Twice malignant transformation of hypertrophic lichen planus

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Abstract
Lichen planus is a chronic mucocutaneous T-cell-mediated disease, the cause of which remains unknown. The first case of lichen planus that transformed into squamous cell carcinoma was reported in 1903. The presented study concerns the case of a 62-year-old woman in whom twice malignant transformation of hypertrophic lichen planus in the dorsal part of the left foot developed. Several studies have pointed out the malignant transformation potential of lichen planus. Epidemiological studies from the last 20 years have revealed a malignant transformation rate of 0.27% per year, emphasizing the importance of the clinical follow-up of lichen planus patients.

Key words
autoimmune disease, lichen planus, malignant transformations, squamous cell carcinoma.

Introduction
Lichen planus (LP) is a mucocutaneous disease, characterized by an unspecific chronic inflammatory process which leads to an intense destruction of the basal layer of the epithelium. Lichen planus affects about 1% of the population. The exact cause of lichen planus (LP) is still not known. The first case of lichen planus (LP) is not still known. The lichen planus is an immunologically-mediated disease. Langerhans cells process the foreign antigens, which are then presented to T lymphocytes. They stimulate lymphocytic infiltration into the dermis and attack the keratinocytes. During this lymphocytotoxic process, the keratinocytes release cytokines that attract more lymphocytes. This process has been referred to as the lichenoid tissue reaction. In addition, recent studies reveal a disruption in the epithelial anchoring system [1, 2].

The hypertrophic or warty variant of LP is a type of the disease better known as lichen planus hypertrophicus (LPH) [3]. Although it is a benign disorder, malignant changes may happen and less than 50 such cases have been reported [4, 5]. SCC complicating cutaneous LP has an incidence of 0.4% [3, 6, 7, 8, 9, 10, 11, 12, 13, 14] An average time interval of 12 years has been documented between the diagnosis of LP and the development of carcinoma [10]. However, both LP and SCC are not uncommon diseases, and the simultaneous finding of both conditions in a patients does not provide evidence of a definite cause-and-effect relationship [3, 4, 6, 7, 8, 9, 10]. The aim of the presented study was to present a case of a patient with hypertrophic lichen planus in whom SCC developed [4, 15].

Case report
The presented case report concerns a 62-year-old woman who has lived and worked in the country. The place of residence highly influenced her work and lifestyle. The woman used to spend most of her time outside, therefore the results of sun exposure were visible on her body. The patient was Caucasian with skin photo type 3. She has been suffering for 30 years from long-lasting and histologically-documented hypertrophic lichen planus, with very short periods of remission. She was treated orally with cyclosporine (2.5mg/kg daily, for 6 months) and steroids with only periodical improvement; recurrences happened (on average, 2 exacerbations a year). The disease was accompanied by severe itching. Upon examination, polygonal hypertrophic violaceous papules were seen on the lower limbs, the flexural areas of the wrists, the elbows and the loins, and plaques located predominantly on the dorsal part of the feet were present. They were accompanied by a lot of erosions. Three years ago, the SCC lesions located on her dorsal part of the left foot were operated on [16].

She was hospitalized because of the presence of new and well-outlined, hard, exophitic nodule among hypertrophic lichen planus lesions in the dorsal part of her left foot (Fig.1). The biopsy, taken from the nodule, revealed squamous cell carcinoma. The patient was referred to the Oncology Department where she underwent surgical excision, with subsequent full thickness skin graft from the unaffected thigh (Fig. 2). The regional lymph nodes were normal on physical examination. Examination of the mouth disclosed reticulated white striae on the buccal mucosa, bilaterally. Nails and hair were unaffected. The general medical examination and laboratory testing of the patient were unremarkable. Hepatitis C Virus (HCV) antibodies were negative. Topical steroid ointments and oral antihistamines were administered on the LP lesions. The follow-up, 6-months after the surgery, showed no recurrence of LP or SCC in the area of the skin.
graft. However, LP hypertrophic lesions remained persistent around the graft and on the previously affected regions of the skin.

DISCUSSION

The presented paper concerns the case of twice development of SCC in the course of hypertrophic lichen planus. There are reports of a few such cases from India where the patients had multiple lesions of LP, one or two of which underwent malignant change [6, 17, 18, 19]. In the presented case, during the long duration of the disease, solitary lesions occurred twice. Sometimes, such cases may mimic SCC clinically, but histopathology reveals LPH with pseudo-carcinomatous hyperplasia without any evidence of malignancy. However, these cases require regular and vigilant follow-up. Histopathology in such lesions shows marked hyperkeratosis, acanthosis, papillomatosis and hypergranulosis [20, 21].

Our patient had a well-differentiated SCC with a size less than 2 cm and absence of overlying ulceration, which is an indicator of a good prognosis; she has been doing well with the treatment applied. Hence, careful vigilance of a long-standing LPH is necessary to allow early detection of a developing SCC.

The patient in the presented case was diagnosed with hypertrophic lichen planus on the dorsal aspect of the left foot. Malignant transformation of lichen planus of the skin is rarely described, in contrast with malignant transformation of lichen ruber of the mucous membranes of the mouth. Squamous cell carcinoma is more frequently found among patients with hypertrophic lichen planus than in those with plain lesions. Interestingly, squamous cell carcinoma is mostly found on the distal extremities (79%) in patients with lichen planus, in contrast with only 2-7% at that location in other cases unrelated to lichen planus [7, 22].

Hypertrophic lichen planus is a chronic variant of lichen planus characterized by hypertrophic or warty lesions most often found on the pretibial area of the lower limbs [6, 23, 24]. In the literature, 41 cases of lichen planus, mainly of the hypertrophic or verrucous types, with consecutive carcinoma have been described [3, 7, 8, 11, 18, 22, 25]. X-ray and arsenic treatment of lichen ruber often preceded malignant transformation by many years [8]. Several authors have stressed the possible association between LP and SCC due to underlying similarities in the pathogenesis of these diseases [3, 7, 8, 9, 10, 11, 12, 26]. Immune alterations associated with LP, together with other cofactors, for example, a history of arsenical or ionizing or ultraviolet radiation treatment, may play an important role in the development of SCC in patients suffering from LP [3, 7, 8, 11, 12]. Furthermore, both chronic inflammation and the accelerated cellular turnover in LP provide a fertile environment for cancer development [3, 7, 8, 11, 12, 26, 27].

This association could be explained by the fact that patients with pruritic and chronic dermatosis tend to scratch the lower part of their legs more often and more intensely, causing chronic inflammation, which is a well-established risk factor for carcinogenesis. Malignant change should be taken into consideration when a proliferative area appears in a lesion of hypertrophic LP located on the legs, particularly in long-standing lesions [4].

CONCLUSIONS

In the patient in the presented case, long-lasting severe itching skin lesions, together with sun expositions and treatment with immunosuppressive drugs, may influence the SCC development.

Patients with unusual clinical presentations during the course of hypertrophic LP should be closely followed-up with skin biopsies to exclude malignant transformation.

REFERENCES


