Review Article

Reflectance skin confocal microscopy of basal cell carcinoma

Microscopia confocal reflectante a laser: carcinoma basocelular

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ABSTRACT

Basal cell carcinoma is the most common malignant skin tumor. Reflectance confocal microscopy is a non-invasive technique that provides real-time, in vivo, horizontal tissue images, at a quasi-histological resolution, by employing a low-power laser beam of 830 nm. In this paper, we review the major morphological criteria for diagnosing this tumor using reflectance skin confocal microscopy.

Keywords: Neoplasms; basal cell; microscopy confocal; diagnosis

RESUMO

O carcinoma basocelular é o tumor cutâneo maligno mais comum. A microscopia confocal reflectante a laser é uma técnica não-invasiva que proporciona imagens horizontais in vivo do tecido com resolução próxima à histológica e em tempo real, através do emprego de um feixe de laser de 830nm. O presente estudo apresenta uma análise dos principais critérios morfológicos utilizados na diagnose do carcinoma basocelular através da microscopia confocal reflectante a laser

Palavras-chave: *Carcinamo basocelular; microscopia confocal; diagnóstico*

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INTRODUCTION

Basal cell carcinoma (BCC), first described by Jacob in 1827, is the most common type of malignant skin tumor, accounting for 80% of non-melanoma skin cancers. [1]

In vivo reflectance confocal microscopy (RCM) is a non-invasive diagnostic tool that uses an 830 nm low-power laser beam to obtain real-time, high resolution (cellular) imaging of the superficial layers of the skin down to a 250 mm depth. In this technique, contrast is provided by differences in the refractive index of different cellular organelles within the tissue. Images obtained are similar to those of conventional histopathology.

A number of reports on RCM and BCC have been published, and five major morphological criteria have been defined for its diagnosis to date.[2]

REFLECTANCE CONFOCAL MICROSCOPY

Under skin confocal microscopy, BCC presents different features that have direct histological correlations, which can be

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used in pre-surgical diagnosis. Since RCM allows the visualization of horizontal sections of the skin, the description of BCC's characteristic features seen through RCM are listed from the epidermis down to the dermis, for practical reasons.

The epidermis usually presents variable degrees of keratinocytic atypia that can reach a marked pleomorphism of the keratinocyte shape and nuclei, along with parakeratotic nuclei in the stratum corneum, which are linked to the degree of actinic damage. Conversely, the presence of elongated monomorphic keratinocytes, with polarization of the nuclei oriented along them (Figure 1), seemed to be the most sensitive and specific feature to help diagnose BCC. [2,3]

At the dermal-epidermal junction, one of the most characteristic features of BCCs is the identification of compact aggregates of tightly packed tumor cells, which form tubercles or cord-like structures and nodules. [4] Those structures usually present a peripheral nuclear palisading that corresponds to peripheral basaloid nuclei that are arranged perpendicularly to the axis of the tumoral island (Figure 2). It is possible to observe a high reflectivity (combined with intervening areas of low reflectivity) in the tumoral islands. Bright dendritic structures that correspond to melanocytes, [5] usually with small cellular bodies, round large plump cells, and/or small bright particles, which correspond to inflammatory infiltrate, are likewise found within the tumoral islands – particularly in the BCC pigmented type. Those islands may be surrounded by a dark zone that corresponds to the separation of the tumor from the stromal tissue, which is also typically seen in histopathological analysis. This tumor-stroma "border" corresponds to an area that is particularly rich in mucin, which surrounds the tumor parenchyma. [6] In hypopigmented/amelanotic BCC, tumor cords and islands are barely visible and appear as hyporeflective areas (dark silhouettes) that are darker than the epidermis or dermal collagen (Figure 3). [7]

The stroma surrounding the tumor is highly refractive; collagen bands display a "frayed" appearance. Scattered bright particles, which correspond to leukocytes, and/or plump bright cells, which correspond to melanophages, can be detected

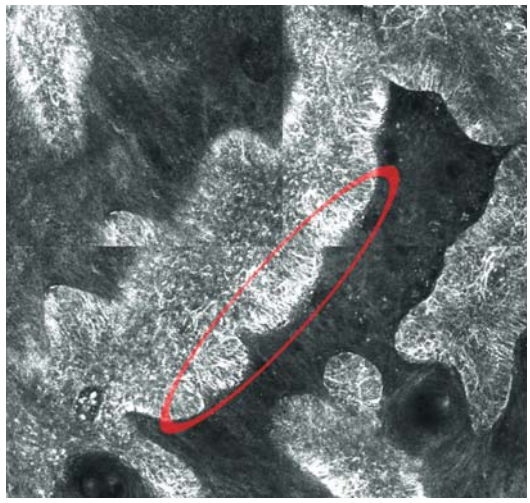

Figure 2: 0.5 mm x 0.5 mm confocal image showing a tumoral island with peripheral nuclear palisading (red circle)

between tumoral cords and islands. In addition to these features, BCC presents abundant elongated and/or twisted blood vessels, visible immediately beneath the epidermis and juxtaposed to the tumor parenchyma, sometimes presenting the rolling of leukocytes along the endothelial lining. [8]

In sum, RCM diagnosis of BCC has been defined based on five major criteria: elongated monomorphic basaloid nuclei, polarization of those nuclei along the same axis, prominent inflammatory infiltrate, increased dermal vasculature with twisted tumor vessels, and pleomorphism of the overlying epidermis, with the disappearance of the normal honeycomb pattern. In the analyzed studies, the presence of polarized nuclei presented the highest sensitivity (91.6%) and specificity (97%). Moreover, the presence of four or more criteria suggested a sensitivity of 82.9% and specificity of 95.7%.

