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CORRESPONDENCE

Large cell acanthoma manifesting as multiple white papules on extremities

Case reports

Case 1

A 39-year-old woman with essential hypertension and diabetes mellitus presented with multiple asymptomatic white papules on her bilateral upper extremities for more than 10 years. They were small well-defined, flat-topped white papules measuring 0.2–0.5 cm (Figure 1A). A skin biopsy taken from her left upper arm showed basket weave hyperkeratosis and a well-demarcated area of slightly thickened epidermis composed of enlarged cells with nuclei larger than those of the adjacent normal epidermal cells (Figure 2A).

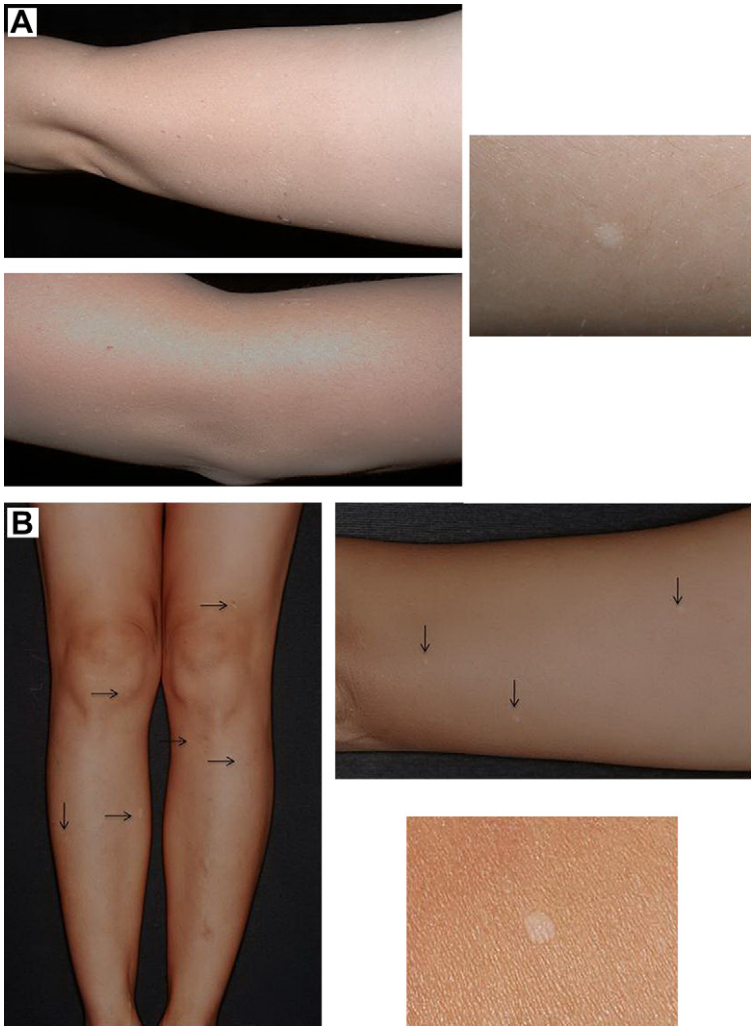

Figure 1 (A) A 39-year-old woman with multiple whitish papules on her upper extremities. (B) Scattered depigmented papules on the extremities in a 38-year-old woman.

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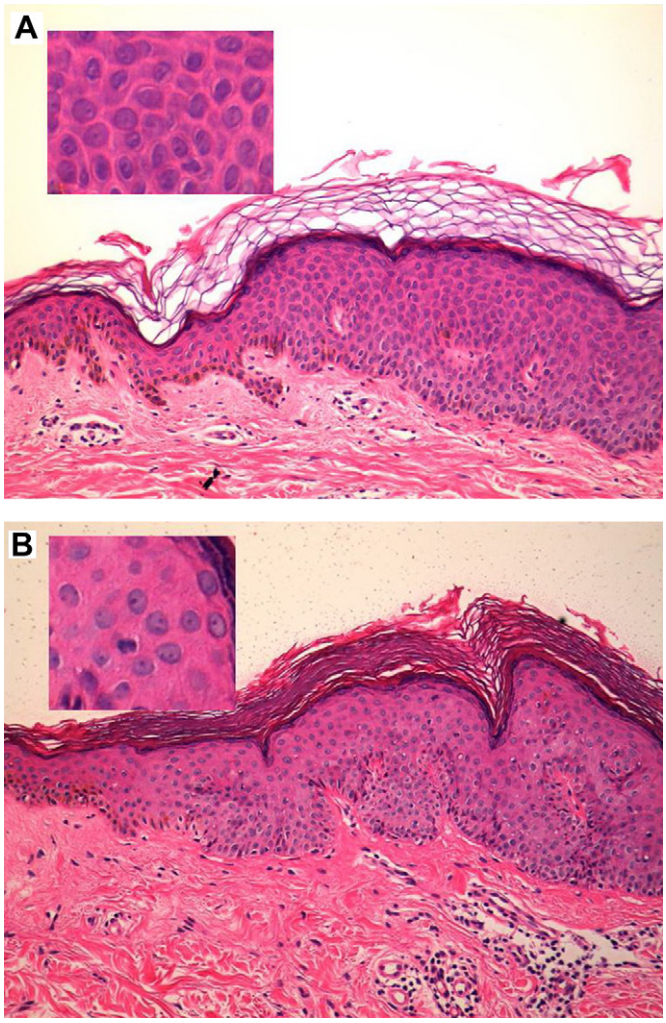

