Chapter

Dermatoscopic Features of Basal Cell Carcinoma

Tina Zagar, Nika Hlaca and Larisa Prpic-Massari

Abstract

Basal cell carcinoma is the most common type of non-melanoma skin cancers, frequently observed in fair-skinned individuals. The major risk factors for developing basal cell carcinoma are environmental exposures, phenotypic and genetic traits, and immunosuppression. The diagnosis of basal cell carcinoma is based upon clinical examination and dermatoscopy findings and finally confirmed by histopathological analysis. There are five main clinicopathologic types of basal cell carcinoma, specifically, superficial, nodular, pigmented, morpheaform, and fibroepithelial variant. The dermatoscopic feature of all BCC is the absence of a pigment network. Dermatoscopy structures are further classified as vascular, pigment-related, and non-vascular/non-pigment-related structures. Vascular structures include arborizing vessels and short fine telangiectasias, while pigmented structures comprise maple leaf-like areas, spoke-wheel areas, multiple blue-gray globules, in-focus dots, and concentric structures. Additional structures such as ulcerations, multiple small erosions, multiple aggregated yellow-white globules, shiny white-red structureless areas, and white streaks are considered non-vascular/non-pigmented structures. As treatment options highly depend on the type of BCC, dermatoscopy is of great value in management strategy, assessment of margins, and evaluation of response to non-ablative therapies.

Keywords: algorithms, dermatoscopy, disease management, carcinoma, basal cell, carcinoma, basal cell/diagnosis, skin neoplasms

1. Introduction

Basal cell carcinoma (BCC) is the most common type of non-melanoma skin cancers (NMSCs), most frequently observed in fair-skinned individuals. BCCs originate from the pluripotent cells of the bulge region of the hair shaft and the interfollicular epidermis. Even though BCCs rarely metastasize, they are locally invasive and destructive, and thus if not treated on time, present a therapeutic challenge. There are five main clinicopathologic types of BCC, specifically, superficial, nodular, pigmented, morpheaform, and fibroepithelial (also familiar as fibroepithelioma of Pinkus) [1].

Regarding epidemiology, the incidence of BCC correlates well with geographic location, with the southern hemisphere and regions closer to the equator having higher incidence. The average amount of annual exposure to ultraviolet radiation (UVR) has insignificant correlation with the incidence of BCCs. Additionally, fair skin phototypes and increasing age are also well correlated with the incidence of

BCC [1, 2]. The median age for acquiring BCC is 68. However, the development of BCC is mostly related to skin color, with white populations being particularly prone to the development of BCC. Moreover, men have a higher risk for acquiring BCC than women, although the rise in BCC among younger women has been noted lately. According to the American Cancer Society, currently, the incidence of BCCs is on the rise by more than 10% per year in the United States. Similar increases in incidence have been observed worldwide over the last two decades [3, 4].

The risk factors for developing BCC are environmental exposures, phenotypic characteristics, genetic traits, and immunosuppression. UVR is the most significant risk factor, particularly intermittent intense episodes of UV exposure and sunburns early in life [4, 5]. Among phenotypic traits, fair skin pigmentation, light hair and eye color, and poor tanning ability are the most common risk factors for BCC [5]. Furthermore, indoor tanning usage, chronic immunosuppression, and to a certain degree long-term photochemotherapy (PUVA) as well as ionizing radiation influence the risk for BCC development [6–8]. Additionally, chronic immunosuppression may increase the risk for BCC [9]. Some inherited diseases such as nevoid basal cell carcinoma syndrome (NBCCS) or Gorlin-Goltz syndrome, xeroderma pigmentosum, Bazex-Dupré-Christol syndrome, Rombo syndrome, and oculocutaneous albinism (OCA) carry a great risk for developing BCC at an early age [10, 11]. Specific gene polymorphisms in regions responsible for pigmentary traits, such as melanocortin-1 receptor (MC1R), the human homolog of agouti-signaling protein (ASIP), and tyrosinase (TYR), are additionally associated with an increased risk for BCC [12].

Pathogenetically, UVR induces mutations in several tumor suppressor genes and proto-oncogenes that consequently lead to BCC formation [13, 14]. Mutations in genes causing hyperactivation of the hedgehog (HH) protein family pathway, including PTCH1 receptor, SMO signal transducer, and GLI transcription factors, are strongly associated with BCC development [15, 16]. Furthermore, the TP53 tumor suppressor gene is also linked to BCC formation. The PTCH1 and TP53 are considered UV signature mutations due to the strong association with UVR-induced mutagenesis [13, 16].

Almost 70% of BCCs arise on the face and 15% on the trunk, while they rarely develop in the genital area [17]. The diagnosis of BCC is based upon clinical examination and dermatoscopy findings and finally confirmed by histopathological analysis. Since dermatoscopic features of BCC strongly assist the clinical diagnosis of BCC, clinicians must be familiar with typical dermatoscopic findings of various subtypes of BCC [17–19].

2. Dermatoscopy of basal cell carcinoma

Dermatoscopy or epiluminescence microscopy is a widely used tool that increases BCC detection accuracy and distinguishes BCC subtypes. Dermatoscopy features of BCC are classified into three main categories: vascular, pigment-related, and non-vascular/non-pigment-related. Vascular structures include arborizing vessels and short fine telangiectasias. Pigment-related structures consist of maple-leaf-like areas, spoke-wheel areas, multiple blue-gray globules (ovoid nests), in-focus dots (peppering/buckshot scatter), and concentric structures. Structures such as ulcerations, multiple minor erosions, shiny white blotches and strands, red structureless areas, and multiple aggregated yellow-white globules are classified as non-vascular/non-pigmented structures [20].

The most significant vascular dermatoscopic feature is arborizing vessels. More than three decades ago, arborizing vessels were described as the main feature

of BCC, with high diagnostic accuracy and predictive value of over 90% [21]. However, arborizing vessels are not limited to BCC but to any fast-growing lesions such as cysts and tumors, including benign skin tumors.

