Dermoscopic Features in Different Morphologic Types of Basal Cell Carcinoma

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BACKGROUND Many different phenotypic presentations of basal cell carcinoma (BCC) are possible.

OBJECTIVE This study aims to highlight the similarities and differences in dermoscopic features between different morphologic types of BCC.

METHODS A prospective observational study was performed using contact polarized dermoscopy to evaluate the presence of various dermoscopic features. Images were evaluated for a range of dermoscopic colors, structures, and vessels. Features were compared according to the histopathologic subtype.

RESULTS Of the 151 BCCs, 39.7% were nodular, 37.7% superficial, 13.9% ulcerated, 3.97% pigmented, 2.65% morpheaform, and 1.99% infiltrative BCCs. The dermoscopic features that showed a highly significant difference ($p < .001$) in distribution between various histologic groups were large blue-gray ovoid nests, leaf-like areas, arborizing vessels, short fine telangiectasias, annular distribution of telangiectatic vessels, structureless hypopigmentation, annular hypopigmentation, translucency, multiple erosions, and ulceration. A significant difference ($p < .05$) between evaluated groups was found in structureless hyperpigmentation, arborizing microvessels, milky red background, and pigment network.

CONCLUSION The results of the study indicate that the combination of relevant dermoscopic features in different morphologic types of BCC depends on the thickness of the tumor, and not on its histologic nature. In addition, dermoscopy was shown to be not particularly useful in identifying which BCCs are more aggressive.

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The skin is the organ most affected by cancer, with basal cell carcinoma (BCC) being the most frequent of all cancers in the fair-skinned population. Epidemiologic data indicate that the global incidence and prevalence rates are increasing, particularly in younger population; therefore, BCC emerges as a growing public health problem.[1,2]

Basal cell carcinomas rarely cause death related to metastases, but they destroy underlying tissues and should be removed at the earliest possible stage. Therefore, early detection of BCCs is of crucial importance. Basal cell carcinomas typically arise de novo on normal skin and may exhibit a large variety of clinical and dermoscopic characteristics that are the result of a wide range of combinations of its histopathologic features.[3] Therefore, clinical diagnosis of BCC may not always be easy and implicates a variety of differential diagnoses, especially in its rare variants.

Dermoscopy usually helps in identifying BCC and establishing the diagnosis. Most of the dermoscopic literature on BCCs to date primarily concerns pigmented variants, and little is known about other morphologic variants of BCCs. The aim of this study was to determine the differences and similarities between phenotypic variations of this tumor.

Materials and Methods

A prospective observational study was performed based on demographic data and digital records of

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clinical and dermoscopic images to collect patient and tumor characteristics. The following variables were recorded for all patients: gender, age, tumor location, tumor diameter, duration, number of tumors, histologic BCC subtype, and primary or recurrent BCC.

The study focused on differences in the frequency of dermoscopic features between different morphologic forms of BCC. The aim was to evaluate the association of relevant dermoscopic features with various types of BCCs.

Patients of both gender, aged above 18 years, attending the University Clinic of Dermatology between January 2009 and January 2011, and who had clinically suspected BCC were eligible for the study. The anatomic location of tumors was classified as head and neck, trunk, and extremities. Patients who were diagnosed with 2 or more BCCs were counted as 2 or more BCC cases. If a BCC occurred within 5 mm of a scar (from a previously excised BCC), the case was defined as a recurrent BCC.

Skin lesions were photographed in JPEG format using a digital camera (Nikon Coolpix 4500, 4.0 megapixels, 4× zoom; Nikon Corporation, Tokyo, Japan). Dermoscopic images of lesions were obtained with polarized contact dermoscopy using a DermLite Photo dermatoscope (3Gen LLC, Dana Point, CA) mounted on the above-mentioned digital camera. The study was approved by the Institutional Review Board and Ethics Committee.

The diagnostic system used for dermoscopic examination was pattern analysis. All clinically suspected lesions for BCC were scored for the presence of 21 various dermoscopic features relevant to the diagnosis of BCC (Table 1). The presence of a dermoscopic feature was considered as positive to diagnose BCC. Afterward, all lesions were excised or biopsied and then subjected to standard histopathologic examination. Histopathology was considered the diagnostic gold standard. A pathologist classified the BCC subtypes into 6 histologic categories. In mixed-type lesions, the superiority rule was applied according to the most unfavorable subtype: aggressive > nonaggressive. In cases of 2 mixed nonaggressive subtypes, the predominant subtype was considered. Dermoscopic images of each lesion were presented in mixed order to 2 other observers, who scored the images blinded to the histopathologic diagnosis and without the knowledge of any clinical data on the patients and lesions.

