction was performed 2 weeks later using a frontal flap.

Oncology meeting board advised adjuvant radiation on the tumor location because of high-risk recurrence tumor site, tumor volume, and pathology criteria (perineural neoplastic invasion, tumor vascular emboli). The patient is followed up regularly and remains free of disease for a year now. Patient's care episodes timeline is reported in Fig. 4.

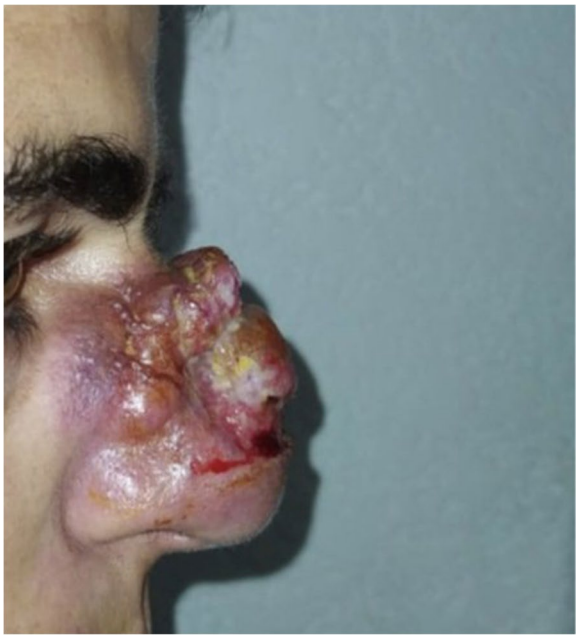

Fig. 1 Patient's photo showing 5cm large tumor of the dorsum nasi involving the right paranasal region

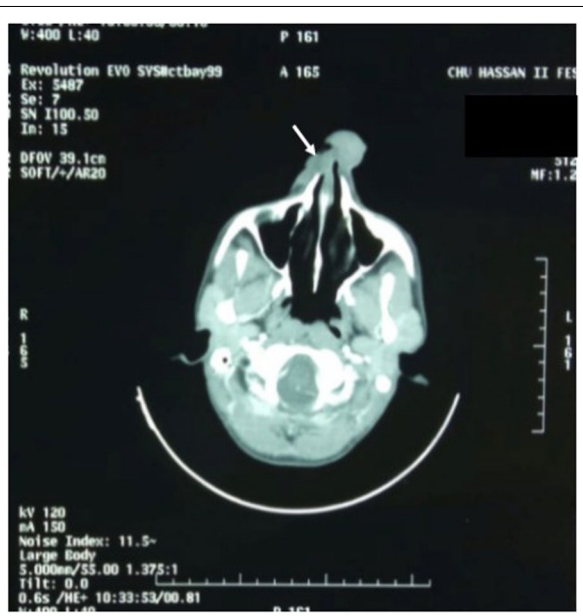

Fig. 2 CT scan axial view with contrast showing an enhanced tumor involving the dorsum nasi and the septum with no evidence of bone destruction (white arrow)

Discussion

Cutaneous squamous cell carcinoma (cSCC) is a widely spread cancer, its incidence varies depending on the skin tone of population and the importance of sun ultraviolet

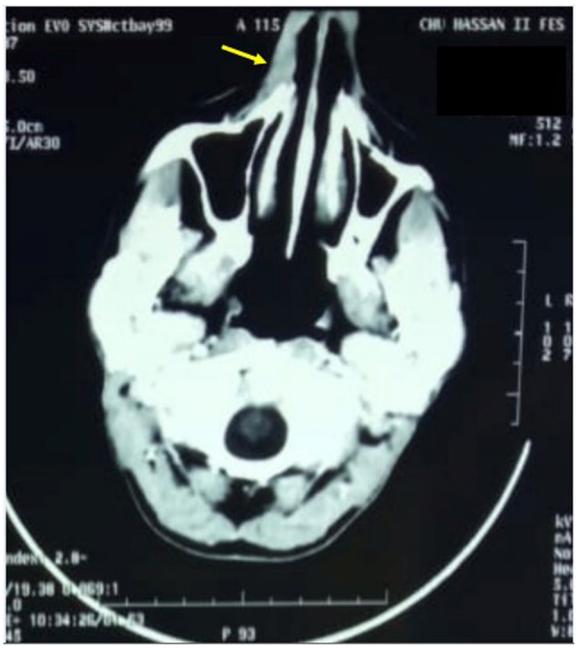

Fig. 3 CT scan axial view with contrast showing subcutaneous spread of the tumor into the right cheek with no destruction of the anterior wall of maxillary sinus (yellow arrow)

radiations unprotected exposure. In the West, the incidence varies from 10 to 20/100,000 person in France to 250/100,000 person in Australia [6]. In Morocco, the prevalence reported was 20% [7]. Cutaneous SCC is the second most common non melanoma skin cancer after basal cell carcinoma. Rochester Epidemiology Project, conducted by the Mayo Clinic, demonstrated a cSCC's incidence increase of 263% increase between 1976 to 1984 and 2000 to 2010 periods [8]. Rates are likely to increase given the growing elderly population and the increased focus on skin cancer screening [9]. cSCC usually happens around 60s, younger cases are associated with pre-existing skin conditions such as xeroderma pigmentosum and burns scares.

