Statistical Evaluation of Dermoscopic Features in Basal Cell Carcinomas

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BACKGROUND Early detection of basal cell carcinoma (BCC) is of crucial importance, as serious morbidity may result from undiagnosed tumor.

OBJECTIVE To evaluate diagnostic significance (specificity, sensitivity, positive and negative predictive value) of dermoscopic features in BCCs.

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

SETTING Specialized University Clinic.

PATIENTS A sample of 151 histopathologically verified BCCs was collected from 116 patients (64 males and 52 females). The populations included predominantly Caucasian individuals.

MAIN OUTCOME MEASURES The sensitivity, specificity, positive and negative predictive values of the various dermoscopic features seen in BCCs were calculated according to standard formulas.

RESULTS The highest diagnostic value (specificity [Sp] = 100%, positive predictive value [PPV] = 100%) for BCC had spoke-wheel areas, short fine telangiectasias, white rosette, annular hypopigmentation, multiple erosions, and ulceration. Arborizing vessels (Sp = 96%, PPV = 98%) and microvessels (Sp = 93%, PPV = 97%) had significant diagnostic value for BCC. Annular distribution of telangiectatic vessels (Sp = 96%), translucency (Sp = 93%), and multiple blue–gray globules (Sp = 89%) had the same PPV of 95% for BCCs. Other dermoscopic features of this study are not strongly associated with the diagnosis of BCC.

CONCLUSION Dermoscopic features relevant for diagnosis of BCC have different diagnostic "weight." Clinicians should have known the sensitivity and specificity of each relevant feature before they can make an accurate dermoscopic diagnosis of BCC.

The author has indicated no significant interest with commercial supporters.

The skin is the most affected organ by cancer with basal cell carcinoma (BCC) as the most frequent of all cancers in the fair-skinned population. Although these tumors rarely cause death related to metastases, they destroy underlying tissues and should be removed at the earliest possible stage.

Basal cell carcinoma may exhibit a large variety of clinical and dermoscopic characteristics that are the result of a wide range of combinations of histopathologic features. Therefore, clinical diagnosis of BCC may not be always easy and implicates a variety of differential diagnoses, especially in its rare variants.

Dermoscopy usually helps in identifying BCC and establishing the diagnosis. Many dermoscopy features of BCC have been described. However, formal statistical evaluation of these features has been reported mainly on pigmented BCCs. For this reason, the diagnostic value of various dermoscopic features of a large set of 151 different BCC subtypes were analyzed.

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ISSN: 1076-0512 • Dermatol Surg 2014;40:718–724 • DOI: 10.1111/dsu.0000000000000031

Materials and Methods

A prospective observational study was done based on demographic data, digital records of clinical and dermoscopic images to collect patients, and tumor characteristics. The following variables were recorded for all patients: gender, age, tumor location, tumor diameter, duration, number of tumors, histological BCC subtype, and primary or recurrent BCC.

Eligible were patients of both gender, aged older than 18 years attending the University Clinic of Dermatology, between January 2009 and January 2011, who had a clinically suspected BCC. The anatomical 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 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 (Table 1, Figure 1) relevant for diagnosis of BCC. Presence of dermoscopic feature was considered as positive to diagnose BCC. Afterward, all lesions were excised or biopsied and subjected to standard histopathologic examination. Histopathology was regarded as the diagnostic gold standard. The BCC subtypes were categorized into 1 of 6 histological categories by the pathologist. In mixed-type lesions, superiority rule was used according to the most unfavorable subtype: aggressive > nonaggressive. In cases of mixed 2 nonaggressive subtypes, the predominant subtype was considered.

All clinically suspected lesions for BCC that were histologically confirmed as non-BCC lesions, comprised the control group. The study was approved by the Institutional Review Board and Ethics Committee. The interobserver error of method did not formally test but the model provides stringent morphologic definitions for each feature and uses only present or absent scoring criteria.

Statistical Analysis

Sensitivity (Sn), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) for the dermoscopic features of BCCs were calculated according to standard formulas (Table 2).

Sensitivity is the probability that a positive dermoscopic feature will indicate BCC among those with the BCC. It is equal to the number of scored true-positive dermoscopic feature in BCCs divided by the total number of BCCs (expressed as a percentage). Sensitivity: $A/(A + C) \times 100$. Specificity is the fraction of those lesions with true-negative dermoscopic feature who are not BCC. The specificity is equal to the number of scored negative dermoscopic feature in non-BCC lesions divided by the total number of non-BCC lesions (expressed as a percentage). Specificity: $D/(D + B) \times 100$.