Statistical Analysis

To examine whether there was a significant statistical difference between categories, χ^2 and Fisher exact tests were applied. The χ^2 statistic for trend was used to test the null hypothesis of no association between the proportion of variation and the categorical variables. All p values cited were 2-sided, and p values less than .05 and .001 were considered statistically and highly statistically significant, respectively.

Results

Patient Characteristics

The final test set included 151 histologically confirmed BCCs collected from 116 patients (64 males [55.2%] and 52 females [44.8%]). The mean age was 67.7 years (range, 29–92 years [SD, 12.2]). All test groups consisted of more males than females (Table 2). According to the age between test groups, the highest mean age had patients with infiltrative BCCs, whereas the lowest mean age was in the group of morpheaform BCCs. No statistical difference ($P > .05$) in the age and gender of patients was found between tests groups.

Multiple BCCs were present in 15.6% of patients (n = 116). Nine patients had 2 BCCs (7.8%), 5 had 4 (4.3%), 3 had 3 (2.6%), and 1 had 6 (0.9%). The study population included predominantly white individuals.

Tumor Characteristics

Histologically, 39.7% were nodular BCCs (n = 60), 37.7% superficial (n = 57), 13.9% ulcerous (n = 21), 3.97% pigmented (n = 6), 2.65% morpheic (n = 4), and 1.99% infiltrative (n = 3). Basal cell carcinomas were most frequently located in the head/neck region (61.6%) in all test groups (Table 2). Forty-seven tumors (31.1%) were located on the trunk, and 11 (7.3%) on the extremities.

TABLE 1. Frequency of Dermoscopic Features in Different Morphologic Forms of BCC

Dermoscopic Features	*Nodular BCC (%)*	*Superficial BCC (%)*	*Ulcerated BCC (%)*	*Pigmented BCC (%)*	*Morpheaform BCC (%)*	*Infiltrative BCC (%)*	*p*
Classical dermoscopic features of BCC							
Arborizing vessels	31 (51.7)	7 (12.3)	12 (57.1)	0	1 (25)	2 (66.7)	**.000**
Arborizing microvessels	32 (53.3)	20 (35.1)	14 (66.7)	2 (33.3)	1 (25)	2 (66.7)	.024
Large, blue-gray ovoid nests	17 (28.3)	16 (28.1)	3 (14.3)	6 (100)	0	1 (33.3)	**.000**
Leaf-like areas	6 (10)	20 (35.1)	0	3 (50)	0	0	**.000**
Spoke-wheel areas	8 (13.3)	11 (19.3)	0	1 (16.7)	1 (25)	1 (33.3)	.089
Multiple blue-gray globules	20 (33.3)	24 (42.1)	5 (23.8)	2 (33.3)	1 (25)	2 (66.7)	.292
Ulceration	12 (20)	1 (1.8)	21 (100)	0	0	1 (33.3)	**.000**
Nonclassical dermoscopic features of BCC							
SFT	2 (3.3)	22 (38.6)	3 (14.3)	0	3 (75)	0	**.000**
Multiple erosions	19 (31.7)	35 (61.4)	0	0	2 (50)	3 (100)	**.000**
Milky red background	46 (76.7)	56 (98.2)	16 (76.2)	3 (50)	4 (100)	1 (33.3)	.002
Translucency	35 (58.3)	0	0	3 (50)	0	1 (33.3)	**.000**
Structureless hyperpigmentation	24 (40)	26 (45.6)	3 (14.3)	4 (66.7)	2 (50)	2 (66.7)	.039
Structureless hypopigmentation	12 (20)	31 (54.4)	0 (0)	1/6 (16.7)	3/4 (75)	0/3 (0)	**.000**
White, shiny areas	35 (58.3)	24 (42.1)	9 (42.9)	4 (66.7)	3 (75)	3 (100)	.175
White, shiny lines	16 (26.7)	21 (36.8)	6 (28.6)	2 (33.3)	2 (50)	1 (33.3)	.475
White, shiny rosette	0	3 (5.3)	0	0	1 (25)	0	.113
Annular distribution of telangiectasias	0	0	19 (90.5)	0	0	0	**.000**
Annular hypopigmentation	2 (3.3)	0	14 (66.7)	0	1 (25)	0	**.000**
Melanocytic dermoscopic features							
Multiple dots	15 (25)	15 (26.3)	2 (9.5)	1 (16.7)	1 (25)	1 (33.3)	.269
Polymorphous vessels	3 (5)	1 (1.8)	1 (4.8)	0	0	0	.615
Pigment network	1 (1.7)	6 (10.5)	0	0	0	0	.050

