DERMATOLOGY PRACTICAL & CONCEPTUAL
www.derm101.com

In vivo reflectance confocal microscopy features of a large cell acanthoma: report of a case

Neda Shahriari[1], Jane M. Grant-Kels[1], Harold S. Rabinovitz[2], Margaret Oliviero[2], Alon Scope[3]

1 Department of Dermatology, University of Connecticut Health Center, Farmington, CT, USA
2 Department of Dermatology, University of Miami Miller School of Medicine, Miami, FL, USA
3 Department of Dermatology, Sheba Medical Center and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Key words: RCM, large cell acanthoma, reflectance confocal microscopy

Citation: Shahriari N, Grant-Kels JM, Rabinovitz HS, Oliviero M, Scope A. In vivo reflectance confocal microscopy features of a large cell acanthoma: report of a case. Dermatol Pract Concept 2016;6(3):14. doi: 10.5826/dpc.0603a14

Received: June 13, 2016; **Accepted:** June 18, 2016; **Published:** July 31, 2016

Funding: None.

Competing interests: The authors have no conflicts of interest to disclose.

All authors have contributed significantly to this publication.

Corresponding author: Jane M. Grant-Kels, MD, UCONN, Dermatology Department, 21 South Rd, Farmington, CT 06032, USA. Email: grant@uchc.edu

ABSTRACT Reflectance confocal microscopy (RCM) is an FDA approved noninvasive optical imaging technique that acquires cellular level-resolution skin images in vivo. Herein, we report a case of histopathologically proven large cell acanthoma (LCA) whose RCM features simulate those of squamous cell carcinoma in situ.

Case presentation

A 73-year-old man with a history of non-melanoma skin cancers presented with a brown-tan 5 mm flat papule on the left arm (Figure 1). Dermoscopic evaluation revealed a pink pseudonetwork with focal gray-brown dots (Figure 2). The differential

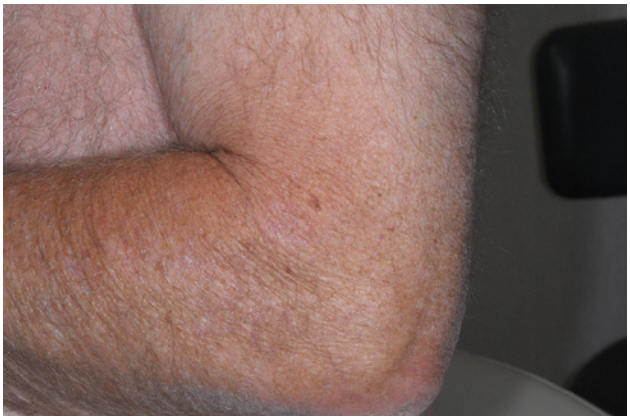

Figure 1A. Brown-tan 5 mm flat papule on the left arm. [Copyright: ©2016 Shahriari et al.]

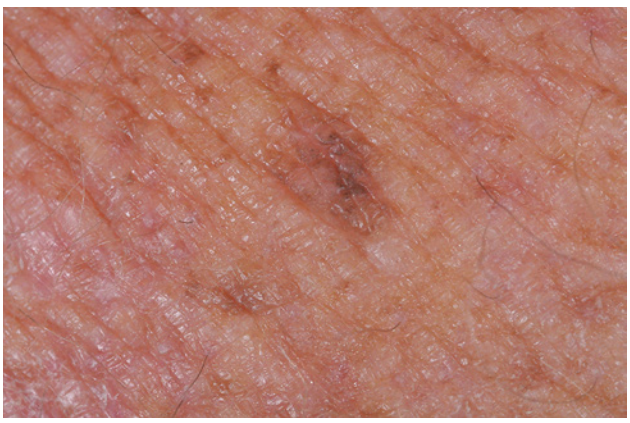

Figure 1B. Close up clinical image of lesion. [Copyright: ©2016 Shahriari et al.]

