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Case report

In vivo characterization of large cell acanthoma by cellular resolution optical coherent tomography

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To the Editor

Large cell acanthoma (LCA) was first described in 1970 by Pinkus as a sharply demarcated brown patch, often present on photodamaged skin and diagnosed by biopsy. It is sometimes difficult to distinguish LCA from other solar-induced pigmented lesions, such as lentigo maligna (LM) and lentigo maligna melanoma (LMM). Dermoscopy has improved the diagnostic accuracy of these facial spots, but there are overlapping features between benign and malignant lesions [1]. Reflectance confocal microscopy (RCM) can help discriminate them but requires significant training and experience [1].

Optical coherence tomography (OCT) is an established medical imaging technique in which biological images are captured using light deflected by optical scattering media. It is a noninvasive real-time device with good tissue penetration depth that could potentially be used in the diagnosis of skin lesions. High-definition OCT can provide an axial/lateral resolution of 3 μm/3 μm [2]. Recently, a Mirau-type full-field cellular resolution OCT was developed. A unique technology was introduced using a high-brightness broadband light source based on a glass-clad Ti^{3+}: sapphire crystal fibre that provided Gaussian-like near-infrared spectrum and hence an even higher axial resolution for OCT [3]. The Gaussian-like spectrum eliminates the ghost image due to the interpixel crosstalk from adjacent depths. The continuous-wave light source reduces the risk of skin burn due to multi-photon processes. Combining high-numerical-aperture objective lens and dynamic focusing, high lateral resolution can be maintained within the scanning range. The system provided cross-sectional scans with an axial resolution of 1.35 μm, lateral resolution of 1.3 μm, and scanning depth of 400 μm. The field of view is 500 × 400 um^2. Each scan required 2 s to acquire an image. In this article, we report the features of a facial and nonfacial LCA, using this in vivo cellular resolution full-field OCT provided by Apollo Medical Optics Inc., Taipei, Taiwan. This study was approved by our institutional review board (17CT062Be).

The first patient was a 54-year-old man who presented with a 3 × 3-cm round, thin brownish plaque on the left forearm for several years (Fig. 1a). Under the dermoscope, milia-like cysts, crypts, and fingerprint-like structures were found (Fig. 1b). The lesion centre and peripheral normal skin were scanned with the prototype of in vivo OCT using a probe attached on a swing arm. After the OCT images were captured, the lesion was excised for histopathological examination (Fig. 1c-e). The OCT images showed a thicker epidermis in the lesion than that in the normal skin (Fig. 1f, g). There were no hyperechogenic scales in the stratum corneum, and the dermal-epidermal junction of both sites was clearly outlined. The lesion had larger keratinocyte nuclei in the spinous layer. They were regularly distributed without disorganisation or disorientation. A prominent hyperechoic basal cell layer corresponded to the hyperpigmented basal cell layer. The OCT findings were consistent with the pathological features of LCA. The size of keratinocyte nuclei in these OCT images was measured by the Image J software. The mean nucleus size in LCA and normal skin was 42.72 ± 11.52 μm^2 (range, 20.16–70.16) and 16.99 ± 3.70 μm^2 (range, 8.60–25.80), respectively (1 area pixel = 0.2688 μm^2, $P < 0.0001$, *t*-test by SPSS version 19).

The second patient was a 48-year-old woman who presented with an enlarging brown patch on the lateral cheek in a background of sun-damaged skin (Fig. 2a). Under the dermoscope, most areas displayed milia-like cysts and crypts; however, some areas showed asymmetric pigmented follicular openings, dark rhomboidal structures, and