The mean tumor diameter was 1.55 cm (range, 0.3–7 cm [SD, 1.17]). Morpheaform BCCs had the largest mean diameter at 4.07 cm (range, 1.8–7 cm), whereas pigmented BCCs had the smallest mean diameter at 0.97 cm (range, 0.5–2.7 cm) among the tested groups (Table 2).

The time of development was recorded for 106 tumors (70.6%). The mean tumor duration was 29.6 months (range, 1–240 months [SD, 48.8]). Morpheaform BCCs had the longest mean time of development at 78 months (range, 36–120 months); infiltrative BCCs had the shortest tumor duration, with a mean of 8.7 months (range, 2–12 months) (Table 2).

Statistical analysis revealed a highly significant ($p < .001$) difference only in tumor size between test groups. No statistical difference ($p > .05$) in tumor location and duration was found. Almost all the tumors included in this study (99.3%) were primary BCCs; 1 (0.7%) was a recurrent BCC (infiltrative type). Nearly five percent (4.64%) of the tumors were aggressive forms of BCCs.

All lesions showed asymmetry in the dermoscopic examination in morphologic structures, pigmentation, and vessels. Dermoscopic evaluation showed an overall pattern of an absent pigment network (144 of 151, 95.3%) and the presence of 1 or more positive features. In total, 21 dermoscopic features

TABLE 2. Demographic Data and Tumors Characteristics in Different Subtypes of BCC

Characteristics	*Nodular BCC*	*Superficial BCC*	*Ulcerated BCC*	*Pigmented BCC*	*Morpheaform BCC*	*Infiltrative BCC*	*p*
Gender, %*							>.05
Females	45	38.6	33.3	33.3	25	33.3	
Males	55	61.4	66.7	66.7	75	66.7	
Age, years*	29–92	43–89	44–89	54–80	51–78	65–76	>.05
Mean age	67.5	69.2	68.4	69.3	66.5	72	
Size, cm†	0.3–4.5	0.5–6.5	0.5–4.5	0.5–2.7	1.8–7	1.2–4.5	<.001
Mean size	1.25	1.7	1.46	0.97	4.07	2.9	
Location, %†							>.05
Head & neck	71.7	31.6	90.5	100	100	100	
Trunk	20	57.9	9.5	0	0	0	
Extremities	8.3	10.5	0	0	0	0	
Duration, months†	1–240	1–192	3–240	3–30	36–120	2–12	>.05
Mean	30.7	32.4	27.1	15	78	8.7	

*Based on number of persons, $n = 116$.
†Based on number of tumors, $n = 151$.

were scored for every lesion. Table 1 shows the distribution of dermoscopic features among test groups and the p values.

Milky red background (Sn = 76.7%), translucency (Sn = 58.3%), white areas (Sn = 58.3%), arborizing vessels (Sn = 53.3%), and microvessels (Sn = 51.7%) were most frequently observed in nodular BCCs (Figure 1A). Arborizing vessels and translucency were highly significantly associated with nodular BCCs ($p < .001$), whereas arborizing microvessels were significantly ($p < .05$) associated with these BCCs.