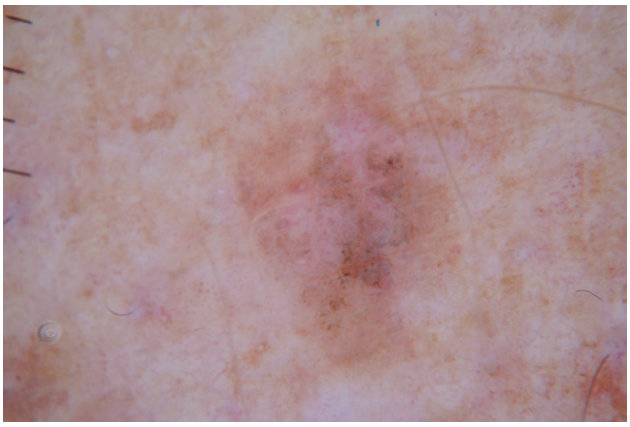

Figure 2. Dermoscopic (contact non-polarized) image of lesion revealing a pink pseudonetwork with focal gray-brown dots. [Copyright: ©2016 Shahriari et al.]

diagnosis based on dermoscopy included irritated seborrheic keratosis, pigmented squamous cell carcinoma (SCC), and traumatized nevus. Reflectance confocal microscopy (RCM) of the lesion showed an uneven surface contour with both raised and depressed areas. The granular and spinous layers of the epidermis demonstrated an irregular honeycomb pattern with large keratinocytes showing some variability of size and shape (Figure 3). At the dermo-epidermal junction (DEJ), there were bright, small, closely set edged papillae (Figure 4). The RCM findings were suggestive of a pigmented SCC in situ and the lesion was biopsied. Histopathologic analysis revealed a sharply circumscribed lesion composed of an acanthotic epidermis with enlarged keratinocytes, consistent with the diagnosis of large cell acanthoma (LCA) (Figure 5).

Conclusion

LCA clinically presents as a discrete scaly 3-10 mm papule, or rarely as a plaque, on sun-exposed body areas, most commonly on the head and extremities [1]. Hermann Pinkus was the first to histopathologically characterize LCA as being composed of keratinocytes with nuclei and cytoplasm twice the size of average adjacent keratinocytes and demonstrating acanthosis, hyperkeratosis, and polyploidy [2]. It was also noted that LCA is usually devoid of any signs of cytologic or mitotic atypia. Later, analysis of LCA DNA distribution established the presence of peaks of diploidy, aneuploidy and tetraploidy [2,3].

Currently, the origin of this lesion has not been unequivocally established. There is debate within the literature as to whether LCA is a distinct neoplastic entity or simply a derivative of seborrheic keratosis or solar lentigo, Bowen's disease, or actinic keratosis with cells displaying large nuclei.

Pinkus initially theorized that LCA was a variant or a derivative of solar lentigo due to shared features, including both lesions occurring on sun-exposed skin regions and presenting as a scaly brown-tan lesion [4]. He argued that LCA is unlikely related to an actinic keratosis, however, due to its lack of predilection for development into an SCC [4]; and indeed, to the best of our knowledge, no case of LCA