Regarding the differences between subtypes of BCC, nodular variants also present aggregated tumor cell nests in the upper dermis that are often adjacent to large and dilated blood vessels.

Superficial BCCs are concentrated in the lower part of the epidermis and the superficial dermis. Aggregates of polarized

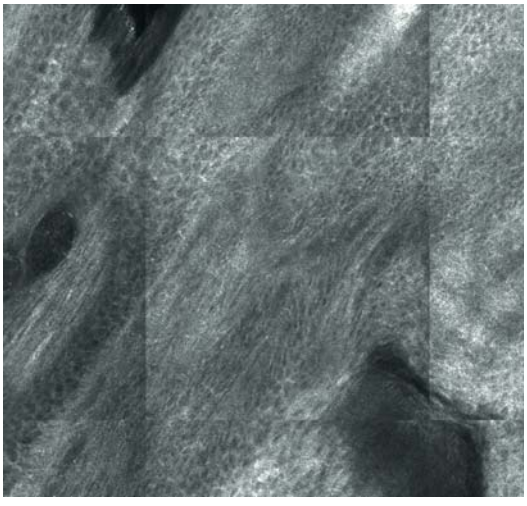

Figure 1: Presence of elongated monomorphic keratinocytes with polarization of the nuclei oriented along the same axis

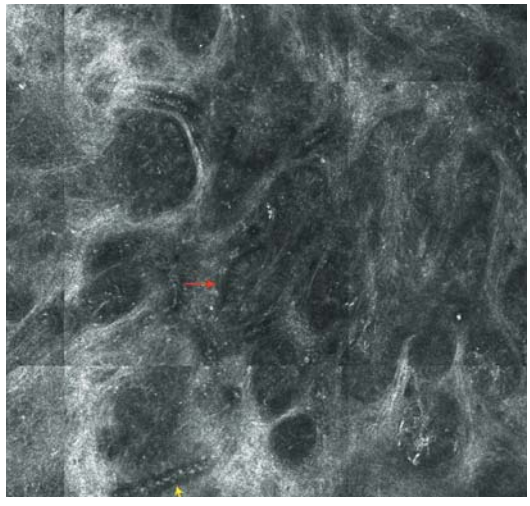

Figure 3: Dark zone surrounding a tumoral island (red arrow); Arborizing vessels (yellow arrow)

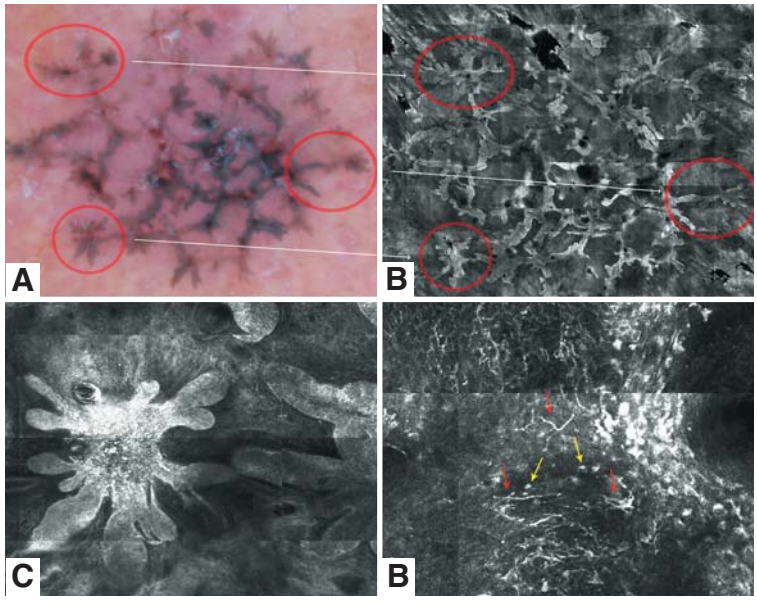

Figure 4: A,B: Pigmented BCC presenting the perfect correlation between dermoscopy and RCM; C: Tumoral island; D: Dendritic structures (red arrows) and granular structures (yellow arrows) corresponding to melanocytes and melanin, respectively

cells with elongated nuclei oriented along the same axis can be seen in the basal cell layer and in the superficial dermis, though the diagnosis is not straightforward in all cases.

In addition to the aggregates of monomorphic cells with elongated nuclei in the upper dermis, infiltrative BCCs present a dense and cell-rich stroma. Peripheral palisading is usually absent, and the borders between tumor cell aggregates and stroma are poorly defined, making the diagnosis of this variant even more challenging.

Conversely, the diagnosis of pigmented variants of BCC is usually straightforward with RCM, due to the marked brightness of the tumoral islands, which also show highly refractive dendritic cells (which correspond to melanocytes) and bright oval- and star-shaped structures with indistinct borders (which correspond to melanophages in traditional histology) (Figure 4).

CONCLUSION

Real-time, near-infrared laser-scanning RCM provides a way to diagnose BCCs in vivo with reliable sensitivity and specificity, and may potentially eliminate the need for invasive diagnostic biopsies. This is particularly useful in cases of flat or barely palpable lesions located in aesthetically sensitive areas, where non-surgical treatments such as imiquimod or photodynamic therapy are most frequently recommended. ●

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