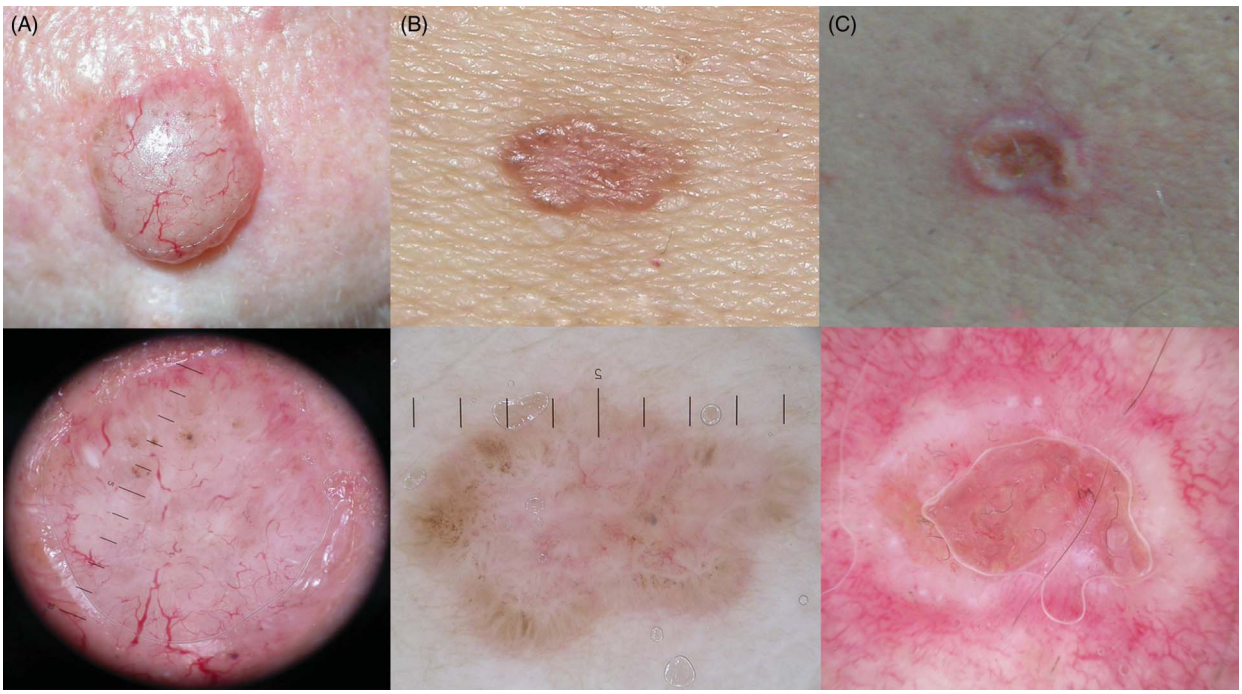

Figure 1. (A) Nodular BCC, arborizing vessels, milky red background, spoke wheel areas (clinical and dermoscopic view); (B) Superficial BCC, arborizing microvessels, leaf-like areas, multiple dots, structureless hyperpigmentation (clinical and dermoscopic view); (C) Ulcerated BCC, ulceration, annular hypopigmentation, arborising vessels (clinical and dermoscopic view).

The features most frequently found in superficial BCCs (Figure 1B) were milky red background (Sn = 98.2%), multiple erosions (Sn = 61.4%), structureless hypopigmentation (Sn = 54.4%), and hyperpigmentation (Sn = 45.6%). The features highly significantly ($p < .001$) associated with superficial BCCs were leaf-like areas, short fine telangiectasias (SFT), structureless hypopigmentation, and multiple erosions. Milky red background, structureless hyperpigmentation, and pigment network were significantly ($p < .05$) associated with the above-mentioned subtype.

Ulceration (Sn = 100%), annular distribution of telangiectatic vessels (Sn = 90.5%), milky red background (Sn = 76.2%), arborizing microvessels (Sn = 66.7%), annular hypopigmentation (Sn = 66.7%), and arborizing vessels (Sn = 57.1%) were the most frequent structures in ulcerated BCCs (Figure 1C). Ulceration, arborizing vessels, annular distribution of telangiectatic vessels, and annular hypopigmentation were highly significantly ($p < .001$) present in ulcerous BCCs. Milky red background and arborizing microvessels were significantly ($p < .05$) present in these BCCs.

Blue-gray ovoid nests (Sn = 100%), structureless hyperpigmentation (Sn = 66.7%), white areas (Sn = 66.7%), leaf-like areas (Sn = 50%), translucency (Sn = 50%), and milky red background (Sn = 50%) were most frequently observed in pigmented BCCs (Figure 2A). Blue-gray ovoid nests and leaf-like areas were highly significantly ($p < .001$) present in pigmented BCCs, whereas structureless hyperpigmentation was significantly ($p < .05$) present in these BCCs.