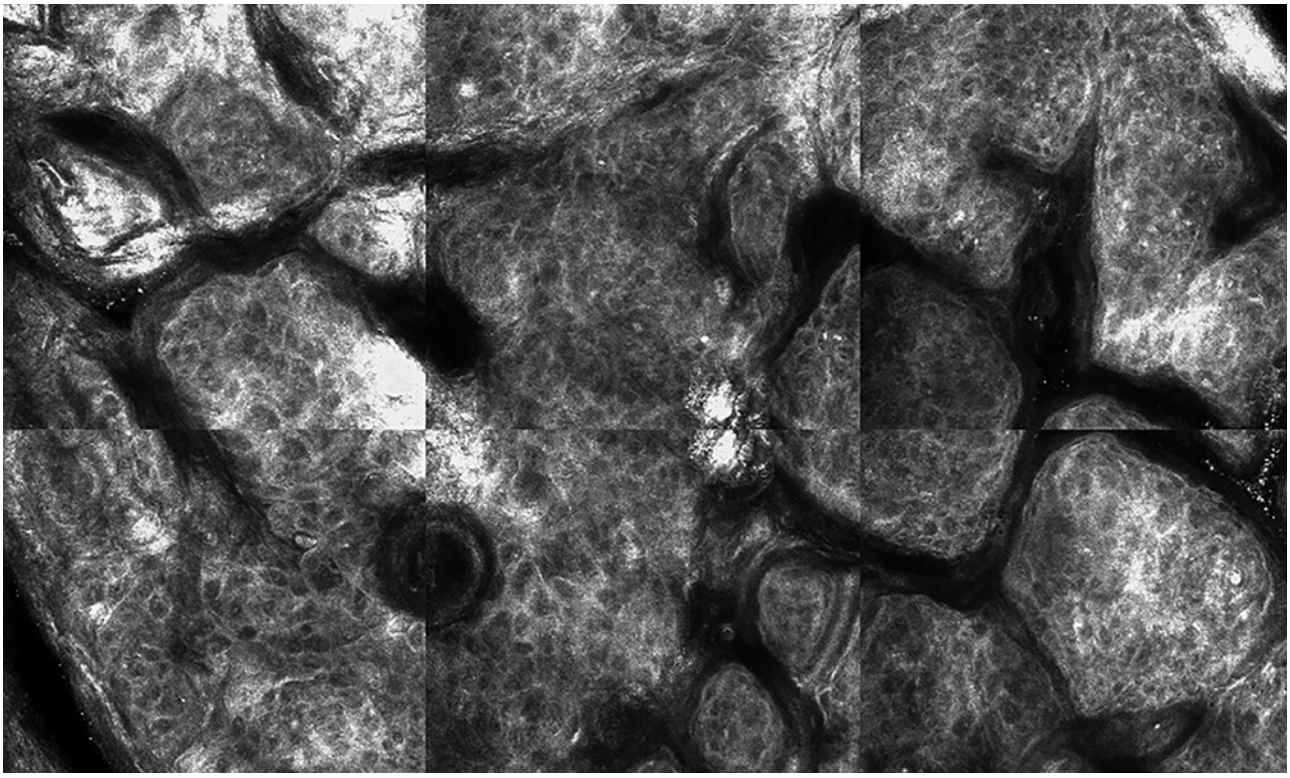

Figure 3. RCM at the granular and spinous layers of the epidermis demonstrated an irregular honeycomb pattern with large keratinocytes showing some variability of size and shape. [Copyright: ©2016 Shahriari et al.]

