Dermatology Practical & Conceptual

Non-Invasive Imaging of Basal Cell Carcinoma with Neuroendocrine Differentiation with Line-Field Confocal Optical Coherence Tomography

Lorenzo Barbarossa[1], Arianna Lamberti[1], Costantino Ricci[2,3], Mariano Suppa[4,5], Elisa Cinotti[1], Pietro Rubegni[1], Linda Tognetti[1]

1 Dermatology Section, Department of Medical, Surgical, and Neurological Sciences, Santa Maria Alle Scotte Hospital, Siena, Italy
2 Pathology Unit, Maggiore Hospital, AUSL Bologna, Bologna, Italy
3 Department of Medical and Surgical Sciences (DIMEC), University of Bologna, Bologna, Italy
4 Department of Dermatology, Hôpital Erasme, HUB, Université Libre de Bruxelles, Belgium
5 Department of Dermatology, Institut Jules Bordet, HUB, Université Libre de Bruxelles, HUB, Brussels, Belgium

Key words: basal cell carcinoma, LC-OCT, non-invasive, imaging, neuroendocrine differentiation

Citation: Barbarossa L, Lamberti A, Ricci C, et al. Non-Invasive Imaging of Basal Cell Carcinoma With Neuroendocrine Differentiation With Line-Field Confocal Optical Coherence Tomography. *Dermatol Pract Concept*. 2024;14(3):e2024173. DOI: https://doi.org/10.5826/dpc.1403a173

Accepted: March 13, 2024; **Published:** July 2024

Funding: None.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication.

Corresponding Author: Lorenzo Barbarossa, MD, Dermatology Section, Santa Maria alle Scotte Hospital, Viale Mario Bracci, 53100, Siena – Italy. Email: lorenzobarbarossa1993@gmail.com

Introduction

Basal cell carcinoma (BCC) is the most frequent tumor with incidence increasing worldwide. It can exhibit different and bizarre differentiation, among which squamous (basosquamous BCC), sarcomatoid, adnexal (follicular, sebaceous, and apocrine/eccrine), and -rarely- a neuroendocrine differentiation (BCC-NED) [1,2]. Among the reported cases of BCC-NED, the majority arose on the head and neck areas (especially cheek and lower eyelid), followed by the thigh, inguinal region and umbilicus [1,2].

Case Presentation

A 44-year-old man presented for routine skin check screening: a scar-like lesion was noted on the upper back (Figure 1A), firm and indurated at palpation; the patient referred only to had memory of an epidermal cyst in that area. An examination by line-field confocal optical coherence tomography (LC-OCT), a recently developed technique able to provide, in real time, vertical and horizontal skin images with cellular resolution up a depth of 500 µm (lateral FOV of 1200 µm) was required to rule-out inflamed

