Squamous cell carcinoma arising from long-term (50-year) Lupus vulgaris: is there a need for a close medical follow-up in such chronic diseases?

Lupus vulgaris: evoluzione in carcinoma squamocellulare dopo 50 anni: e se fosse necessario un follow-up più stretto?

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INTRODUCTION

Tuberculosis is a systemic infectious disease caused by Mycobacterium tuberculosis. Although this infection showed a remarkably decline in past decades, the immigration phenomenon and the increasing number of patients affected by acquired immunodeficiency syndromes could explain the well-established increase in incidence observed in European countries. Lupus vulgaris (LV) represents the most common cutaneous manifestation of tuberculosis. Even if it is a rare condition, squamous cell carcinoma (SCC) is the most frequent malignancy arising from LV, probably due to the chronic status of inflammation [1-6].

A case of SCC on the left parotid region, arising from a pre-existing, misdiagnosed and under-treated LV, is herein reported.

CASE REPORT

A 67-year-old female farmer was referred to the Head and Neck Surgery Department of the Second University of Naples for a nodular, ulcerated and bleeding lesion, involving the left ear lobe and the parotid region. The patient reported the onset of a small, nodular, erythematous lesion in the same region since she was 19-year-old, first diagnosed as an abscess and partially resolved with antibiotics. The persistence of the lesion led the General Practitioner to suggest the diagnosis of angioma; thus the patient underwent electrodesiccation therapy. Ten years later, the recurrence of the lesion led to a clinical diagnosis of LV and an anti-tuberculosis therapy was instituted with Etanicozid B6 (a combination of ethambutol-400 mg, isoniazid-125 mg, pyridoxine-50 mg) three capsules per day and rifamycin (locally administered), with a slight improvement.

Since the patient’s clinical conditions worsened in 2006, she presented to the dermatologist for a slight extension of the eruption to the parotid region and to the pinna (Figure 1A). A skin biopsy at the periphery of the lesion was performed, and all the specimens were fixed in a 10% solution of formaldehyde and embedded in paraffin.

Five-micrometer thick sections were stained with haematoxylin-eosin and processed for histological examination and evaluation. Histopathological features showed a granulomatous dermatitis associated with a dense inflammatory infiltrate close to the granulomas, involving both superficial and deep dermis. Areas of hyperparakeratosis of the covering
epithelium and vacuolar changes of the basal layer were also detected. Such histological findings suggested the diagnosis of a tuberculous lesion. A Tuberculin Skin Test was performed resulting in a strong positivity of 21 mm (Figure 2).

The patient was commenced on three capsules per day of Miazide B6 (a combination of ethambutol-400 mg, isoniazid-125 mg, pyridoxine-50 mg) for 6 months, with considerable improvement in the lesion (Figure 1B-C).

A year later, the patient presented once again with a nodular lesion in the same area. Dermoscopic examination revealed a spoke-wheel pattern of vessels, which strongly suggested cancer. A skin punch biopsy revealed a well-differentiated (G1) squamous cell carcinoma (SCC) (Figure 3 A-B).

When admitted to the surgical unit the patient showed a 3 x 3.5 cm, erythematous, nodular, ulcerated and bleeding lesion, involving the earlobe and the parotid region, of hard consistency and undefined borders, which seemed to reach the soft tissue (Figure 1D). A left facial nerve paralysis suggested nervous involvement by the lesion. Two enlarged lymph nodes of 30 mm and 25 mm in diameter were detected by ultrasound imaging, whereas computed tomography revealed extensive ipsilateral parotid involvement. Full blood count, serum urea and electrolyte concentrations and liver function tests were normal. Chest X-ray showed no evidence of any active or metastatic disease. A radical excision of the lesion including the earlobe, the parotid gland with sacrifice of facial nerve and a functional neck dissection were performed. The final diagnosis was of a well differentiated (G1) squamous cell carcinoma (SCC), pT4 pN1 M0. Post-operative radiotherapy (65 Gy) was administered and 18 months later the patient was healthy, with no recurrence.

