ATYPICAL PRESENTATION OF DISSEMINATED ACTINIC KERATOSES IN AN IMMUNOCOMPETENT PATIENT

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Abstract

Introduction: Actinic keratoses are frequent precancerous lesions, caused by cumulative UV radiation, especially UVB, which involve sun-exposed areas such as the face, ears or dorsum of hands in fair-skinned people. The risk of malignant transformation into squamous cell carcinoma is 10%.
Material and methods: A 66 years old female, with Fitzpatrick photo type II skin, with no significant personal history, presented for consultation with multiple, disseminated, more than 20 erythemato-squamous, hyperkeratotic, well-circumscribed lesions, localized on the ears, chest, dorsum of the upper limbs and lower legs, that spared the face, in evolution for 10 years. In the inferior region of the right leg, a well circumscribed ulcer, 3 centimeters in diameter, was present for 2 years. The lesions were asymptomatic and topically treated for psoriasis vulgaris for several years with emollients and topical corticoids, with no improvement.
Results: All laboratory investigations for immunosuppression and an aggressive evolution of these precancerous lesions, such as HIV-infection, neoplasia and autoimmune diseases, were negative. The pathology investigations (3 punch biopsies) showed actinic keratosis KIN II-III and KIN III. The biopsy from the leg ulcer revealed an ulcerated squamous cell carcinoma. A multidisciplinary approach of the patient had been chosen in order to evaluate the medical status.
Discussions: Actinic keratoses, as precancerous lesions, require a strict follow-up and a histopathological examination of any lesion suspected of having a neoplastic transformation. An accurate and prompt diagnosis is essential. Close monitoring with the analysis of different diagnostics is necessary in chronic skin diseases in order to adapt a long-term treatment. In this case, the psoriasis vulgaris treatment was maintained by the patient despite the poor outcome.
Conclusions: This patient typically illustrates the necessity of sun protective measures for all exposed skin, not only for the face (patient with photo type II skin, blue eyes and lesions that involve sun-exposed areas such as dorsum of hands, ears and chest, but sparing the face).
The diagnosis of skin lesions in older persons should consider not only common diseases such as vascular leg ulcer due to chronic venous insufficiency, but also ulcerated skin carcinomas and not every erythemato-squamous lesion should be considered psoriasis vulgaris. Patients with actinic keratoses require a strict clinical follow-up. It is extremely important that the patient understands the necessity of reporting any changes in the preexisting lesions as soon as possible.

Keywords:

actinic keratoses,
squamous cell carcinoma,
sun protection.

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Introduction

Actinic keratoses (solar keratoses) are frequent precancerous lesions characterized by UV-induced dysplasia of epidermal keratinocytes (1). The main pathogenic mechanisms include inflammation, oxidative stress, genetic mutations and dysregulations of cellular proliferation and cellular growth (2). They usually affect Fitzpatrick photo type I and II (usually fair-skinned persons) and are frequently localized on sun-exposed areas such as the face, dorsum of the hands or the auricula (3).

There are numerous clinical forms such as pigmented, atrophic, Bowenoid, lichen planus-like or hypertrophic actinic keratoses (4).

Regarding the risk of malignant transformation into squamous cell carcinoma, there seems to be a ten-fold increase in patients presenting with more than ten lesions (5).

Management of actinic keratoses depends on several classifications such as KIN (keratinocyte intraepithelial neoplasia), PAK (proliferative actinic keratosis), IAK (inflamed actinic keratosis) (6) and includes different therapies, from topical treatment to cryotherapy, photodynamic therapy or classical surgical excision. Management costs represent a significant burden, adding up to 1.2 billion dollars *per* year in the US (7). Therefore, effective preventive measures and efficient methods of early diagnosis are essential.

Case report

A 66-year-old, fair-skinned, blue-eyed female, from rural environment, with no significant personal history, presented for consultation with multiple, disseminated, more than 20 erythemato-squamous, hyperkeratotic, well-circumscribed lesions, 0.5–5 cm in diameter, localized on the ears, chest, dorsum of the upper limbs (Figures 1 and 2), lower legs and sparing the face, with a 10-year evolution. Two years before presentation, the patient noted the transformation of an erythematous, scaly patch into a well circumscribed ulcerated lesion in the inferior region of the right leg (Figure 3). It increased in size and reached 3 centimeters in diameter at the moment of clinical examination.

The lesions were asymptomatic and topically treated for several years for psoriasis vulgaris with emollients and topical corticoids with no improvement.