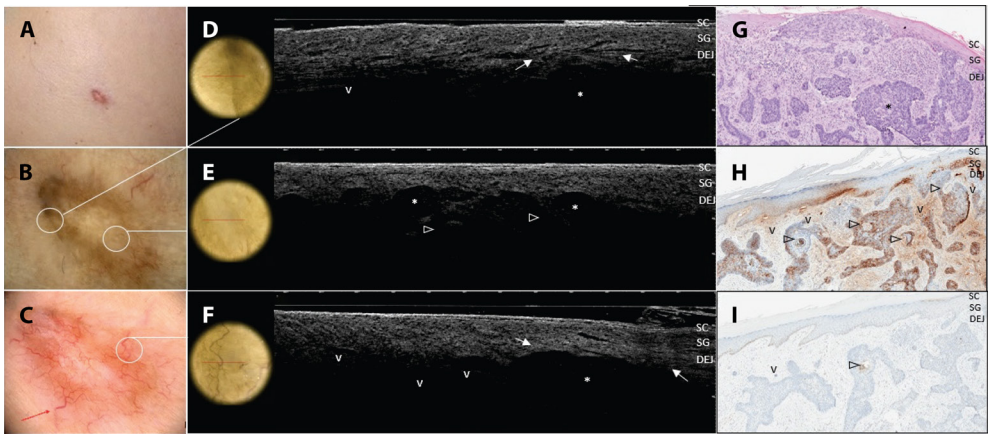

Figure 1. Clinical appearance at presentation time. (A) A scar-like lesion, 10.5 x 6.20 mm, located in right scapular region. (B) Polarized dermoscopy ×40 enlargement) highlights an oval lesion characterized by a brownish/yellowish peripheral pigmentation with a focal grayish spot and a whitish center with cobblestone-like pattern. (C) Non-polarized dermoscopy. (×40x enlargement) highlighted multiple in-focus arborizing vessels (red arrow) arranged in a radial pattern. Each vertical LC-OCT image is paired with a corresponding dermoscopic frame. (D-F) The red line inside the dermoscopic frame indicates the exact position of the probe tip inside the lesion and corresponds to the 1.2- mm field of view on a vertical plane of the LC-OCT probe. Navigating inside the lesion, multiple lobules (asterisks) separated from the epidermis were visible in all lesional point with dense cellularity (ie hyperreflective small structures, millefeuille pattern) delimited by well-defined margins; hyperreflective linear structures corresponding to connective strands (arrows) and non-reflective roundish structures corresponding to dilated capillary and dermal vessels (v) were also visible. Lobules were smaller in size and tightly disposed in superficial dermis, interspersed with microcystic areas (arrowheads) and larger in deep dermis. (G) H&E staining (×40) showed BCC lobules characterized by basaloid epithelium with typical palisade form and cleft from the adjacent tumor stroma, infiltrating the deep dermis. (H) Immunohistochemistry analysis showed strong chromogranin-positivity was present inside the lobular and microcystic structures, while (I) synaptophysin staining was negative.

dermatofibroma [3,4]. LC-OCT scan revealed multiple lobules separated from the epidermis (Figure 1, D-F) with dense cellularity (ie millefeuille pattern) and well-defined margins, dense connective strands and dilated capillary and dermal vessels. In superficial dermis, lobules were smaller and tightly disposed (Figure 1E), while in deep dermis were larger and interspersed with microcystic areas (Figure 1, D and F). BCC was suspected and surgical excision planned. The histologic exam showed nodular BCC infiltrating of the subcutaneous tissue (thickness: 3.5 mm), with cytologic features suggestive of neuroendocrine differentiation (salt-and-pepper chromatin, no nucleoli, high N/C ratio and nuclear molding); the tumor diffusely stain for chromogranin (granular and cytoplasmatic) but turned out negative for synaptophysin (Figure 1I), cytokeratin 20, and NSE, thus allowing us to make the diagnosis of BCC-NED.

Conclusions

The BCC-NED variant is a very rare instance. Not uncommonly, BCC-NED has been reported associated to scars, suggesting the surgical trauma as potential trigger [3]. Clinical features may be misleading (ie scar-like lesions) and the dermoscopic features (in-focus arborizing vessels, cobblestone appearance of microcysts) are shared with other BCC subtypes. Thus, histological and immunohistochemical analyses are required for the diagnosis, showing neuroendocrine cytological features and diffuse stain for at least one neuroendocrine markers [3].

To date, LC-OCT has been successfully employed to detect several epidermal and/or upper dermal alterations [3]. In particular, our group demonstrated that LC-OCT was able to realize a "virtual biopsy" in basal cell carcinoma subtypes [4]. Here in this case, with an atypical picture and confounding patient history, the *in vivo* LC-OCT examination allowed us to detect specific BCC features (eg BCC- lobules with millefeuille pattern, microcysts, fibrotic structures) and to individuate the lesion depth extension. Moreover, a thorough co-localization of the LC-OCT image with the exact lesional point of the dermoscopic frame was possible (ie red bar, Figure 1).

In conclusion, we report on a rare case of BCC-NED with LC-OCT. This device is thus proposed as a rapid and easy-to-use tool to support clinicians in orienting the diagnostic suspect and the appropriate lesion management. Moreover, thanks to a co-localization software that matches

the LC-OCT with the dermoscopic images, this device can be employed for a *real time* for preoperative mapping of surgical margins [5].

References

1. Houcine Y, Chelly I, Zehani A, et al. Neuroendocrine differentiation in basal cell carcinoma. *J Immunoassay Immunochem*. 2017;38(5):487-493.DOI:10.1080/15321819.2017.1331170. PMID: 28548901.
2. Chung IY, McKelvie P, Chen Y. Eyelid basal cell carcinoma with neuroendocrine differentiation: a case report and literature review. *Orbit*. 2021;40(4):316-319.
3. Monnier J, Tognetti L, Miyamoto M, et al. In vivo characterization of healthy human skin with a novel, non-invasive imaging technique: line-field confocal optical coherence tomography. *J Eur Acad Dermatol Venereol*. 2020;34(12):2914-2921.
4. Suppa M, Fontaine M, Dejonckheere G, et al. Line-field confocal optical coherence tomography of basal cell carcinoma: a descriptive study. *J Eur Acad Dermatol Venereol*. 2021;35(5): 1099-1110.
5. Venturi F, Pellacani G, Farnetani F, Maibach H, Tassone D, Dika E. Noninvasive diagnostic techniques in the preoperative setting of Mohs micrographic surgery: A review of the literature. *Dermatol Ther*. 2022 Nov;35(11):e15832. doi: 10.1111 /dth.15832.