Milky red background (Sn = 100%), arborizing microvessels (Sn = 100%), SFT (Sn = 75%), white areas (Sn = 75%), structureless hypopigmentation (Sn = 75%), structureless hyperpigmentation (Sn = 50%), white lines (Sn = 50%), and multiple erosions (Sn = 50%) were most frequently found in morpheaform BCCs (Figure 2B). Short fine telangiectasias and structureless hypopigmentation were highly significantly ($p < .001$) present in morpheaform BCCs, whereas milky red background, arborizing microvessels, and structureless hyperpigmentation were significantly ($p < .05$) present in these BCCs.

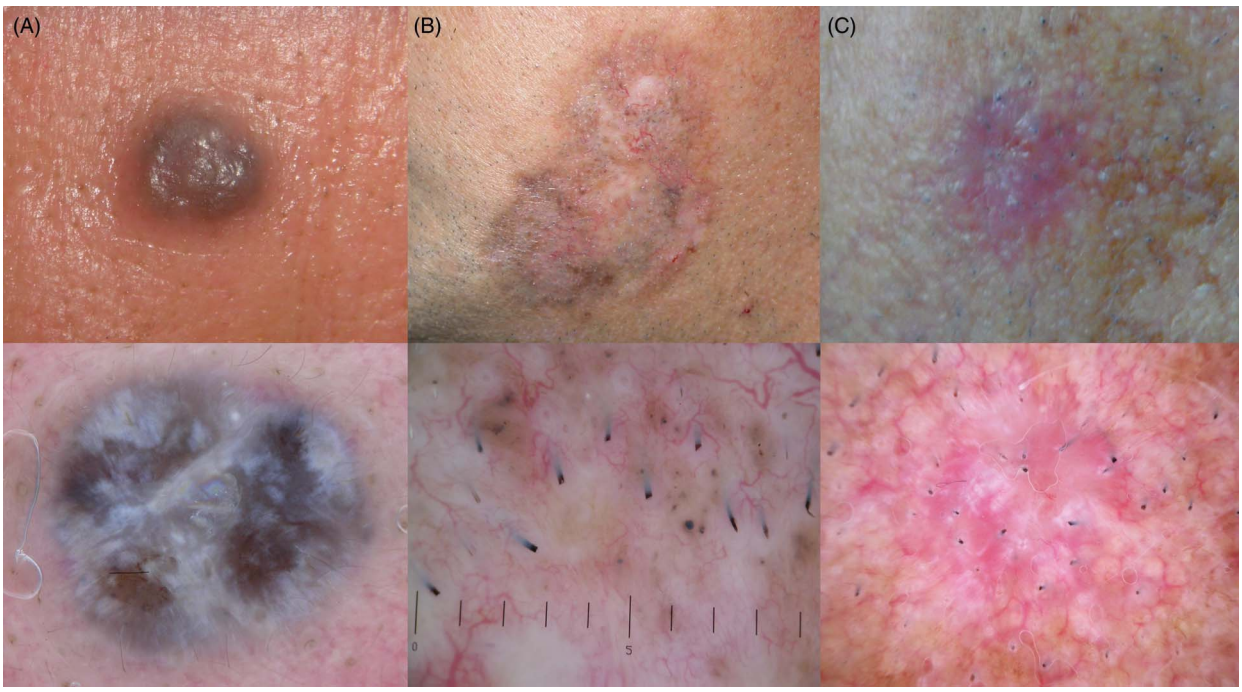

Figure 2. (A) Pigmented BCC, blue-gray ovoid nests, white line (clinical and dermoscopic view); (B) Morpheaform BCC, arborizing vessels, multiple dots, structureless hypopigmentation (clinical and dermoscopic view); (C) Infiltrative BCC, milky red background, white lines (clinical and dermoscopic view).

The most frequent features in infiltrative BCCs (Figure 2C) were multiple erosions (Sn = 100%), white areas (Sn = 100%), multiple blue-gray globules (Sn = 66.7%), structureless hyperpigmentation (Sn = 66.7%), arborizing vessels (Sn = 66.7%), and microvessels (Sn = 66.7%). Arborizing vessels and multiple erosions were highly significantly ($p < .001$) present in infiltrative BCCs, whereas arborizing microvessels and structureless hyperpigmentation were significantly ($p < .05$) present in these BCCs. Figure 3 shows the association of the most relevant dermoscopic features with specific morphologic forms of BCC.