Figure 2 (A) Case 1. Microscopic details show basket weave hyperkeratosis and acanthosis with enlarged keratinocytes compared to the adjacent epidermal cells (enlarged in inset). (B) Case 2. The skin shows hyperkeratosis, acanthosis composed of large keratinocytes with large nuclei (enlarged in inset). Both skins are depigmented.

Case 2

A 38-year-old woman presented with multiple asymptomatic white papules on her four extremities for 6 months. They were well-demarcated and slightly elevated white papules measuring 0.5 cm (Figure 1B). The number of these lesions was increasing gradually over a 2-month period. A skin biopsy taken from her left upper arm showed a focal slightly elevated lesion with moderate hyperkeratosis and thickened epidermis composed of larger epidermal cells with enlarged nuclei, and mild perivascular mononuclear cell infiltration in the dermis (Figure 2B).

Discussion

In 1970, Pinkus[1] reported large cell acanthoma (LCA) as epidermal lesions with epidermal orthokeratosis with or without papilomatosis; the size of the keratinocytes was at least twice as large as that of the nearby normal keratinocytes. Sanchez Yus et al[2] proposed that LCA was a disease entity which was different from solar lentigo. Unlike solar lentigo, the keratinocytes in LCA were definitely larger than normal ones and hyperkeratosis was also a distinct feature. Different deoxyribonucleic acid (DNA) content was demonstrated in LCA and solar lentigo by Rabinowitz et al.[3]

Table 1 The relationship between human papillomavirus (HPV) and large cell acanthomas.

Case	Reference	Method	HPV type
1.	Berger et al[4]	PCR	6
2.	Garrido-Rios et al[5]	PCR	16,53
3. Present case	Present case	PCR	33

PCR = polymerase chain reaction.

As to the pathogenesis of LCA, human papillomavirus (HPV) has been reported to be associated with LCA (Table 1).[4,5] In 2005, Berger et al[4] claimed that HPV type 6 might be associated with LCA because it was detected on lesional skin by using polymerase chain reaction (PCR). Garrido-Rios et al[5] demonstrated HPV type 16 in conjunction with HPV type 53 not only in lesional skin but also in perilesional skin in 2009. In Case 1, we found HPV type 33 by the PCR-based gene chip method. However, in Case 2, no HPV was detected. Besides, no uniform HPV type is found in the reports mentioned above. The relationship between HPV infection and LCA remains to be investigated.

Clinically, LCA presents as a single or multiple hyperpigmented papules, usually less than 10 mm in size.[2–4] The clinical differential diagnosis includes solar lentigo, Bowen's disease, actinic keratosis, and seborrheic keratosis.[2,3] Achromic LCA is unusual and one case of a verrucous papule on right hand has been reported.[6] The clinical manifestation of the generalized depigmented papules on limbs had not been reported before. Clear cell papulosis could be a clinical differential diagnosis for multiple depigmented papules on the trunk and/or limbs. Histopathological examinations could help to establish the definite diagnosis.

The histological features of LCA can be classified into three patterns as basic, verrucous and hyperkeratotic.[2] In our cases, the basic pattern is favored. Classically, the pathological findings were characterized by acanthosis, hyperkeratosis, and epidermal cells with abundant cytoplasm and larger round nuclei.[3] Basal pigmentation is one of the features in typical LCA, but our two cases are depigmented.

To date, there was no definite treatment modality for multiple LCAs. Because LCA is usually a solitary lesion, an excisional biopsy achieves both therapeutic and examining goals. In Case 1, the patient was treated with topical retinoid and then trichloroacetic acid (TCA), while the other patient received topical corticosteroids. Only TCA gained therapeutic effect, but recurrence of skin lesions was also noted. More therapeutic trials for this entity need to be explored.

In summary, we report two cases of LCA presented as multiple depigmented papules on the extremities. They should be considered in the differential diagnosis of similar clinical lesions. Our results of HPV study raises further question for the role of HPV in the pathogenesis of LCA.

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