Figure 1. Disseminated erythemato-squamous lesions of the upper limbs

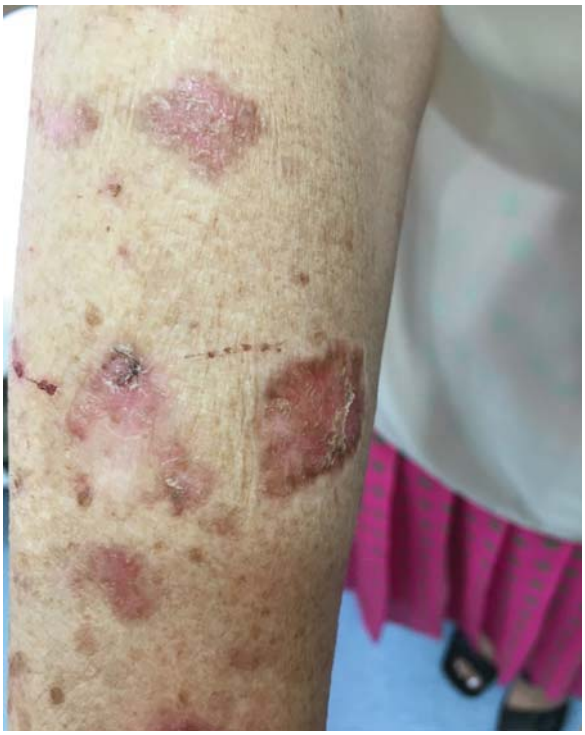

Figure 2. Clinical aspect of the erythemato-squamous patches

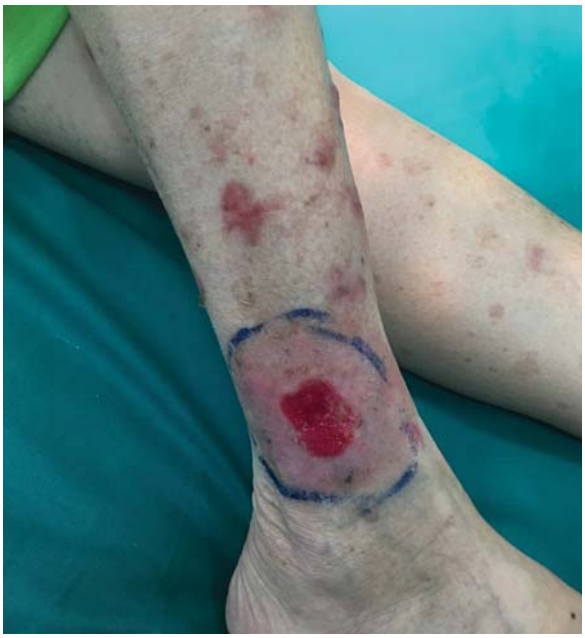

Figure 3. Ulcerated, well-circumscribed lesion on the lower right leg

The patient also associated signs of actinic degeneration such as multiple lentigines, ephelides and solar elastosis, located on the chest and dorsum of the upper limbs.

Dermatology Quality of Life Index (DLQI) was 8 at the initial visit, and clinical examination revealed a round, mobile, infracentimetric, asymptomatic axillar lymphadenopathy, without any other abnormalities of the cardiovascular, osteoarticular, digestive or nervous systems.

Based on clinical findings, the diagnoses of disseminated actinic keratosis and squamous cell carcinoma were made. For confirmation, three punch biopsies were taken from the left arm, upper right arm and from a margin of the ulcerated lesion of the lower right leg.

The biopsy from the left arm revealed an atrophic epidermis, atypical keratinocytes with cytonuclear pleomorphism, orthokeratosis, lymphocytic inflammatory infiltrate with melanophages at the dermo-epidermal junction and important dermal solar elastosis with dilatated capillary vessels, revealing a lichen planus-like actinic keratosis KIN III (Figure 4).

The second biopsy showed similar findings, revealing an actinic keratosis KIN II-III and the punch-biopsy from the ulcerated lesion identified areas of intratumoral keratinization with formation of keratinous pearls, nests of squamous cells and a polymorphic infiltrate, establishing the diagnosis of invasive, ulcerated, moderately-differentiated squamous cell carcinoma (G2) (Figure 5).

Disseminated actinic keratoses can be suggestive of an underlying immunosuppression, such cases being usually associated with HIV infection. Therefore, several serologic investigations were made: the detection of HIV-1 and HIV-2 antibodies was negative, tumor markers (CEA, CA 15.3, CA 125, CA19.9) were also in normal limits and an autoimmune disease was excluded based on the normal value of antinuclear antibodies, serum complement, autoantibodies anti-dsDNA.

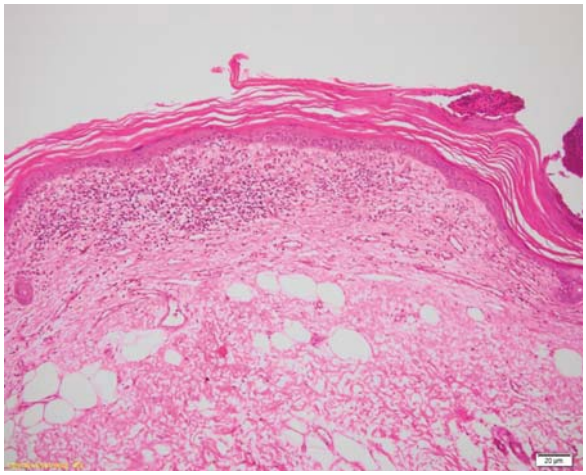

Figure 4. Pathology examination of the left arm revealing a lichen planus-like actinic keratosis KIN III (Courtesy of Prof. Dr. Sabina Zurac)

