Photo Vignette

Large cell acanthoma: A benign lesion masquerading as malignant melanoma

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Abstract

We present the case of a 54-year-old woman with a clinically suspected malignant melanoma. Histology, however, revealed the unexpected diagnosis of large cell acanthoma. This is a benign epidermal neoplasm that is poorly understood and underreported in the literature. The clinical and dermoscopic appearance in our patient differs from previously reported cases. We draw attention to this heterogeneous lesion and encourage further investigation into its classification and distinguishing features, which may ultimately inform optimal management for patients.

Introduction

Since large cell acanthoma (LCA) was first described in 1970, there has been ongoing debate regarding its classification.[1] It is widely considered a benign epidermal neoplasm, presenting as a lightly pigmented, slightly keratotic macule or plaque, most commonly on sun-exposed sites in middle-aged to elderly individuals.[2] Histologically, LCAs are defined by sharply demarcated epidermal hyperplasia with pathognomonically large keratinocytes, approximately twice the size of their unaffected neighboring cells.

Clinically, it is difficult to distinguish LCA from solar lentigo, seborrheic keratosis, and pigmented actinic keratosis. In the 1990s, some authors considered LCA a distinctive entity,[3] while others suggested it is simply a variant of solar lentigo, which itself may be a precursor to seborrheic keratosis.[4] A clinical and histological study of 19 LCA cases published by Mehregan[5] concluded that LCA is likely a variant of lentigo with a reactive pattern of hypertrophic cells. Moreover, the overlap between LCA and solar lentigo was most recently demonstrated by Fraga and Amin[6] in their macroscopic, microscopic, and immunophenotypic evaluation of 90 skin lesions. However, LCAs occurring on non–sun-exposed sites in both children and adults, as well as reports of hypopigmented LCAs, are inconsistent with solar lentigo.[7,8] The present case further highlights the wide clinical spectrum of LCA, with irregular hyperpigmentation leading to consideration of another clinical differential diagnosis for this lesion, namely melanoma.

Case Synopsis

A 54-year-old woman was referred with a strikingly pigmented plaque on her left medial thigh (**Figure 1A**). The longstanding, stable history over several years and well-defined, stuck-on, warty appearance were suggestive of a benign lesion such as seborrheic keratosis. However, the polychromatic nature and irregular pigmentation on clinical assessment were concerning for malignancy. Dermoscopic assessment (**Figure 1B**) revealed a non-specific brown and pink globular background. There were no hallmark melanocytic features, such as a reticular network, nor typical dermoscopic signs of seborrheic keratosis or any other non-melanocytic pigmented lesion. Although the sharply demarcated border suggested a benign lesion, the accentuated skin markings, irregular globules, and asymmetric hyperpigmented blotches all raised suspicion for melanoma in situ. The lesion was therefore urgently excised.

Histopathological examination demonstrated areas of normal epidermis interspersed with epidermal hyperplasia, acanthosis, and strikingly large keratinocytes, without significant cellular atypia (**Figure 2**). Focal hyperorthokeratosis and hypergranulosis were also observed, alongside basal hyperpigmentation. SOX10 immunohistochemistry ruled out a melanocytic lesion and favored a benign squamoproliferative lesion consistent with LCA. On review of further sections, an area of the lesion

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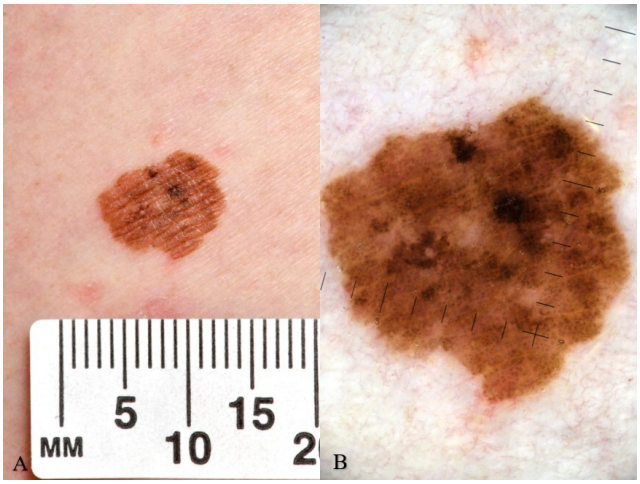

Figure 1. ***(A)*** *Clinical photograph showing a 10 × 9 mm darkly pigmented plaque on the left medial thigh with a well-defined border, multiple shades of pink and brown, and asymmetric distribution of pigment.* ***(B)*** *Dermoscopic photograph of the lesion showing a non-specific light brown background, with accentuated skin markings, irregular globules, and asymmetric hyperpigmented blotches.*