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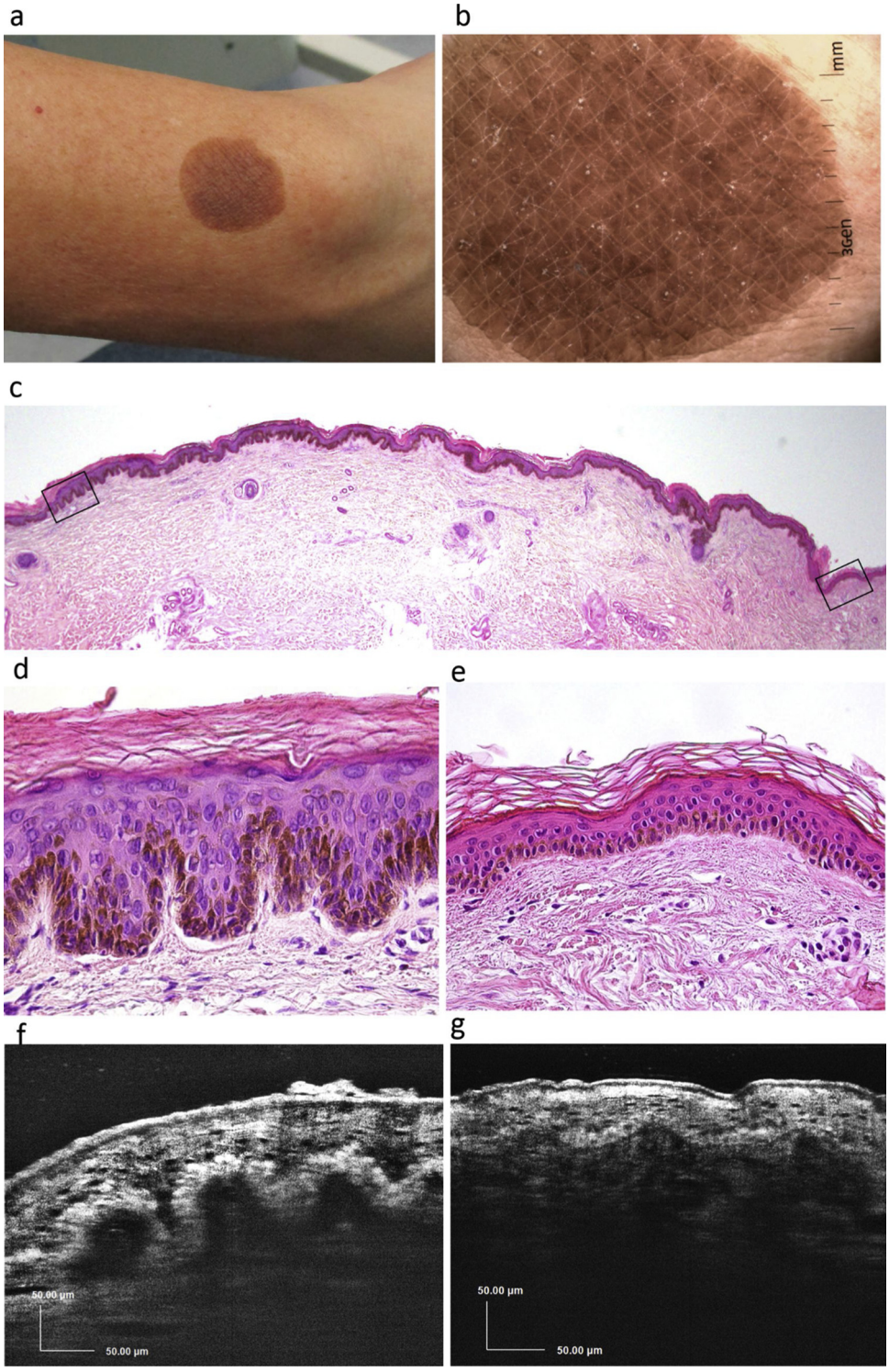

Fig. 1. (a) Clinical presentation. (b) Polarised dermoscopic image. (c) Scanning view of the large cell acanthoma. Haematoxylin and eosin stain, original magnification, 40 × . (d) Centre of the large cell acanthoma and (e) peripheral normal skin corresponding to the black inset in the figure (c). Original magnification, 200 × .
Optical coherence tomography images of (f) large cell acanthoma and (g) normal skin.

homogeneous blotch area (Fig. 2b). The OCT images were captured, and the skin lesion was partially incised for histopathological examination. The OCT images showed similar findings with those of the previous patient (Fig. 2c, d). The mean nucleus size in LCA and normal skin was 49.59 ± 13.92 μm^2 (range, 28.76–92.20) and 18.41 ± 4.46 μm^2 (range, 10.75–30.91), respectively ($P < 0.0001$). The OCT findings and pathological features were consistent.