Various attempts to categorize dermatoscopic features for particular BCC subtypes have been described. Most of the studies focus on the vascular pattern in different forms of BCC. As mentioned before, besides the role in diagnosing BCC, dermatoscopy is of great value in management strategy, evaluation of response to non-ablative therapies, and margin detection before surgical excision. Regarding the management strategy of treatment, the first step is to distinguish between superficial and non-superficial BCC as it determines further management decision, with non-surgical treatments considered the first-line option for sBCC, while surgical excision being the standard for nodular BCC (nBCC) and Mohs micrographic surgery representing optimal choice for more invasive infiltrative forms of BCC [22, 23]. Superficial BCC is characterized by an optimal response to non-ablative therapies, such as imiquimod and photodynamic therapy (PDT). The authors Urech et al. reveal that dermatoscopic findings of erosions or ulcerations strongly predict a favorable response to imiquimod [24]. The pigment-related structures can act as a competitive light-absorbing factor, significantly reducing the response rate of the tumor to PDT. This observation leads to the exclusion of PDT as a treatment option in the presence of pigmented features [25]. In monitoring the outcome of non-ablative therapeutic modalities, dermatoscopic disappearance of pigmented structures, ulceration, and arborizing telangiectasias are indicators of complete tumor clearance.

Further monitoring is recommended to recognize early post-treatment reappearance of BCC-specific structures. However, the detection of white or red structureless areas and superficial fine telangiectasia does not provide explicit information on the possible presence of residual disease since these features might also appear as a result of treatment-induced skin atrophy [26].

In the non-superficial BCC, dermatoscopy is used in presurgical excision margins marking since it can detect a sub-clinical tumor expansion by revealing disease-related features in peripheral areas of clinically healthy skin.

3. Dermatoscopy of various BCC subtypes

3.1 Dermatoscopy of nodular basal cell carcinoma

Nodular BCC clinically manifests as a flesh-colored papule or nodule with a smooth surface typically located in the face region (**Figure 1A–C**). This subtype of BCCs is the most common and comprises approximately 60–80% of all cases of BCCs [1, 22, 27]. NBCCs usually have a pearly appearance and visible arborizing telangiectasias, while their border is raised compared to the central part of the lesion. This elevated rolled border is one of the critical clues to diagnosis. Additional clinical feature of nodular BCC is ulceration, hence the terms "rodent ulcer" or "phagedenic ulcer" for describing the ulcerating forms of nBCC. In contrast to sBCC, which often emerges on the trunk, nBCCs usually arise in the head and neck area, especially on the cheeks, nose, nasolabial folds, forehead, and eyelids, although they may develop in any hair-bearing area of the skin [1, 2, 22, 28]. The clinical differential diagnosis of non-ulcerated nBCC lesions includes adnexal neoplasms, fibrous papules, intradermal melanocytic nevi, amelanotic melanoma, sarcoidosis, cutaneous tuberculosis, and foreign body granulomas. Regarding ulcerating nBCC, squamous cell carcinoma (SCC) and keratoacanthomas are potential differential diagnoses [29].

NBCC is considered low-risk BCC; hence, standard surgical excision with 4-mm clinical margins with postoperative margin evaluation or electrodessication and

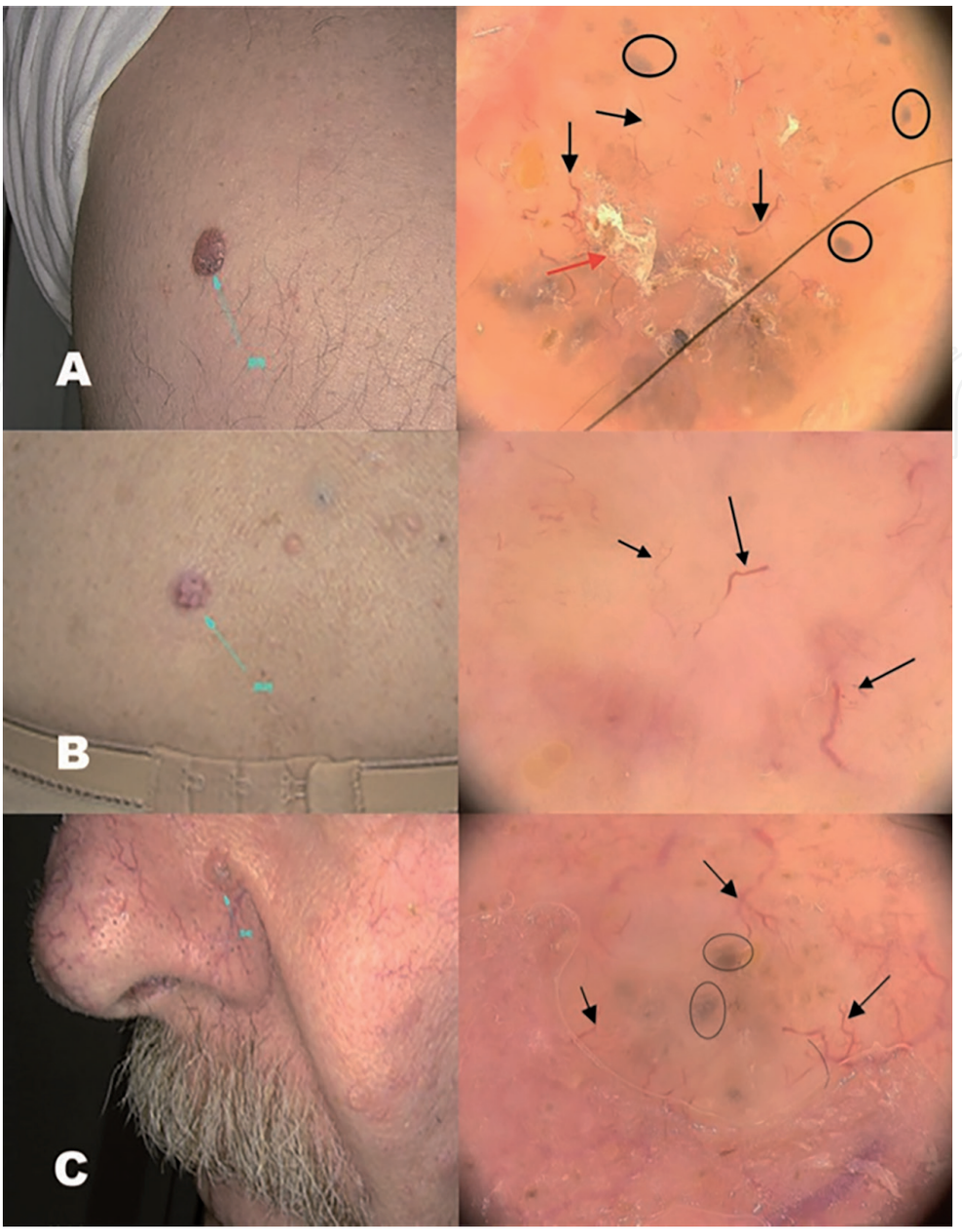

Figure 1.
(A) Left: nodular BCC clinically presented as a pink-colored nodule with a smooth surface. Right: dermatoscopy revealed small arborizing vessels (black arrows), blue-gray globules (circle), and scale due to ulceration (red arrow). (B) Left: nodular BCC may clinically manifest as a growing pink nodule. Right: the hallmark of nodular BCC is arborizing vessels. Be careful, vessels like this may blanch out if you press down hard on the lesion. (C) Left: skin-colored papule on the nose of the patient. Right: arborizing vessels identifiable as larger bright red stem vessels that branch into thinner branches (arrows) and gray-brown ovoid nests (square) are the most distinguishable features of nodular BCC.