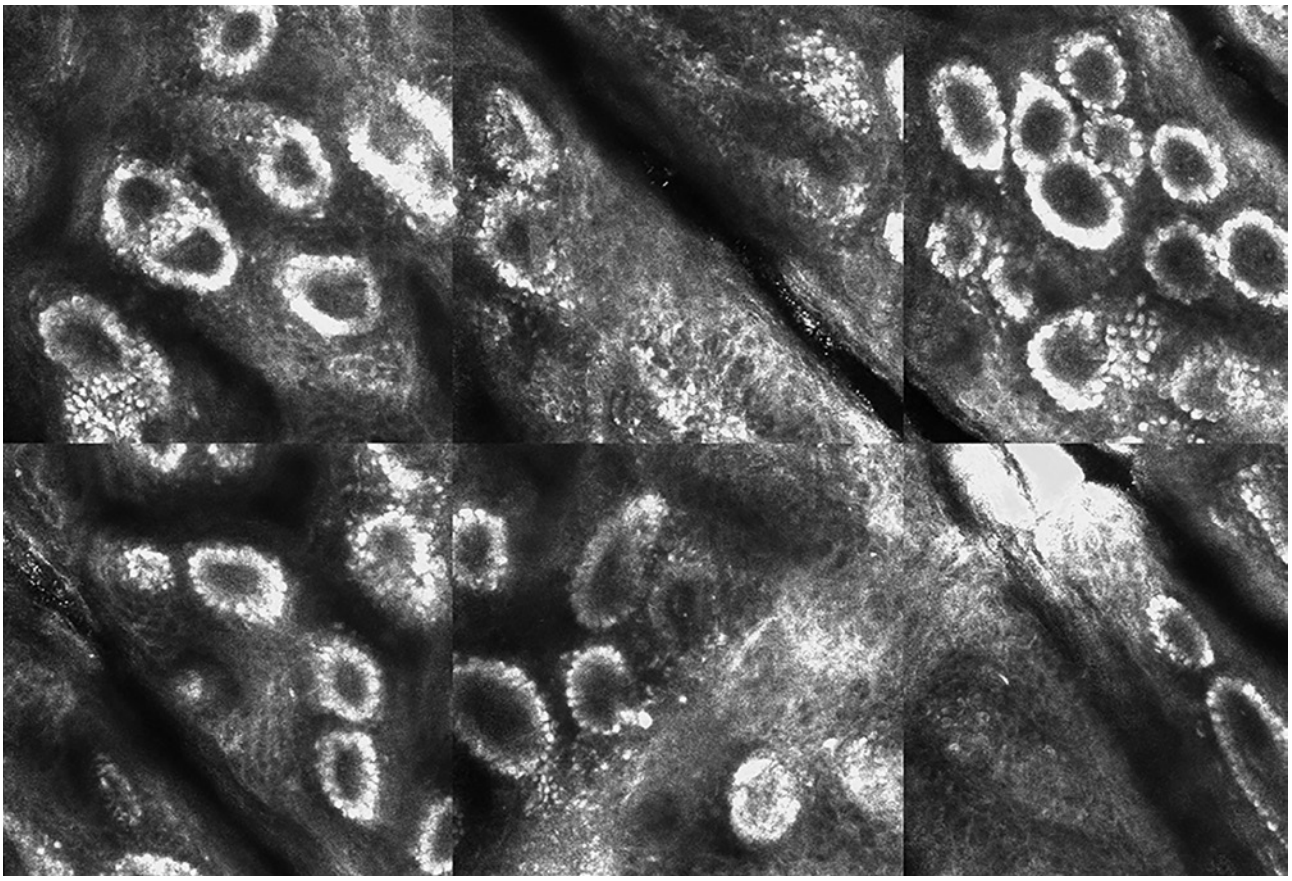

Figure 4. RCM at the dermo-epidermal junction demonstrated bright, small, closely set edged papillae. [Copyright: ©2016 Shahriari et al.]

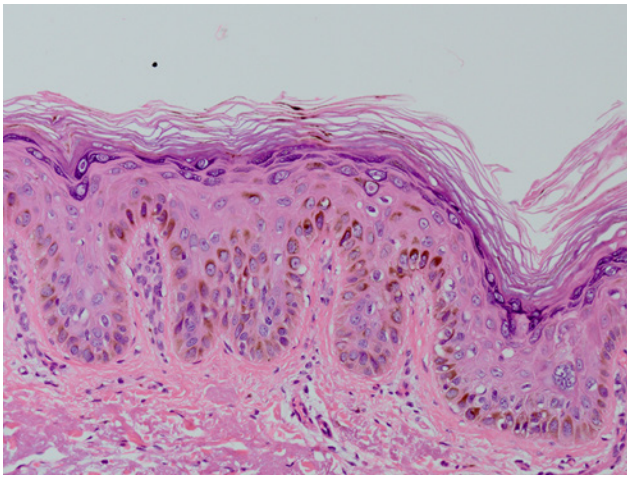

Figure 5. Histopathology revealed a lesion composed of an acanthotic epidermis with enlarged keratinocytes, consistent with the diagnosis of large cell acanthoma. [Copyright: ©2016 Shahriari et al.]

evolving into a SCC has been reported in the literature. In line with Pinkus' theory, Mehregan et al. demonstrated that solar lentigines and LCA have a slight increased number of melanocytes by HMB-45 staining likely due to both lesions occurring on sun-damaged skin of adults [5]. Analysis of proliferating cell nuclear antigen (PCNA) showed an increased epidermal proliferation rate in actinic keratoses compared with LCA and solar lentigines.

In contrast, Sánchez Yus et al. posit that LCA may be a cytologic variant of Bowen's disease. Their assessment was "based on the frequent disordered arrangement of the malpighian cells, its nuclear variability and occasional finding of dyskeratosis and suprabasal mitoses, as well as the involvement of skin appendages." [6] DNA studies showing polyploidy, unlike solar lentigines, have given some credence to this point of view. However, most dermatopathologists and dermatologists classify LCA as one type of solar lentigo [7,8].