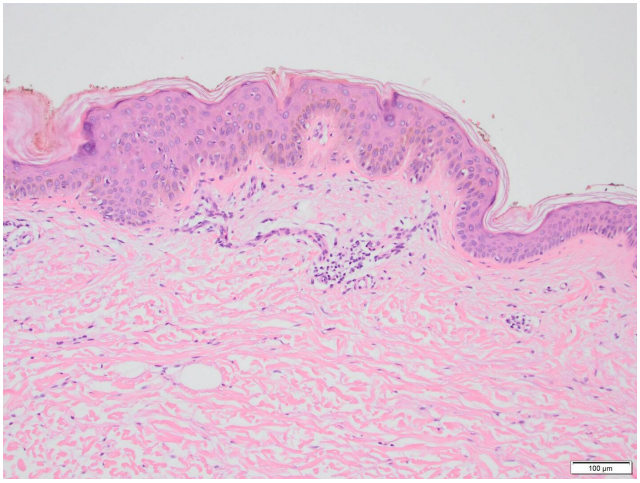

Figure 2. *Histopathological photograph of the lesion (hematoxylin-eosin, original magnification ×200). Focal hyperorthokeratotic and acanthotic lesion with basal hyperpigmentation on the left side and center of the image, with keratinocytes in the basal and spinous epidermal layers strikingly larger than those of the normal epidermis on the right-hand side.*

demonstrated a transition from normal epidermis to flat LCA and subsequently to a seborrheic keratosis–like area of LCA (Figure 3).

Case Discussion

Although the present case provides histologic evidence that LCA may represent a stage in the evolution of other skin lesions, such as seborrheic keratosis, rather than a distinctive entity, it does describe LCA on a non–sun-exposed site, which diverges from the solar lentigo hypothesis. When considering the clinical relevance of the LCA debate, the most important question remains the classification of a lesion as either malignant or benign. Yus et al[9] suggested that LCA is a variant of Bowen's disease owing to occasional suprabasal mitoses and dyskeratoses. However, no invasive behavior or malignant transformation has ever been reported in the literature, and LCA has long been considered a benign entity. Recognition of LCA in clinical practice is therefore important to avoid unnecessary surgical excision. A recent retrospective study evaluating 33 histopathologically confirmed LCAs proposed that dermoscopic features such as a yellow-opaque homogeneous background, brown dots, and a moth-eaten border are useful in distinguishing LCA from other epidermal tumors.[10] Although the present case features a well-demarcated border, the globular structures and irregular dark blotches do not match the previously described features, further highlighting the difficulty of diagnosing LCA. Even the promise of non-invasive techniques, such as reflectance confocal microscopy, has not proved reliable for diagnosing LCA, as a previously reported case was initially mistaken for Bowen's disease.[11]

Conclusion

We describe the vast heterogeneity of LCA, a lesion whose origin remains poorly understood, often misdiagnosed, and underrepresented in the literature. To provide the safest and least invasive care for patients with LCA, we must continue to investigate its pathology, clinical presentation, and dermoscopic features.

Potential conflicts of interest

The authors declare no conflicts of interest.

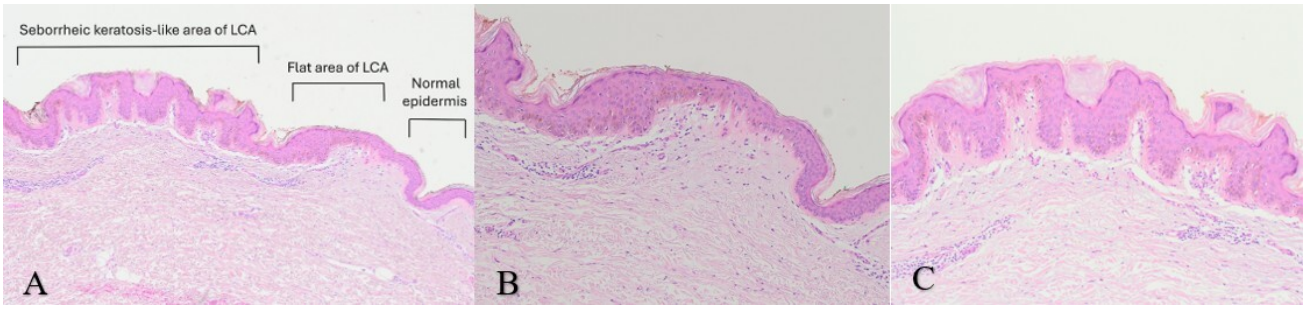

Figure 3. ***(A)*** *Histopathological photograph of the lesion (hematoxylin-eosin, original magnification ×40). Normal epidermis on the right side transitions to large cell acanthoma (LCA) in the center right and further to a seborrheic keratosis–like area of LCA on the left side.* ***(B)*** *LCA area showing keratinocytes transitioning from normal size on the right to large cells consistent with LCA on the left (hematoxylin-eosin, original magnification ×100).* ***(C)*** *Seborrheic keratosis–like area of LCA showing exophytic, papillomatous architecture, acanthosis, hyperkeratosis, and large keratinocytes (hematoxylin-eosin, original magnification ×100).*

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