curettage (EDC) are the two available treatment options according to the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines). EDC is an alternative therapeutic modality for patients who may not tolerate surgery or prefer this non-surgical treatment option [23].

Dermatoscopy findings of nBCC include arborizing vessels, large blue-gray ovoid nests, multiple blue-gray dots/globules, and ulcerations (**Figure 1A–C**). Among the latter, classical arborizing vessels are the most distinguishable feature of nodular BCC (**Figure 1A–C**), easily identifiable as larger bright red stem vessels that branch into thinner branches [28]. Arborizing vessels correspond to dilated tumor vessels in the superficial dermis. Although the pigmentation features are the hallmark of pigmented BCC, they may be present in nodular BCC as well.

The most common pigmentation feature of non-sBCC is blue-gray ovoid nests (**Figure 1A** and **C**). Blue-gray ovoid nests are pigmented structures that histopathologically represent pigmented tumor nests invading the dermis. It is worth noting that nBCCs generally appear more pigmented in contrast to sBCCs. In nBCCs, blue-gray pigmentation usually arises in the center of the lesion, whereas maple leaf-like areas, spoke-wheel areas, and concentric structures are closer to the peripheral part of the lesion [30]. Ulcerations are structureless, red to black-red areas in parts of epidermal loss (**Figure 1A**). In some cases, nBCC can even present with shiny white areas and rainbow patterns that occur when the polarized light illuminates vascular structures of the tumor. Further dermatoscopic findings of nBCC include milia-like cysts and multiple aggregated yellow-white globules [31].

Histopathology of nBCC consists of large, round islands of basaloid keratinocytes that extend from the epidermis to the dermis. The nuclei form palisades at the periphery of the lesions, in addition to a lack of central nuclear organization. In some larger tumor islands, necrosis leads to the development of cystic spaces. As a result of ulceration, an adjacent inflammatory infiltrate develops. Additionally, mucin pools may form in cystic or nodulocystic BCCs [32, 33].

In conclusion, the most specific dermatoscopic features of nodular BCC are arborizing vessels together with ulcerations, while some nodular BCCs additionally present with pigmented structures such as blue-gray ovoid nests. The surgery remains the cornerstone of the therapy of nBCC.

3.2 Dermatoscopy of superficial basal cell carcinoma

The superficial basal cell carcinoma clinically presents as well-circumscribed slightly scaly, shiny, red- to pink-colored non-firm macule, patch, or thin plaque (**Figure 2A** and **B**). The diameter of the tumor can range from a few millimeters to several centimeters. Additionally, the pigmented forms of sBCC may have a variable degree of spotty brown to black pigmentation (**Figure 2C** and **D**). Larger sBCC may also exhibit atrophic areas of hypopigmentation [1]. The central part of sBCC often appears atrophic in contrast to the pearly elevated border. The sBCC is locally destructive as it grows gradually and horizontally over time, reaching several centimeters in diameter if not treated. Induration, ulceration, and nodule all rarely appear as a result of the deeper invasion [2].

SBCC is the second most common subtype of BCC developing in approximately 15% of all BCCs. The predilection sites for sBCCs are the trunk and extremities. Often multiple sBCC may occur in one individual [22]. It is important to distinguish sBCC from other BCCs because of the different treatment strategies available for this entity. Currently, depending on the individual clinical presentation, standard surgical excision with postoperative margin evaluation or electrodessication and curettage (EDC) are the treatments of choice for low-risk sBCC, while topical 5-fluorouracil (5-FU) and 5% imiquimod are second-line treatment modalities [23, 34]. The differential diagnosis for sBCC includes actinic keratosis, Bowen's disease, and solitary lichenoid keratosis, in addition to inflammatory diseases such as nummular eczema, psoriasis, and cutaneous lupus erythematosus. Regarding histopathology, sBCC is marked by foci of palisading basaloid cells connecting in a net-like pattern and extending to the papillary dermis [18, 29].

The diagnosis of sBCC is based upon typical clinical features together with dermatoscopic findings and histopathological analysis. Dermatoscopy facilitates the differentiation of sBCC from other BCCs. The main dermatoscopic features of superficial BCC are maple-leaf-like areas, short fine superficial telangiectasias, shiny white-red structureless areas, concentric structures, spoke-wheel