Clinically, LCA may be difficult to differentiate from solar lentigo, lichen planus-like keratosis, pigmented actinic keratosis, seborrheic keratosis, and LM/LMM. Dermoscopy is a useful method to evaluate the possibility of malignancy. However, the LCA dermoscopic features has not been well-defined. Dermoscopic findings in the two cases included milia-like cysts, crypts, fingerprint-like structures, asymmetric pigmented follicular openings, dark rhomboidal structures, and

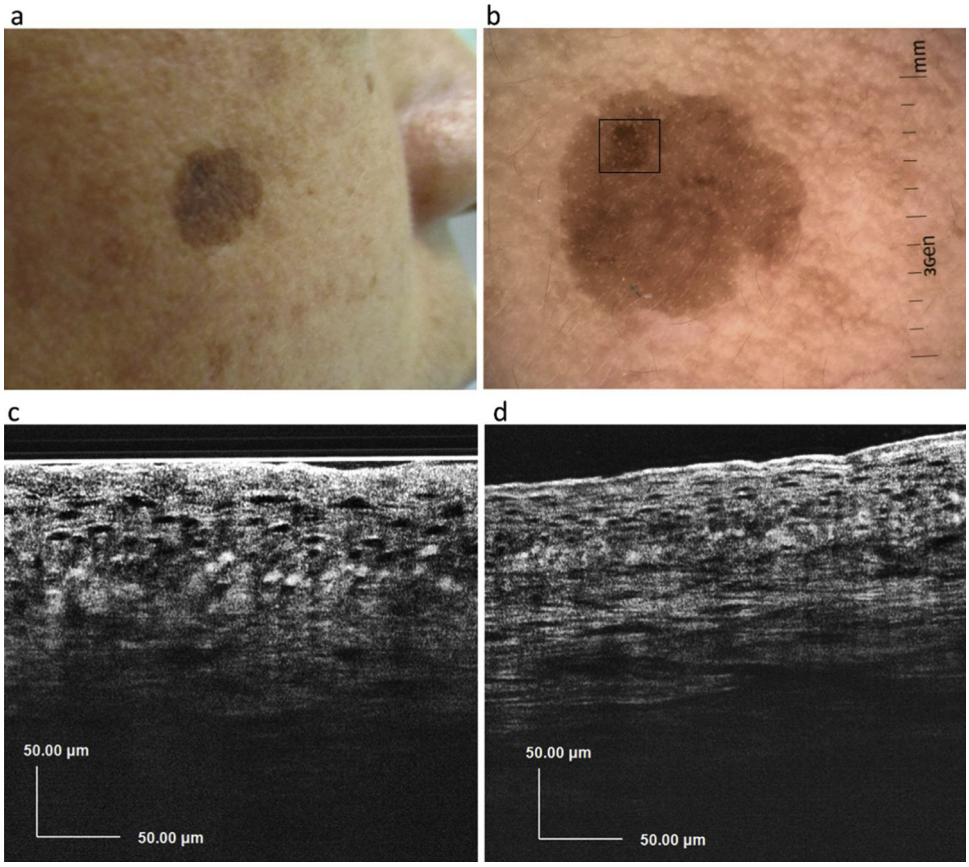

Fig. 2. (a) Clinical presentation. (b) Polarised dermoscopic image. Black inset revealed asymmetric pigmented follicular openings, dark rhomboidal structures, and homogeneous (blotch) area. Optical coherence tomography images of (c) large cell acanthoma and (d) normal skin.

homogeneous blotch areas. While the first three findings suggested a benign lesion, the last three findings were suggestive of LM/LMM. It is better to have another noninvasive device that can provide information on the necessity of skin biopsy.

Carvalho et al. found that en face images provided by RCM were helpful in discriminating LM from other facial pigmented non-melanocytic lesions [1]. However, a case report revealed that RCM findings of LCA included an irregular honeycomb pattern in the granular and spinous layers and small and closely set edged papillae at the dermal-epidermal junction. Therefore, RCM did not allow us to forego a biopsy in this case because these findings were a close simulator of pigmented Bowen's disease [4].

In vivo OCT provided a vertically oriented view that is easier to interpret and compare with conventional histological sections. The well-demarcated dermal-epidermal junction shown in our cases made invasive squamous cell carcinoma and LMM less likely [5]. Disruption of the stratum corneum, which corresponded to histological changes of hyper- and parakeratosis in actinic keratosis and squamous cell carcinoma, was not observed [5]. Cellular resolution full-field OCT also demonstrated information about cellular alterations. Features such as presence of acantholysis or nuclear pleomorphism commonly observed in squamous cell carcinoma [5] and the roundish pagetoid cells clustered at the basal cell layer in LMM [6] were not present in our patients. Therefore, cellular resolution full-field OCT could provide more details than high-definition OCT and might be helpful in the clinical evaluation of these lesions. Nevertheless, a study with large sample size of these lesions are required to determine the diagnostic accuracy of this device.

This preliminary case report demonstrated the in vivo morphological changes in keratinocytes and pigmented basal cells in LCA that had good correlation with the histopathological findings. It provided another useful noninvasive image tool to evaluate skin lesions.

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