Discussion

Basal cell carcinoma shows various types of differentiation (follicular, sebaceous, apocrine, and eccrine)[1,4] and can appear as a papule, nodule, plaque, ulceration, scar, or even as a skin induration. The wide variety of its clinical appearance is the result of various histologic combinations. There are 5 major histologic patterns: nodular (21%), superficial (17%), micronodular (15%), infiltrative (7%), and morpheaform (1%).[4] A mixed pattern (2 or more major histologic patterns) is present in 38.5%.[4]

Because of the general lack of pigment in BCCs, the blood vessels have been widely investigated. Depending on their caliber and configuration, telangiectatic vessels have been described as arborizing vessels, arborizing microvessels, and SFT.[5] The caliber and configuration of blood vessels are positively correlated with tumor growth. Initially, in small BCC,

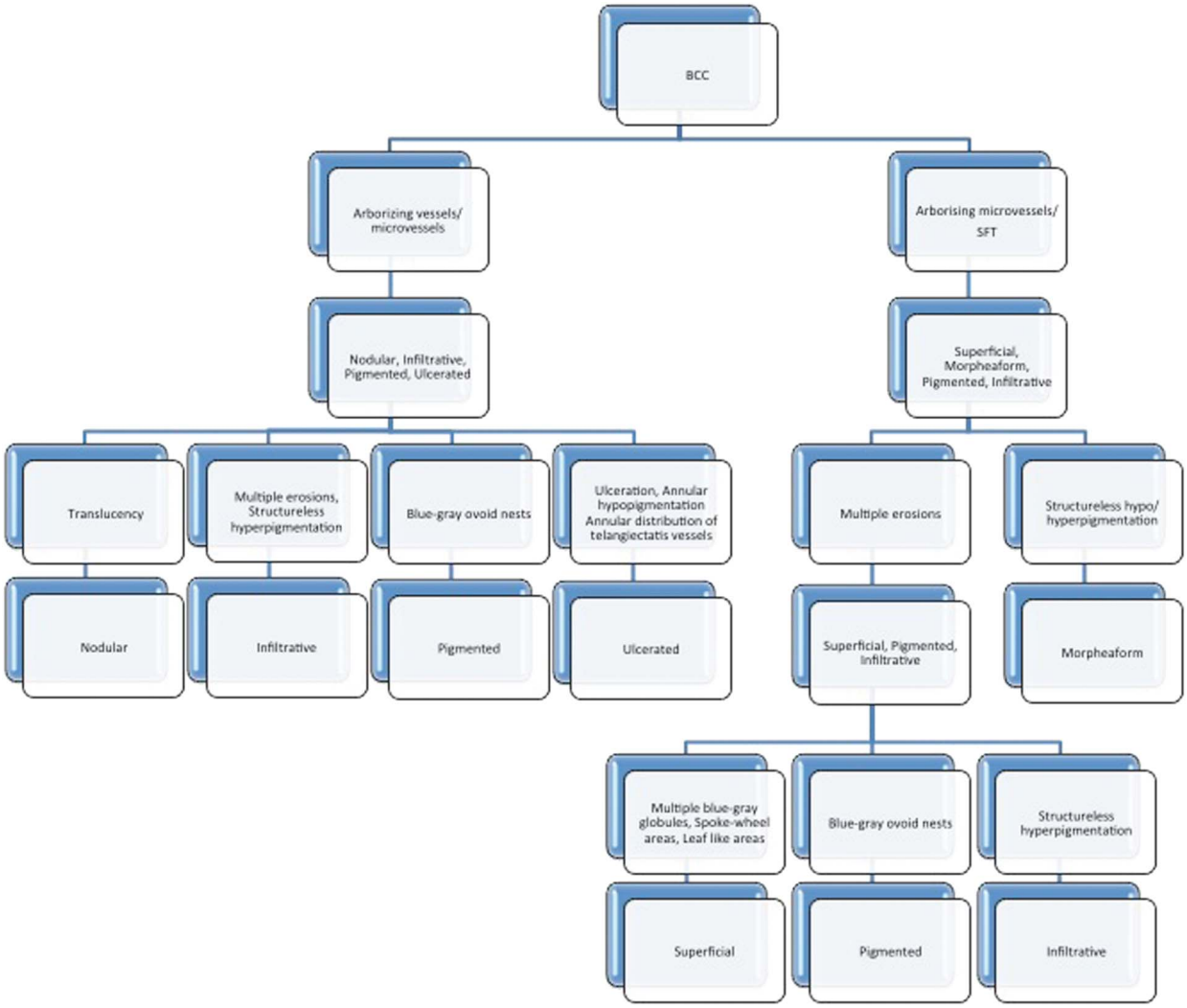

Figure 3. Association of the dermoscopic features with specific morphologic forms of BCC.