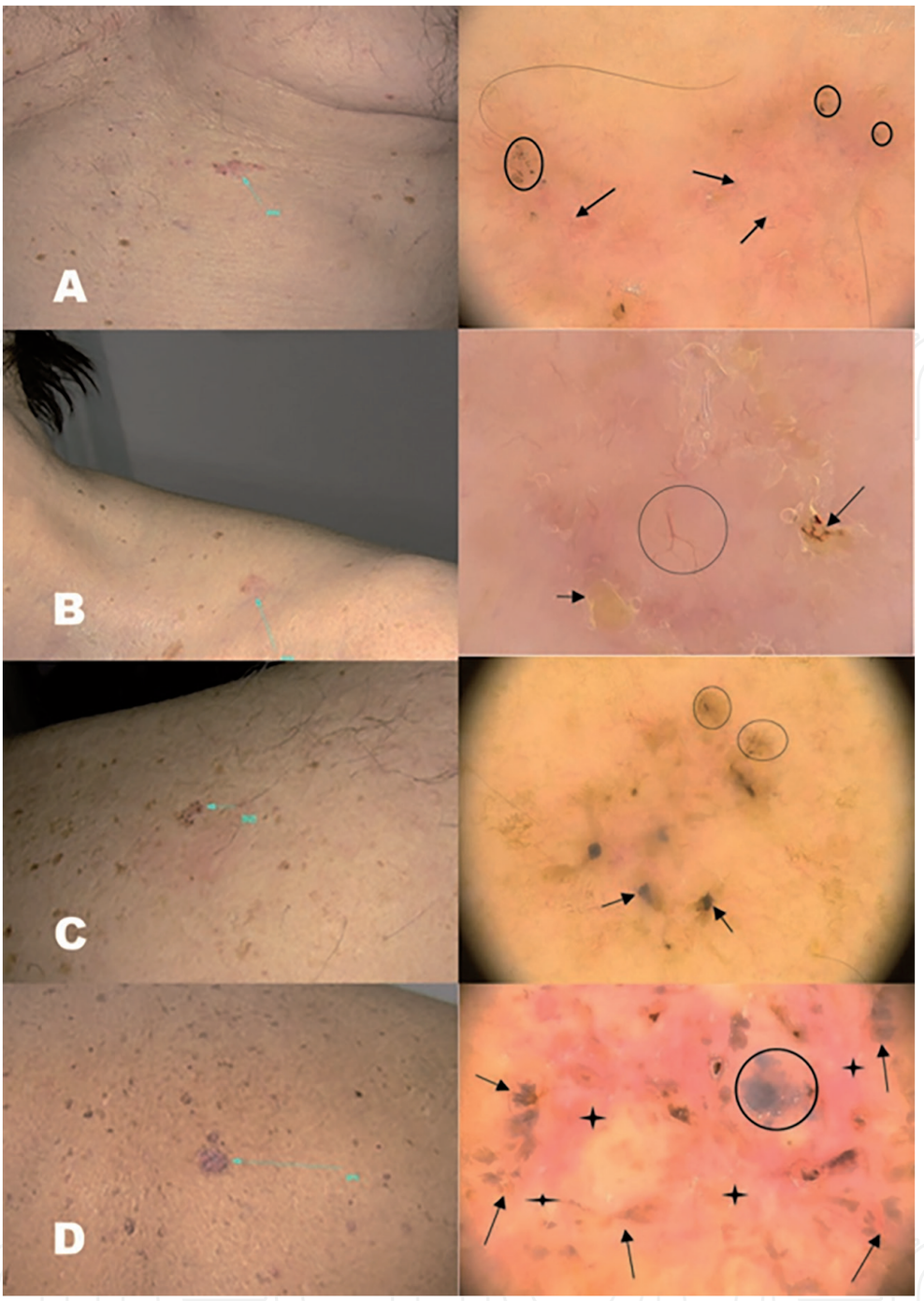

Figure 2.
(A) Left: superficial BCC clinically presented as well-circumscribed red- to pink-colored patch. Right: superficial BCC with short fine telangiectasias (arrows), small brown-gray dots (circles), and white-red structureless areas. (B) Left: well-circumscribed slight scaly, pink-colored macule. Right: arborizing vessels with ramification (black arrows) and multiple yellowish structureless areas representing small ulcerations covered with crust (red arrows). (C) Left: clinical presentation of superficial pigmented BCC. Right: the more experienced dermatoscopist will recognize the leaf-like structures (red circles) and concentric structures (white circles), structures corresponding to dermo-epidermal pigmentation. (D) Left: BCC exhibiting the various amounts of pigment and scale. Right: the dermatoscopic features of superficial BCC are maple leaf-like areas (red circles) and shiny white, red structureless areas (stars) throughout the lesion. In contrast, blue-gray ovoid nests (square) point to the diagnosis of an infiltrative variant of BCC.

areas, and multiple small erosions [29, 35]. However, among the latter, the most positive predictive patterns of sBCC are multiple small erosions and maple leaf-like areas together with short fine superficial telangiectasias (**Figure 2A** and **B**). Under dermatoscopy, short fine telangiectasias appear as fine vascular structures with length up to 1 mm, and only a few branches or commonly, no branching at all [35].

Recently dotted vessels have been described in sBCC located on lower extremities. As the dotted vessels are also a feature of Bowen disease, other features such as white shiny blotches/strands and superficial fine telangiectasia (SFT) should be considered when diagnosing sBCC in this anatomical region [36].

Furthermore, maple-leaf-like areas can be visualized as brown or gray/blue bulbous, leaf-like projections that never arise from the pigmented network or nearby confluent pigmented areas (**Figure 2C** and **D**). Histopathologically, they correspond to pigmented tumor islands that interconnect with lobular extensions. Multiple small erosions are frequently seen in sBCC and they appear as small brown-red to yellow crusts (**Figure 2B**) covering the areas of epidermal loss [30, 37].

Another finding in sBCC is spoke-wheel areas that resemble radial arrays that join at the darker center. They are consistent with tumor nests arising and connecting to the epidermis with finger-like projections and centrally located pigment. The areas of diffuse dermal and tumor fibrosis appear as opaque white to red-colored areas under dermatoscopy, and these are called white-red structureless areas, also familiar as milky-pink areas [38–40]. In addition, short white streaks also correspond to dermal fibrosis and are more commonly seen in sBCCs. Recently, a new dermatoscopic feature of sBCC named negative maple leaf-like areas (NMLLA) has been described. NMLLA are round non-pigmented well-defined bulbous projections similar to maple leaf-like areas on the white-colored background. These areas represent non-pigmented tumor nests at the dermo-epidermal junction and are usually associated with sBCC in the trunk region [41].

Furthermore, loosely arranged, well-defined focused fine brown-to-gray dots can also represent an unspecific feature of sBCC. They correlate with pigment deposition at the dermo-epidermal junction or melanophages in the papillary dermis [42].

Finally, negative predictive patterns of sBCC are ulceration, blue-gray ovoid nests, and arborizing vessels. These findings are suggestive of non-sBCCs subtypes. Among the listed criteria, blue-gray ovoid nests strongly support the diagnosis of infiltrative non-sBCC, which is especially relevant in differentiating clinically flat pigmented lesions. The blue-gray color results from pigment deposition deeper in the dermis, whereas brown pigment corresponds to melanin accumulation at the dermo-epidermal junction [39].

Some authors also suggest clinical subdivision of sBCC to patch, patch-to-plaque, and plaque forms, as more palpable forms of BCC often exhibit dermatoscopic features of nodular BCC (nBCC) [43]. Another helpful finding, highly suggestive of sBCC is multiple small erosions in clinically flat lesions [44].