**DISCUSSION**

Skin manifestations by tuberculous infection are rare (less than 0.1% of dermatologic patients), and they may be a consequence of a direct inoculation of tubercle bacilli in the skin.
(tuberculosis verrucosa cutis) or secondary to systemic infection. The most common cutaneous lesion is represented by Lupus vulgaris (LV), which is a typical expression of the presence of the tubercle bacilli in the dermis of patients with a previous tubercular infection, usually at pulmonary level [1-6].

LV is a chronic and progressive condition, which usually occurs on the face, especially on the nose, as a solitary small, sharply margined, red-brown papule of gelatinous consistency (“apple-jelly” nodules), with slow growing into large plaques with central atrophy. Not uncommonly several bacilli persist at the periphery of the lesion, leading to a progression directly related to the status of the immune system. The mainstay therapy is represented by well-codified multi-drug anti-tubercular chemotherapy [1-6].

To the best of our knowledge, fewer than 30 similar cases have been reported, most published before 1990 [7-17]. Two cases of SCC arising on a chronic history of LV (about a 40-year history in both patients) have been reported in the last two years: the country context (Turkey and South Africa respectively) could suggest a tuberculotic infection [15, 16]. Ziehl-Neelsen staining proved positive only in the South African patient, whereas Tuberculin Tine Test positivity was detected in both cases. More recently, Zawirska et al. reported a case of a 65-year-old man presented in New Jersey with a 40-year history of LV, misdiagnosed as psoriasis and complicated by the development of a cutaneous SCC. As in our case, the patient was a farmer: thus the authors suggested that chronic sunlight exposure may have played a role in the aetiopathogenesis of malignancy from his long-standing LV [17].

SCC is one of the most common non-melanoma tumours of the skin, which recognizes several risk factors in its aetiology, such as X-ray irradiation, sunlight exposure and chronic inflammation. In 1969 Forstrom et al. among 460 patients affected by LV observed 8% of SCC arising on tuberculous skin lesions and suggested a strict relation between SCC and long-standing chronic inflammation status [18].

Chronic inflammation (at least 10 years) causes an increase in cytokine levels in loco. Cytokines are proteins involved in fundamental mechanisms of tissue repair process, inducing cell

![Histological features of the well-differentiated squamous cell carcinoma: haematoxylin-eosin, original magnification x4 (A) and x20 (B).](image)

Figure 3 - Histological features of the well-differentiated squamous cell carcinoma: haematoxylin-eosin, original magnification x4 (A) and x20 (B).
proliferation. The continuous proliferative status leads to a shortened G2 phase, such that the DNA-repair process is impaired and several mutations are eventually accumulated, with a normal regeneration process easily slipping into carcinogenesis [18-20].

X-ray irradiation and sunlight exposure are well-described risk factors for neoplastic processes due to their direct damage of DNA. Deregulation of the cell cycle and genetic predisposition, after several years or decades, lead to cancer transformation [18-20].

In our patient, malignant transformation of the misdiagnosed and undertreated skin lesion seems to be the result of at least two of the above-mentioned risk factors: chronic (approximately 50-year) inflammation status and sunlight exposure due to the rural environment. In conclusion, the reported case of SCC arising on a 50-year history of LV emphasizes how a chronic inflammation status could represent an important risk factor for skin cancer. A strict medical follow-up in such long-standing lesions, especially when not responding to any therapy, should be considered in order to prevent malignant transformation or achieve a correct diagnosis in earlier stages.

Key words: Lupus vulgaris, Lupus Carcinoma, chronic inflammation

SUMMARY

Skin manifestations of tuberculous infection (Mycobacterium tuberculosis) are represented by miliary tuberculosis of the skin, tuberculous chancre, scrofuloderma, tuberculosis verrucosa cutis, periorificial tuberculosis, and Lupus vulgaris (LV). Among this group, LV is the most common skin condition, diagnosed in 10% of tuberculotic patients. The authors report herein a case of squamous cell carcinoma (SCC) arising from long-standing (50-year) LV and underline the need of an extensive follow-up of tuberculotic lesions.

REFERENCES

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