Multiple reactive keratoacanthomas in a patient with hypertrophic lichen planus treated with cyclosporine: Successful treatment with acitretin

Sir,

Keratoacanthoma is a common cutaneous neoplasm that most often affects males (M:F = 3:1) with skin phototype 1 and 2, and within the fifth to seventh decade of life. The real nature of the tumor is controversial; the tendency toward spontaneous regression suggests a benign course, but it may rarely metastasize.[1] For this reason and because its histopathologic pattern often resembles that of a typical squamous cell carcinoma (SCC), keratoacanthoma is now best regarded as a subtype of SCC (SCC keratoacanthoma type).[1] Although the exact etiology is unknown, sun exposure, mechanical trauma, ionizing radiations, chemical carcinogens, infections by human papilloma virus, genetic and

immunological factors may all be considered to be possible etiologic factors. Finally, immunosuppressive therapy and chronic inflammation related to some dermatologic disorders such as hypertrophic lichen planus or psoriasis has been suggested to play an etiological role.[2-4]

A 64-year-old man presented with a 4-week history of pruritic papules located on the trunk and extensor surface of hands and legs. There was no family history of dermatological diseases. The patient was known to be suffering from chronic obstructive pulmonary disease, hypertension, stroke and epileptic attacks. The patient denied allergies to medications and past surgical interventions. Dermatologic examination revealed multiple violaceous, hyperkeratotic papules, some of which were confluent to form plaques, located on the trunk and legs [Figure 1a]. A clinical diagnosis of hypertrophic lichen planus was confirmed by histopathological examination of a papular lesion located on the right clavicular region, showing apoptotic keratinocytes, vacuolar degeneration, pigment incontinence and marked lympho-histiocytic infiltrate [Figure 1b]. Cyclosporine was initiated at a dose of 5 mg/kg/day and after 4 weeks of treatment, hypertrophic lichen planus improved and the dosage was reduced to 3 mg/kg/day. After another 8 weeks, complete remission was observed leaving behind residual hyperpigmentation. However, around 20 nodules ranging from 0.5 to 1.2 cm in diameter, with a central keratin filled crater appeared on the legs [Figures 2a and b]. Dermatoscopy of all lesions showed the same pattern characterized by a central mass of keratin surrounded by white structureless areas, dotted and hairpin vessels. Histopathologic evaluation of a biopsy from a lesion on the right leg showed a peripheral zone formed of squamous cells with atypical mitotic figures, hyperchromatic nuclei and loss of polarity to some degree [Figure 2c], consistent with a diagnosis of keratoacanthoma.

The diagnosis of multiple reactive keratoacanthomas was made and acitretin 0.5 mg/kg/day was prescribed. After three months, the lesions disappeared except for a persistent nodule on the right leg which reached a size of approximately 4 cm in diameter. However, this residual lesion disappeared after another three months of treatment at the same dosage [Figure 2d]. After a six-month follow-up, no recurrence was observed.

Keratoacanthoma usually appears as a solitary lesion but multiple or generalized forms and unusual variants have been described [Table 1].[1] Reactive keratoacanthomas have been reported as a consequence of inflammatory or infectious dermatoses (psoriasis, lichen planus, hypertrophic lichen planus, prurigo nodularis, pemphigus foliaceous, discoid lupus erythematosus, herpes zoster) and physical trauma (vaccination, radiation, thermal burns, cryotherapy, surgery, chronic scratching, tattoos).

Two cases of multiple keratoacanthomas associated with hypertrophic lichen planus[3-4] and one of multiple keratoacanthomas in a psoriatic patient treated with cyclosporine[2] have been reported in the literature. The etiological factors of hypertrophic lichen planus and cyclosporine therapy were present in our patient, in whom keratoacanthomas occurred after 12 weeks of treatment. It is likely that the onset of multiple reactive keratoacanthomas was triggered by chronic inflammation and/or repeated scratching related to hypertrophic lichen planus; moreover, the

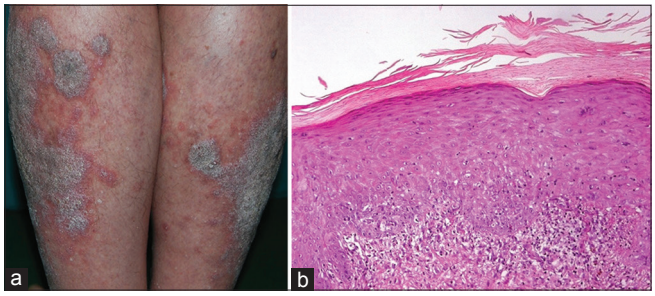

Figure 1: (a) Clinical (multiple violaceous, hyperkeratotic papules and plaques) and (b) histopathological (apoptotic keratinocytes, vacuolar degeneration, pigment incontinence and lympho-histiocytic infiltrate; H and E, ×150) aspects of hypertrophic lichen planus

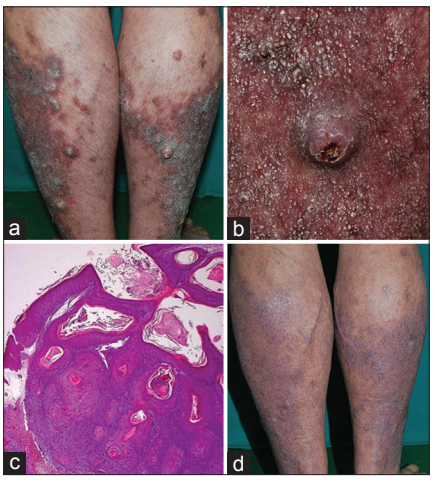

Figure 2: (a and b) Clinical and (c) histopathological (H and E, ×25) aspects of keratoacanthomas (d) the lesions completely disappeared after 3 months of treatment with acitretin

Table 1: Keratoacanthoma: Clinical variants and classification

Solitary KA
Typical
Unusual types
Agglomerated form
Enlarging type up to 20 cm in diameter (KA centrifugum)
Giant up to 9 cm or larger
Subungual
Plate-shaped
Multiple KAs
Intraoral and other mucous membrane KAs
Multiple eruptive KAs of Ferguson Smith type
Multiple familial KAs of Witten and Zak
Multiple persistent KAs
Generalized eruptive KAs of Grzybowski type (thousands of tiny disseminated 2-3 mm KAs)
KAs in special conditions
Muir-Torre syndrome
Xeroderma pigmentosum
Florid cutaneous papillomatosis
Nevus sebaceous of Jadassohn
Pseudorecidive KAs
Reactive KAs
Occupational (chemical induced-mainly tar) KAs
KAs in immunosuppressed patients

Modified from Schwartz RA, 2004,[1] KA: Keratoacanthoma

immunosuppressant effects of cyclosporine may also have contributed.

Although the gold standard for the treatment of keratoacanthoma is surgical excision, oral retinoids have been successfully used for the treatment of multiple lesions,[4-5] thus avoiding surgery. The exact mechanism of action of retinoids on keratoacanthomas is unknown: modulation of terminal differentiation of epidermal cells has been suggested to induce inhibition of keratinization.[5] Our patient had a positive response without recurrence during a six-month period of follow-up, as also noted in a previous report.[5]

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DOI: 10.4103/0378-6323.136984