In brief, pigmented sBCC is defined by patterns corresponding to dermo-epidermal pigmentation, particularly maple leaf-like areas, spoke-wheel, and concentric structures, with the absence of blue-gray ovoid nests, arborizing vessels and ulceration [30]. By adhering to the latter, the diagnosis of sBCC can be made with the sensitivity of 81.9% and specificity of 81.8%. On the contrary, non-pigmented sBCC demonstrates superficial short fine telangiectasia, multiple small erosions, and translucent-to-opaque shiny white-red structureless areas. Dermatoscopy is a reliable method for distinguishing sBCC from other BCCs, and neoplastic and inflammatory disorders. Adding current dermatoscopy algorithms to clinical practice is of crucial importance for making the correct prebiopsy diagnosis [29, 35].

3.3 Dermatoscopy of pigmented BCC

Pigmented BCC is a variant of basal cell carcinoma that histologically exhibits increased melanin pigmentation. It is clinically presented as a nodular

pigmented lesion or pigmented macule (**Figure 3A–E**). However, around 30% of BCCs that are clinically classified as non-pigmented reveal pigmented features under dermatoscopy; thus, the pigment-related structures may be found in all BCC subtypes, both superficially and non-superficially [30, 45]. Based

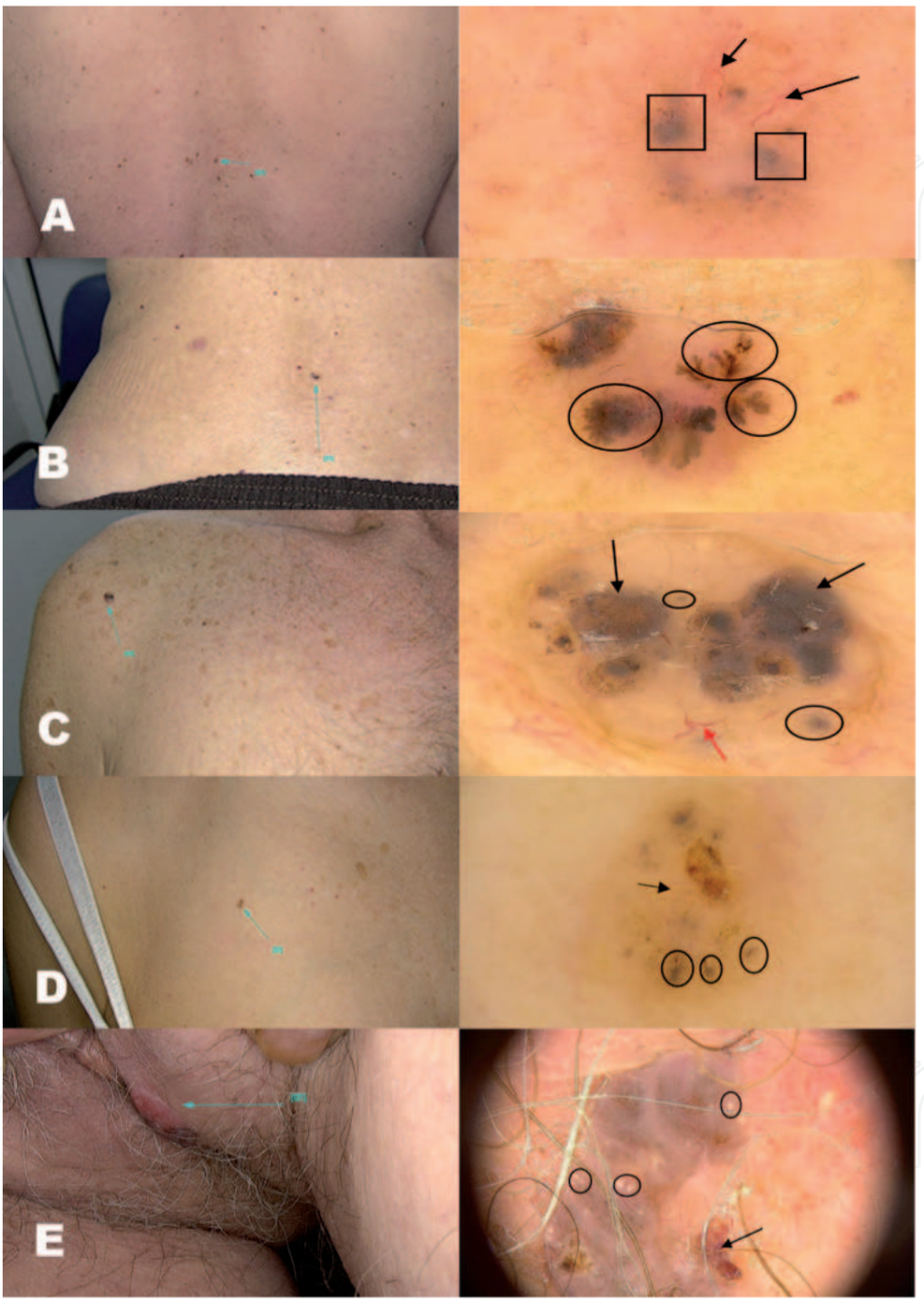

Figure 3.
(A) Left: BCC clinically presented as firm pigmented papule. Right: pigmented basal cell carcinoma with arborizing vessels (arrows) and blue-gray ovoid nests (squares). (B) Left: clinical presentation of pigmented BCC. Right: this pigmented BCC shows the so-called maple leaf-like features (red circles). (C) Left: nodular pigmented BCC clinically presented as firm pigmented papule. Right: the heavily pigmented BCC with large blue-gray blotches (squares), blue-gray ovoid nests, and globules (circle) and arborizing vessels at the periphery of the lesion (arrow). (D) Left: clinical examination revealed small pigmented papule. Right: dermatoscopic picture of classic BCC with spoken wheel structures at the periphery (white circles) and fine arborizing telangiectasia (black arrows) in the middle of the lesion. (E) Left: unusual localization of BCC at labia major. Right: atypical presentation of nodular pigmented BCC with large blue-gray areas, ulceration covered by crust (red arrow), and milia-like cysts (triangles). This nodular BCC is hardly distinguishable from nodular melanoma.