SFTs are the dominant blood vessels. As the tumor enlarges, either in thickness or width, the growing need of the tumor tissue for blood leads to the development of branched vasculature with a larger diameter, situated parallel to the tumor surface. In addition, fibromucinous stromas increase with the thickness of the tumor.

Nodular BCC was the most common subtype in this study. Clinically, it presented as a papule, plaque, or nodule. Dermoscopically, arborizing telangiectasias and translucency showed a highly significant association with nodular BCCs. Milky red background was the common feature in nodular BCCs, which is not surprising because most nodular BCCs included in this study were overall nonpigmented lesions; however, this finding was without statistical significance for this variant of BCCs. White areas were frequently observed in nodular variants, but there was no statistically significant predisposition for any specific subtype. Among the pigmented features, multiple blue-gray globules, large blue-gray ovoid nests, and structureless hyperpigmentation were the most frequently observed. The other evaluated features showed rare presence in nodular BCCs.

Ulcerated BCCs clinically presented as ulcerated papules and nodules. In this group, ulceration, arborizing vessels, annular distribution of telangiectatic vessels, and annular hypopigmentation were highly significantly associated with this tumor subtype. Because of destruction the central area of tumor body, ulceration was the dominant feature observed with dermoscopy, together with remnants of a vascular network and hypopigmentation around the ulcer. Translucency was completely absent in the ulcerated tumors, whereas the combinations of the other evaluated dermoscopic features were similar to those found in nodular BCCs.

Superficial and morpheic subtypes represented thin variants of tumor. Clinically, superficial BCCs presented as papules or plaques, whereas morpheic subtypes presented as large sclerotic plaques. The dermoscopic features highly significantly associated with both types were SFT and structureless hypopigmentation, whereas milky red background and structureless hyperpigmentation were significantly present in both groups. Morpheaform BCCs often reach large dimensions before the correct diagnosis is made, leading to the development of arborizing microvessels; these were significantly associated with the above-mentioned variant, whereas multiple erosions and leaf-like areas were highly significantly present in superficial BCCs. Pigment network as a melanocytic feature was rarely but significantly observed in superficial tumors. The combinations of the other evaluated structures were similar in both groups.

Of the 3 infiltrative BCCs, 1 had a nodular and 2 had a sclerotic clinical presentation. Therefore, the dermoscopic findings were a mixture of features typical for both variants. Arborizing vessels and multiple erosions were highly significantly associated with infiltrative BCCs, whereas arborizing microvessels and structureless hyperpigmentation were significantly associated with these BCCs. White areas and multiple blue-gray globules were frequently observed in the infiltrative group, but this finding had no statistical significance for this group.

Pigmented variants account for only approximately 7% of all BCCs, but these have been the most investigated subtype.[3,6] The most frequent pigmented features in this study were multiple blue-gray globules and multiple dots. These features were distributed in a scattered pattern and were present in all test groups, without a significant difference between the groups. Leaf-like areas were significantly more frequent in pigmented and superficial types of BCC than in the other tested groups. Spoke-wheel areas as the most specific pigmented feature were rarely found in test groups, without statistical significance for any particular type of BCC. As pigmentation increased, blue-gray ovoid nests became the most common and a highly significant feature in pigmented variants of tumor. Moreover, structureless hyperpigmentation showed a significant association with pigmented BCCs.

Despite the widespread opinion among dermatologists that BCC is the easiest to diagnose, the clinical diagnosis of BCC is surprisingly weak at about 60%. Furthermore, a correct clinical diagnosis does not

imply a correct diagnosis of the histologic subtype. Clinically, the nodular and plaque lesions in this study presented with both nodular as nonaggressive and infiltrative and morpheaform as aggressive histologic patterns. The absence of a strong correlation between clinical presentation and histopathology puts greater importance on dermoscopic examination, which has been shown to increase the diagnostic accuracy for BCC up to 90%.[7]

However, the results of this study indicate that dermoscopy is not particularly useful in identifying which BCCs are more aggressive. Careful dermoscopic examination did not find any distinctive feature(s) that would point to an aggressive nature of the tumor. In addition, this study shows that the numerous combinations of dermoscopic features in various BCCs depend on the thickness of the tumor, and not on its histologic nature.

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