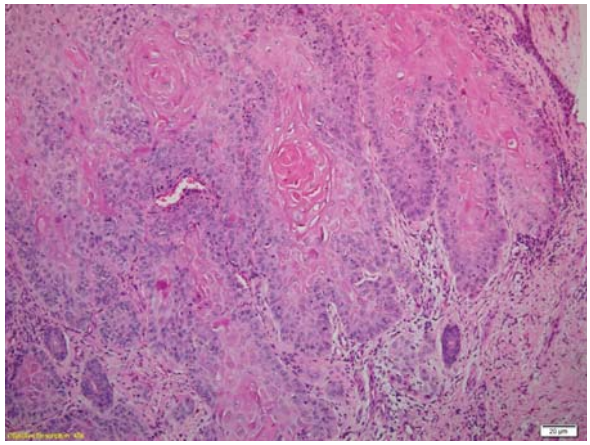

Figure 5. Pathology findings of the ulcerated lesion of the lower right leg revealing an invasive, ulcerated squamous cell carcinoma G2 (Courtesy of Prof. Dr. Sabina Zurac)

The extent of the disease has been evaluated by an interdisciplinary team, including different specialty consultations of oncology, internal medicine, plastic surgery and gynecology. Also, a bilateral mammography excluded any primary or secondary malignant involvement.

Discussions

Actinic keratoses, as precancerous lesions, require a strict follow-up of all cutaneous lesions and a histopathological examination of any suspect lesion. They usually imply a long-term evolution with possible malignant transformation into squamous cell carcinomas (8). Once transformed, the mortality and morbidity of this pathology cannot be neglected, with a 5-year survival rate of only 25-40% in advanced cases and significant disfigurement, especially post treatment (9).

In this case report, it is worth mentioning the presence of risk factors such as age, fair skin complexion, blue eyes, and signs of actinic degeneration such as multiple lentigines, ephelides and solar elastosis.

A correct and early diagnosis of this pathology is essential. Several differential diagnoses for this erythematous, scaly eruption could have been considered, such as disseminated superficial actinic porokeratosis, discoid lupus erythematosus, psoriasis vulgaris, etc. Taking into consideration the patient's risk factors and the affected sun-exposed areas, the diagnosis was oriented towards a non-melanocytic precancerous lesion.

Furthermore, the presence of an ulcerated lesion in a middle-aged patient, localized on the lower leg, could suggest the diagnosis of a vascular leg ulcer due to chronic venous insufficiency. Other differentials should also be considered, such as ulcerated squamous cell carcinoma in this case, or even pyoderma gangrenosum, HSV infection, ulcerated basal cell carcinoma or a posttraumatic lesion.

A correct and prompt diagnosis could have been essential in preventing a malignant transfor-

mation in this case. Periodical strict dermatologic follow-ups are extremely important for patients with actinic keratoses. Another important aspect is that the patient understands the necessity of reporting any changes observed in the preexisting lesion.

In this case, DLQI of 8 (ranging from 0 to 30) suggests important impairment of the patient's quality of life.

Regarding the management of this condition, several treatments can be used, depending on the number of lesions and location and on the presence or absence of immunosuppression. They include topical therapies (0.5% 5-fluorouracil, 3.75% imiquimod, 0.015% ingenol mebutate (lesions on face and scalp) and 0.05% ingenol mebutate (lesions on trunk and extremities), cryotherapy, photodynamic therapy or surgical excision (10). In this case, cryotherapy was applied, two sessions of 10 seconds each along with emollients and antiseptics. Also, the patient has been referred to plastic surgery for excision with reconstruction of the ulcerated lesion.

Another important aspect of the management of non-melanoma skin cancer is that strict and efficient sun protective measures should be taken. Not only sun protective creams with a SPF of 30+, but also adequate clothing (long sleeves, broad-brim hats) and staying indoors in the period of maximum sun intensity, between 10:00 am and 04:00 pm. In this case, the patient stated that protection of the face was frequently insured by a broad-brimmed hat and sun protective creams, but all other areas were neglected, giving a justification for the location of the lesions.

Conclusion

This patient typically illustrates the necessity of sun protective measures for all exposed skin, not only for the face (fair-skinned patient with blue eyes and lesions that involve sun-exposed areas such as dorsum of hands, ears and chest, but sparing the face).

The diagnosis of skin lesions in older persons should consider not only common diseases such as vascular leg ulcer due to chronic venous insufficiency, but also ulcerated skin carcinomas, and not every erythemato-squamous lesion should be considered psoriasis vulgaris.

Patients with actinic keratoses require a strict clinical follow-up. It is extremely important that the patient understands the necessity of reporting any changes in the preexisting lesions as soon as possible.

Conflicts of interest: none declared.

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