on histopathology correlation, features representing pigment at the dermo-epidermal junction, such as maple-leaf-like areas, spoke-wheel areas, concentric structures, and focus dots, are in brown and appear more frequently in the superficial and infiltrating variant of BCC (**Figure 3B** and **D**). In contrast, features representing pigment in deeper layers of the dermis such as blue-gray ovoid nests and blue-gray globules are in blue or gray, and they are characteristic of the nodular subtype of BCC [37, 39, 45]. Multiple blue-gray globules are defined as numerous, loosely arranged round to oval, well-circumscribed structures similar but smaller than the ovoid nest (**Figure 3A**, **C**, and **E**). They histopathologically correlate with small tumor nests in the papillary or/and reticular dermis. On the other hand, large blue/gray ovoid nests are well-circumscribed, confluent, or near-confluent pigmented or elongated areas, more prominent than globules and not intimately connected to a pigmented tumor body (**Figure 3A**, **C**, and **E**). Regarding pathophysiology, they correspond to large tumor nests with pigment aggregates invading the dermis. Blue-gray blotches together with arborizing vessels represent pathognomonic findings of pigmented basal cell carcinoma. In-focus dot terms describe loosely arranged, well-defined small brown-gray dots, which appear sharply in focus. They correspond to small tumor aggregates in the superficial dermis or at the dermo-epidermal junction, although they may also represent free pigment deposits or melanophages at the junction. Maple leaf-like areas are translucent brown-to-gray/blue peripheral bulbous extensions, mainly localized on the lesion's periphery that never arises from a pigmented network or adjacent confluent pigmented areas (**Figure 3B**). Histologically, they represent pigmented nests at the dermo-epidermal junction and in the superficial papillary dermis. Spoke-wheel areas are well-circumscribed radial projections, usually tan but sometimes blue or gray, meeting at an often darker (dark brown, black, or blue) central axis. They are a rare dermatoscopic feature, highly specific for BCC. Occasionally radial projections are not clearly defined, and they appear as globular structures with a darker center. In such cases, we call them concentric structures [37, 39, 45]. Heavily pigmented BCCs may show dermatoscopic features associated with melanocytic lesions, such as brown globules, a blue-white veil and peppering. It is not always possible to distinguish melanoma from BCC with dermatoscopy; therefore in that clinical setting, the correct management decision is more relevant than the diagnosis (**Figure 3E**).

3.4 Dermatoscopy of infiltrative BCC

Infiltrative BCC is an aggressive and recurrent BCC variant that constitutes 5–10% of the BCCs. It is a histologic variant characterized by invasive growth patterns with clinically indistinct borders. This subtype of BCC is more aggressive and requires wider surgical margins or Mohs surgery, in contrast to non-infiltrative variants such as nodular or superficial BCC, which are commonly treated with standard surgical excision. The most common dermatoscopy features that point to infiltrating growth of BCC are arborizing vessels, fine telangiectasia, shiny white structureless areas, ulceration, and whitish background. Vessels found in the infiltrative variant of BCC are more delicate and more scattered, with fewer branches than nodular subtypes. A pigmented subtype of infiltrative BCC can exhibit blue-gray ovoid nests or multiple blue-gray in-focus dots [28, 37]. The novel dermatoscopic feature linked to the infiltrative form of BCC is called a circumferential stellate pattern. It is defined as a geometric star-shaped pattern extending outward from the circumferential peripheral edge of the tumor and identified by white lines, vessels, or uneven skin surface morphology [46].

3.5 Dermatoscopy of morpheaform/sclerodermiform BCC

Morpheaform BCC is an uncommon variant of BCC in which tumor cells induce proliferation of fibroblasts within the dermis and an increased collagen deposition with sclerosis that clinically resembles a scar. The histologic extent often exceeds the clinical impression, leading to high recurrence rates after standard excision. Morheaform BCC displays dermatoscopic features at a later stage of development than other subtypes of BCCs [47]. Approximately 75% of tumors show a structureless hypopigmented porcelain area. Arborizing vessels are expected in morpheaform BCC, and they tend to have less evident branching. This subtype of BCC is rarely pigmented, but when they are, dermoscopy shows blue-gray ovoid nests [36]. If pink-white areas and fine arborizing vessels are seen in high-risk zones such as the nose, cheek, and periauricular area, clinician should consider a diagnosis of sclerodermiforme BCC.

3.6 Dermatoscopy of fibroepithelial BCC

Another uncommon variant of BCC is fibroepithelial BCC. Fibroepithelial BCC, also known as Pinkus tumor, clinically appears as erythematous, flesh-colored dome-shaped papule or plaque. Differential diagnoses include benign skin lesions such as dermal nevus, fibroma, seborrheic keratosis, and even malignant tumors such as amelanotic melanoma [48]. Dermatoscopy patterns seen in fibroepithelioma of Pinkus are fine arborizing vessels that have less evident ramification and are smaller in caliber in contrast to telangiectasia seen in other forms of BCC accompanied by white streaks under polarized dermatoscopy that are called crystalline structures similar to those in other forms of BCC. Pigmented variants show brown-gray structureless areas and blue-gray dots. Other common but unspecific findings are milia-like cysts and ulceration [48, 49].

3.7 Dermatoscopy of basosquamous carcinoma

Basosquamous carcinoma (BsC) is a controversial entity and has both diagnostic and therapeutic challenges. BsC combines histopathologic and dermoscopic characteristics of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) [1]. Like SCC, BsC is more locally invasive and aggressive, and metastasizes more often than other forms of BCC. Dermatoscopy features comprise both features of BCC and SCC. Therefore, besides arborizing vessels, ulceration, and blood crust that are standard features of BCC, BsC is characterized by keratin masses, surface scaling, and white structureless areas, and dermoscopic features are mainly seen in SCC [27].

3.8 The dermatoscopic findings of other uncommon variants of BCC

The nevoid BCC that typically develops in Gorlin-Goltz patients together with palmar pits may show blue-gray dots, globules, or nests and arborizing vessels at the periphery.

Micronodular basal cell carcinoma is a histopathological term that applies to BCCs in which smaller aggregations of basaloid cells infiltrate the dermis. They have destructive behavior, with subclinical spread and high rates of recurrence. Only a few studies have specifically analyzed dermatoscopic features of micronodular BCCs. The main features were truncated vessels and multiple blue-gray globules [42].

BCCs with a linear appearance are sporadic, sometimes seen in association with different histological subtypes. The most frequently affected sites are the periorbital

area and the neck. The linear subtype of BCC may show any dermatoscopic features associated with BCC in general.