Reflectance confocal microscopy (RCM) is an FDA approved noninvasive optical imaging technique that acquires cellular level-resolution skin images in vivo. A review of the RCM patterns of the aforementioned pathological entities may be informative. RCM of solar lentigo reveals variable bright particles (probably due to melanin-containing granules in the stratum corneum) and a regular cobblestone or honeycomb pattern with distinct refractile keratinoyctes with central dark nuclei in the stratum granulosum and spinosum layers [9]. At the level of the DEJ, there are different sized dermal papillae with bright rings (termed "edged papillae") and bulbous projections of epithelium [9]. The RCM features of seborrheic keratosis include bright horn pseudocysts (milia), a cobblestone pattern or broadened honeycomb pattern in the stratum spinosum, bulbous projections of epidermal rete ridges, and distorted papillary rings at the DEJ [10].

In contrast to solar lentigines and seborrheic keratoses, the histopathologically established LCA in our case with RCM was a close simulator of SCC in situ demonstrating an irregular honeycomb pattern in the granular and spinous layers as previously described for Bowen's disease [11] The associated small and closely set edged papillae at the DEJ is also a feature frequently seen in cases of pigmented Bowen's disease. Thus, unfortunately RCM did not allow us to forego a biopsy, as we needed to exclude SCC in situ.

To be able to distinguish LCA from SCC, as is readily done by dermatopathologists nowadays, more cases of LCA imaged with RCM are needed. Identifying the distinctive RCM features of LCA will allow more precise bedside diagnosis to reduce unnecessary biopsies of this benign entity.

References

1. Sánchez Yus E, del Rio E, Requena L. Large cell acanthoma is a distinctive condition. Am J Dermatopathol. 1992;14:140-7. PMID: 1566974.
2. Pinkus H. Epidermal mosaic in benign and precancerous neoplasia (with special reference to large cell acanthomas). Acta Dermatol (Kyoto). 1970;65:75-81. PMID: 5533827
3. Argenyi ZB, Huston BM, Argenyi EE, Maillet MW, Hurt MA. Large-cell acanthoma of the skin: a study by image analysis-cytometry and immunohistochemistry. Am J Dermatopathol 1994;16:140. PMID: 8030765.
4. Rahbari H, Pinkus H. Large cell acanthoma: one of the actinic keratoses. Arch Dermatol. 1978;114(1):49-52. PMID: 619783.
5. Mehregan DR, Hamzavi, F, Brown K, Large cell acanthoma. Int J Dermatol 2003;42(1):36-9. PMID: 12581141. DOI: 10.1046/j.1365-4362.2003.01587.x.
6. Sánchez Yus E, de Diego V, Urrutia S. Large cell acanthoma: a cytologic variant of Bowen's disease? Am J Dermatopathol 1988;10:197-208. PMID: 3232750.
7. Patsatsi A, Lazaridou E, Fotiadou C, Kyriakou A, Sotiriadis D. Large cell acanthoma: a debate throughout the decades. Dermatol Pract Concept 2014;4:43-5. PMID: 24520512. DOI: 10.5826/dpc.0401a05.
8. Roewert HJ, Ackerman AB. Large-cell acanthoma is a solar lentigo. Am J Dermatopathol 1992;14:122–32. PMID: 1533104.
9. Sanchez VP, Gill M, Gonzalez S. Lentigo. In: Gonzalez S, Ahlgrimm-Seiss (eds.). *Reflectance Confocal Microscopy in Dermatology: Fundamentals and Clinical Applications*. Aula Médica. 2012:31-4.
10. Sanchez VP, Gill M, Gonzalez S. Seborrheic keratosis. In: Gonzalez S, Ahlgrimm-Seiss V (eds.). *Reflectance Confocal Microscopy in Dermatology: Fundamentals and Clinical Applications*. Aulamedica; 2012: 57-59.
11. Ulrich M, Kanitakis J, Gonzalez S, et al. Evaluation of Bowen disease by in vivo reflectance confocal microscopy. Br J Dermatol 2012;166:451-3. PMID: 21824125. DOI: 10.1111/j.1365-2133.2011.10563.x.