The most relevant risk factors include long-term unprotected sun exposure, age over 60s, immunosuppression and fair skin tone [9]. Although cSCC is common in Caucasian people and most frequent in men than women. It might happen also in African, Asian, and Hispanic patients [3, 10, 11]. Unlike Caucasian individuals, these populations' cSCC mostly develop on sites of previous trauma, scarring, unhealed burns, or chronic wounds [9]. Also, it carries higher mortality rate (18%) and worse prognosis [9, 12]. Solid organ transplant recipients are the immunodepression group of patients that bears the most risk of cSCC [13]. Although many cancers are known to be triggered by a chronic infection, such as human papillomaviruses and epidermoid carcinoma, Epstein-Barr virus, and undifferentiated carcinoma of nasopharyngeal type, hepatitis B and C viruses, and liver adenocarcinoma, human T cell lymphotrophic virus I and hematologic malignancy, there still no evidence

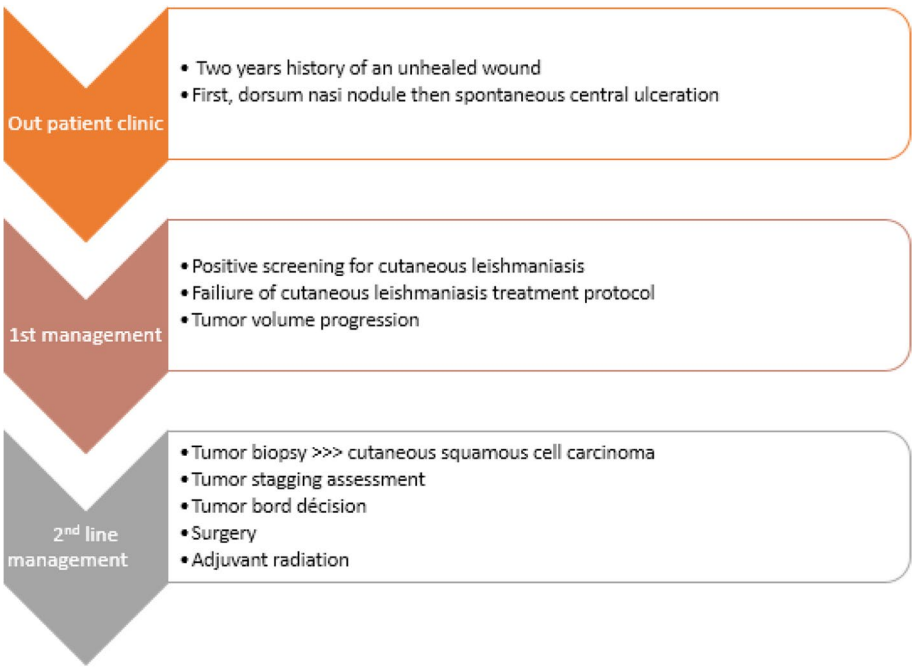

Fig. 4 Timeline of the patient's episodes of care

of the involvement of cutaneous leishmaniasis on the pathogenesis of the cutaneous SCC [14, 15]. In fact, few reports have been published on cSCC associated with cutaneous leishmaniasis in immunocompetent patients [1, 2, 16, 17]. In most cases, cSCC developed on the scarring tissue of cutaneous leishmaniasis years later [11, 12]. However, two cases were reported an association of cSCC and active cutaneous leishmaniasis [1, 2].

According to WHO, cutaneous leishmaniasis (CL) is a chronic skin infection due to protozoan parasites transmitted by the bite of infected female phlebotomine sandflies. An estimated 700,000 to 1 million new cases occur annually [18]. However, only a small fraction of those infected by parasites causing leishmaniasis will eventually develop the disease [18].

About 95% of CL cases occur in the Americas, the Mediterranean basin, the Middle East and Central Asia. In 2019, over 87% of new CL cases occurred in 10 countries: Afghanistan, Algeria, Brazil, Colombia, Iran, Iraq, Libya, Pakistan, the Syrian Arab Republic, and Tunisia [18].

Cutaneous leishmaniasis in Morocco is an endemic disease with few locations in the central part of the country for L. *tropica* and other locations in the South and the South Est for L. *major* [19, 20].