4. Conclusion

Generally observing, classic arborizing vessels are typically found in a nodular variant of BCC, while short fine telangiectasia points forward the superficial form of BCC. Structures associated with pigment could be roughly divided into two categories based on melanin deposition. All dermatoscopic subtypes of BCC can exhibit various amounts of pigment. Maple leaf-like areas, spoke-wheel areas, concentric structures, and in-focus dots indicate the presence of melanin at the dermo-epidermal junction and are a feature of superficial BCC. On the other hand, large blue-gray ovoid nests and multiple blue-gray dots and globules correspond to melanin at the dermal level. They are the characteristic of a non-superficial variant of BCC. Spoke-wheel areas are a rare dermatoscopic feature, but they are highly particular for BCC. Ulceration represents a loss of epidermis and portion of the dermis and is primarily seen in nodular lesions. Ulcerated areas are frequently covered with coagulated blood or crust, sometimes making it difficult for further dermatoscopic review. Multiple small erosions are the characteristic of a superficial variant of BCC, and they are smaller than ulcerations and clinically observed as a yellowish crust.

Diagnosis of BCC is not established on a single dermatoscopy feature, but rather on the coexistence of several dermatoscopic features together with clinical presentation. Histopathology essentially yields the final and decisive diagnosis. Besides a prominent position in diagnosis, dermatoscopy holds an essential role in managing BCC, significantly improving the treatment and post-treatment outcome assessment, possessing a beneficial role during all the stages of BCC management.

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References

[1] Tan ST, Ghaznawie M, Heenan PJ, Dosan R. Basal cell carcinoma arises from interfollicular layer of epidermis. Journal of Oncology. 2018;**26**:3098940. DOI: 10.1155/2018/3098940

[2] Scrivener Y, Grosshans E, Cribier B. Variations of basal cell carcinomas according to gender, age, location and histopathological subtype. The British Journal of Dermatology. 2002;**147**:41-47. DOI: 10.1046/j.1365-2133.2002.04804.x

[3] Verkouteren JAC, Ramdas KHR, Wakkee M, Nijsten T. Epidemiology of basal cell carcinoma: Scholarly review. The British Journal of Dermatology. 2017;**177**:359

[4] Reinau D, Surber C, Jick SS, Meier CR. Epidemiology of basal cell carcinoma in the United Kingdom: Incidence, lifestyle factors, and comorbidities. British Journal of Cancer. 2014;**111**:203

[5] Savoye I, Olsen CM, Whiteman DC, et al. Patterns of ultraviolet radiation exposure and skin cancer risk: The E3N-SunExp study. Journal of Epidemiology. 2018;**28**:27

[6] Gandini S, Doré JF, Autier P, et al. Epidemiological evidence of carcinogenicity of sunbed use and of efficacy of preventive measures. Journal of the European Academy of Dermatology and Venereology. 2019;**33**(Suppl 2):57

[7] Robinson SN, Zens MS, Perry AE, et al. Photosensitizing agents and the risk of non-melanoma skin cancer: A population-based case-control study. The Journal of Investigative Dermatology. 2013;**133**:1950

[8] Watt TC, Inskip PD, Stratton K, et al. Radiation-related risk of basal cell carcinoma: A report from the Childhood Cancer Survivor Study. Journal of the National Cancer Institute. 2012;**104**: 1240

[9] Silverberg MJ, Leyden W, Warton EM, et al. HIV infection status, immunodeficiency, and the incidence of non-melanoma skin cancer. Journal of the National Cancer Institute. 2013;**105**:350

[10] Castori M, Morrone A, Kanitakis J, Grammatico P. Genetic skin diseases predisposing to basal cell carcinoma. European Journal of Dermatology. 2012;**22**:299

[11] MacDonald DS. A systematic review of the literature of nevoid basal cell carcinoma syndrome affecting East Asians and North Europeans. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology. 2015;**120**:396

[12] Berlin NL, Cartmel B, Leffell DJ, et al. Family history of skin cancer is associated with early-onset basal cell carcinoma independent of MC1R genotype. Cancer Epidemiology. 2015;**39**:1078

[13] Pellegrini C, Maturo MG, Di Nardo L, et al. Understanding the molecular genetics of basal cell carcinoma. International Journal of Molecular Sciences. 2017;**18**:2485

[14] Epstein EH. Basal cell carcinomas: Attack of the hedgehog. Nature Reviews. Cancer. 2008;**8**:743

[15] Stacey SN, Sulem P, Jonasdottir A, et al. A germline variant in the TP53 polyadenylation signal confers cancer susceptibility. Nature Genetics. 2011;**43**:1098

[16] Lin Y, Chahal HS, Wu W, et al. Association study of genetic variation in DNA repair pathway genes and risk of basal cell carcinoma. International Journal of Cancer. 2017;**141**:952

[17] Bonilla X, Parmentier L, King B, et al. Genomic analysis identifies new drivers and progression pathways in skin basal cell carcinoma. Nature Genetics. 2016;**48**:398

[18] Cameron MC, Lee E, Hibler BP, et al. Basal cell carcinoma: Epidemiology; pathophysiology; clinical and histological subtypes; and disease associations. Journal of the American Academy of Dermatology. 2019;**80**:303-317. DOI: 10.1016/j.jaad.2018.03.060

[19] Wang YJ, Tang TY, Wang JY, et al. Genital basal cell carcinoma, a different pathogenesis from sun-exposed basal cell carcinoma? A case-control study of 30 cases. Journal of Cutaneous Pathology. 2018;**45**:688-695

[20] Reiter O, Mimouni I, Gdalevich M, et al. The diagnostic accuracy of dermoscopy for basal cell carcinoma: A systematic review and meta-analysis. Journal of the American Academy of Dermatology. 2019;**80**:1380

[21] Haws AL, Rojano R, Tahan SR, Phung TL. Accuracy of biopsy sampling for subtyping basal cell carcinoma. Journal of the American Academy of Dermatology. 2012;**66**:106

[22] Bastiaens MT, Hoefnagel JJ, Bruijn JA, et al. Differences in age, site distribution, and sex between nodular and superficial basal cell carcinoma indicate different types of tumors. The Journal of Investigative Dermatology. 1998;**110**:880-884

[23] The NCCN Basal Cell Skin Cancer Clinical Practice Guidelines in Oncology (Version 2.2021 – February 25, 2021). © 2021 National Comprehensive Cancer Network, Inc. Available from: http://www.nccn.org

[24] Urech M, Kyrgidis A, Argenziano G, et al. Dermoscopic ulceration is a predictor of basal cell carcinoma response to imiquimod: A retrospective study. Acta Dermato-Venereologica. 2017;**97**:117-119. DOI: 10.2340/00015555-2464

[25] Christensen E, Warloe T, Kroon S, et al. Guidelines for practical use of MAL-PDT in non-melanoma skin cancer. Journal of the European Academy of Dermatology and Venereology. 2010;**24**:505-512. DOI: 10.1111/j.1468-3083.2009.03430.x

[26] Apalla Z, Lallas A, Tzellos T, et al. Applicability of dermoscopy for evaluation of patients' response to nonablative therapies for the treatment of superficial basal cell carcinoma. The British Journal of Dermatology. 2014;**170**:809-815. DOI: 10.1111/bjd.12749

[27] Costantino D, Lowe L, Brown DL. Basosquamous carcinoma—An under-recognized, high-risk cutaneous neoplasm: Case study and review of the literature. Journal of Plastic, Reconstructive & Aesthetic Surgery. 2006;**59**:424-428

[28] Zalaudek I, Kreusch J, Giacomel J, et al. How to diagnose nonpigmented skin tumors: A review of vascular structures seen with dermoscopy: Part II. Nonmelanocytic skin tumors. Journal of the American Academy of Dermatology. 2010;**63**:377-386; quiz 87-8

[29] Pan Y, Chamberlain AJ, Bailey M, et al. Dermatoscopy aids in the diagnosis of the solitary red scaly patch or plaque-features distinguishing superficial basal cell carcinoma, intraepidermal carcinoma, and psoriasis. Journal of the American Academy of Dermatology. 2008;**59**:268-274

[30] Lallas A, Tzellos T, Kyrgidis A, et al. Accuracy of dermoscopic criteria for discriminating superficial from other subtypes of basal cell carcinoma. Journal of the American Academy of Dermatology. 2014;**70**:303-311

[31] Bellucci C, Arginelli F, Bassoli S, Magnoni C, Seidenari S. Dermoscopic yellow structures in basal cell carcinoma. Journal of the European Academy of Dermatology and Venereology. 2014;**28**:651-654. DOI: 10.1111/jdv.12092

[32] Lallas A, Argenziano G, Zendri E, et al. Update on non-melanoma skin cancer and the value of dermoscopy in its diagnosis and treatment monitoring. Expert Review of Anticancer Therapy. 2013;**13**:541-558

[33] Lallas A, Moscarella E, Argenziano G, et al. Dermoscopy of uncommon skin tumours. The Australasian Journal of Dermatology. 2014;**55**:53-62. DOI: 10.1111/ajd.12074

[34] Williams HC, Bath-Hextall F, Ozolins M, et al. Surgery versus 5% imiquimod for nodular and superficial basal cell carcinoma: 5-year results of the SINS randomized controlled trial. The Journal of Investigative Dermatology. 2017;**137**:614-619

[35] Altamura D, Menzies SW, Argenziano G, et al. Dermatoscopy of basal cell carcinoma: Morphologic variability of global and local features and accuracy of diagnosis. Journal of the American Academy of Dermatology. 2010;**62**:67-75

[36] Papageorgiou C, Apalla Z, Variaah G, et al. Accuracy of dermoscopic criteria for the differentiation between superficial basal cell carcinoma and Bowen's disease. Journal of the European Academy of Dermatology and Venereology. 2018;**32**:1914-1919

[37] Lallas A, Apalla Z, Argenziano G, et al. The dermatoscopic universe of basal cell carcinoma. Dermatology Practical & Conceptual. 2014;**4**:11-24

[38] Marghoob AA, Malvehy J, Braun RP. An Atlas of Dermoscopy. 2nd ed. Oxford: CRC Press; 2012

[39] Demirtasoglu M, Ilknur T, Lebe B, et al. Evaluation of dermoscopic and histopathologic features and their correlations in pigmented basal cell carcinomas. Journal of the European Academy of Dermatology and Venereology. 2006;**20**:916-920

[40] Peris K, Altobelli E, Ferrari A, et al. Interobserver agreement on dermoscopic features of pigmented basal cell carcinoma. Dermatologic Surgery. 2002;**28**:643-645

[41] Imbernón-Moya A, Sidro M, Malvehy J, Puig S. Negative maple-leaf-like areas: A new clue for basal cell carcinoma margin recognition. The British Journal of Dermatology. 2016;**175**:818-820. DOI: 10.1111/bjd.14620

[42] Lallas A, Apalla Z, Ioannides D, et al. Dermoscopy in the diagnosis and management of basal cell carcinoma. Future Oncology. 2015;**11**:2975-2984

[43] Scalvenzi M, Lembo S, Francia MG, et al. Dermoscopic patterns of superficial basal cell carcinoma. International Journal of Dermatology. 2008;**47**:1015-1018

[44] Ahnlide I, Zalaudek I, Nilsson F, et al. Preoperative prediction of histopathological outcome in basal cell carcinoma: Flat surface and multiple small erosions predict superficial basal cell carcinoma in lighter skin types. The British Journal of Dermatology. 2016;**175**:751-761. DOI: 10.1111/bjd.14499

[45] Lallas A, Argenziano G, Kyrgidis A, et al. Dermoscopy uncovers clinically undetectable pigmentation in basal cell carcinoma. The British Journal of Dermatology. 2014;**170**:192-195

[46] Pyne JH, Fishburn P, Dicker A, et al. Infiltrating Basal cell carcinoma: A stellate peri-tumor dermatoscopy pattern as a clue to diagnosis.

Dermatology Practical & Conceptual. 2015;**5**:21-26

[47] Husein-ElAhmed H. Sclerodermiform basal cell carcinoma: How much can we rely on dermatoscopy to differentiate from non-aggressive basal cell carcinoma? Analysis of 1256 cases. Anais Brasileiros de Dermatologia. 2018;**93**:229-232

[48] Viera M, Amini S, Huo R, et al. A new look at fibroepithelioma of pinkus: Features on confocal microscopy. The Journal of Clinical and Aesthetic Dermatology. 2008;**1**:42-44

[49] Zalaudek I, Leinweber B, Ferrara G, et al. Dermoscopy of fibroepithelioma of pinkus. Journal of the American Academy of Dermatology. 2005;**52**: 168-169