Regarding its clinical features, cutaneous leishmaniasis due to *L. tropica* is described as a single lesion starting as a nodule at the site of inoculation. A crust develops centrally which may fall away exposing an ulcer which usually heals gradually. The second cutaneous form is that caused by *Leishmania major*, the lesion is often severely inflamed and ulcerated and heals in 4 to 6 months without treatment leaving life-long scars and serious disability or stigma [19]. In addition, in some cases infection can persist [2].

The diagnosis of leishmaniasis is confirmed by identifying the parasite within the lesion [21]. Depending on the species and region, the treatment of meglumine antimonate has cure rates of 80 to 100% [22]. Surgery is not a recommended modality for the treatment of leishmaniasis because of the potential for recurrence at the excision site and the risk of exacerbation of the disease [23].

Whereas some parasitic infections are associated with specific cancers such as schistosomas and liver flukes [3]. Infections caused by parasites, have been related to cancer including cSCC by several mechanisms such as inducing chronic inflammation and producing carcinogenic metabolites [2, 3, 18–20].

Accessible literature has potentially linked leishmaniasis infection to the development of malignancy in humans [3, 24]. Association between leishmaniasis and malignancy can be classified into four categories: leishmaniasis developing in patients with malignancy, malignancy developing in patients with leishmaniasis scar, leishmaniasis mimicking malignancy, and leishmaniasis co-existing with malignancy [3].

Although the majority of cases of association between cutaneous leishmaniasis and cSCC in immunocompetent patients reported malignancy developing in a chronic cutaneous leishmaniasis scar [16, 17, 3], our patient is the third case of coexisting active cutaneous leishmaniasis and SCC [1, 2].

Regarding the pathogenesis, many authors argue that cutaneous leishmaniasis causes a chronic wound that may trigger cellular cytogenetic modifications inducing carcinogenesis such as atypical mitotic features, moderate to marked dysplasia with expression of p53 protein [3–5].

Surgery is not recommended for the treatment of cutaneous leishmaniasis as it may trigger worse outcome [23]. However, biopsy is needed whenever there is an atypical presentation or treatment outcome to rule out associated malignancy. The management of cSCC associated with cutaneous leishmaniasis does not differ from the usually known guidelines of random cSCC. No literature is available on the benefit of associating anti-leishmaniasis treatment to carcinologic surgery in case of active cutaneous leishmaniasis associated with cSCC. There is not enough data to draw conclusions about such cases prognosis. However, our patient's first year follow-up is uneventful.

Conclusions

Although many viruses and parasites can trigger malignancies in human, association between cutaneous leishmaniasis and skin malignancy have been reported but causality is still to be proved. Many pathology features suggest alterations caused by leishmaniasis infection that could trigger carcinogenesis. Therefore, before reluctant cutaneous leishmaniasis, biopsy is mandatory to rule out associated skin malignancy.

Patient's perspective

I am a 30-year-old man, and I work in building construction. Two years ago, I had an itchy pimple on my nose. I thought it was some kind of an insect bite, and it appears in the summer I remember. So, I did not pay that much attention to it but it still did not heal after a few weeks. Since I was so busy working, that pimple does not bother me that much. Few months later, it started growing so I went seeing many doctors. Some gave me medications and creams, while other asked for blood tests. After more than a year, the pimple kept enlarging and all those medications have not made me any better. So, a friend of mine advised me to see a dermatologist at the university hospital of Fes, it was almost 200 Km far from my home town. I went there, my pimple was already big, and I started being preoccupied by it. Doctors advised me to be hospitalized in order to figure out rapidly what that pimple was. After some tests,

they told me that I have leishmaniasis and prescribed some medications to me. I went back home, but when I returned for my routine follow-up consultation, my doctor seemed preoccupied and asked me the permission to perform a biopsy. Few days later, they told me I have skin cancer. I was shocked and angry, I thought they all missed the diagnosis. Doctor explained to me that my case is exceptional and maybe leishmaniasis has set out the conditions for the cancer to develop. Also, if the cancer was evolving since 2 years, I would have been in a worse situation. Then, I started a long journey to get that cancer cured. Now, I finished my treatment protocol a year ago. I still have 4 more years of follow-up. I wish that my case will be published in order to help other patients that might encounter the same problem as I. I hope doctors will be more aware of that situation.

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Authors' contributions
NO was involved in diagnosis, surgery procedure, and manuscript drafting. AT was involved in literature review and drafting of the manuscript. NH was involved in pathology study and reviewed the manuscript. DK was involved in surgery procedure and reviewed the manuscript. MNA reviewed the manuscript for insightful remarks. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets generated and/or analyzed during the current study are not publicly available due to patient's data confidentiality but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
An informed consent for publication purpose was obtain from the patient. Written consent is available.

Competing interests
The authors declare that they have no competing interests.

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