Positive predictive value reflects the probability of a lesion with a positive dermoscopic feature being BCC. Positive predictive value is equal to the number of scored true-positive dermoscopic feature divided by the total (true + false) number of positive feature (expressed as a percentage). Positive Predictive Value: $A/(A + B) \times 100$. Negative predictive values represent the probability of lesion with a negative dermoscopic feature not being BCC. Negative predictive value is equal to the number of true-negative dermoscopic feature divided by the total (true + false) number of negative feature (expressed as a percentage). Negative Predictive Value: $D/(D + C) \times 100$.

Results

Patient Characteristics

The final test set was consisted of 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]).

TABLE 1. Definition of Dermoscopic Features and Theirs Histhopathologic Correlation

Dermoscopic Features	*Definition*	*Histopathologic Correlation*
Classical dermoscopic features of BCCs		
Arborizing vessels	Stem vessels of a large diameter (>0.2 mm) with irregular tree-like branching	Dilated superficial blood vessels in dermis, parallel to the surface
Arborizing microvessels	Arborizing telangiectasias <0.2 mm in diameter	
Large blue–gray ovoid nests	Well-circumscribed, confluent, or near confluent pigmented ovoid or elongated areas, larger than globules and not intimately connected to a pigmented tumor body	Large nests of pigmented basaloid cells in the dermis
Leaf-like areas	Brown to gray/blue discrete bulbous extensions forming leaf-like pattern (never arising from pigmented network and from adjacent confluent pigmented area)	Large complex nodules of pigmented basaloid cells in the upper dermis
Spoke-wheel areas	Well-circumscribed radial projections, usually tan but sometimes blue or gray, meeting at often darker (dark brown, black, or blue) central axis	Nests of pigmented basaloid cells radiating from the follicular epithelium
Multiple blue-gray globules	Well-circumscribed ovoid pigmented areas in smaller dimensions than nests	Small nests of pigmented basaloid cells in the dermis
Ulceration	Brown to reddish areas often associated with congealed blood and without recent history of trauma	Full thickness loss of epidermis and superficial dermis
Nonclassical dermoscopic features of BCCs		
SFT	Fine kinked vessels of a small caliber and length (typically <1 mm) with few branches	Early stage of development of arborizing telangiectasias
Multiple erosions	>5 brown pigmented areas, diameter <1 mm on the lesions surface	Superficial loss of tissue
Milky-red background	Shiny white to red structureless areas that appeared translucent to opaque	Vascularization of the tumor
White shiny areas	White shiny clods or larger structureless areas with a shiny bright white color	Fibrosis in the dermis
White shiny lines	Bright, shiny white lines, often irregular distributed	Fibrosis or altered collagen in the dermis
White shiny rosette	Four bright white points grouped together akin to a 4-leaf clover (individual or multiple)	Interaction of keratin-filled adnexal openings with the polarized light of the dermatoscope
Translucency	Transparency through the depth of the tumor	Transparency of skin which depends of the size and location of the basaloid cells
Structureless hypopigmented areas	Areas devoid of dermoscopic structures and without regression. These areas can be pigmented or nonpigmented	Lack of melanin or presence of melanin in all layers of the skin
Structureless hyperpigmented areas		
Annular distribution of vessels	Arborizing telangiectasias around the ulcer	Dilated superficial blood vessels in dermis
Annular hypopigmentation	Annular hypopigmented area, around the ulcer	Lack of melanin in the skin
Dermoscopic features of melanocytic lesions that were present in BCCs		

TABLE 1. (Continued)

Dermoscopic Features	*Definition*	*Histopathologic Correlation*
Pigment network	Grid-like network consisting of pigmented "lines" and hypopigmented "holes"	Melanin in keratinocytes and/or melanocytes along the epidermal rete ridges
Multiple dots	Small round structures <0.1 mm in diameter that may be black, brown, gray, or bluish	Aggregates of melanocytes or melanin granules. Black dots represent pigment in the upper epidermis or stratum corneum. Brown dots represent pigment at the dermoepidermal junction. Blue–gray dots represent pigment in the papillary dermis
Polymorphous vessels	Any combination of 3 or more different types of vascular structure	Blood vessels in the dermis

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%) BCCs.

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% morpheaform (n = 4), and 1.99% infiltrative (n = 3). Individual lesions were most frequently located in the head/neck region (61.6%). Forty-seven tumors (31.1%) were located on the trunk and 11 (7.3%) on the extremities. The mean tumor diameter was 1.55 cm (range, 0.3–7 [SD, 1.17] cm).

Time of development was recorded for 106 tumors (70.6%). The mean time of tumor duration was 29.6 months (range, 1–240 [SD, 48.8]).

Almost all included tumors (99.3%) were primary BCCs and 1 (0.7%) was recurrent BCC (infiltrative type). Nearly five percent (4.64%) of the included tumors were aggressive forms of BCCs.

All the lesions showed asymmetry in dermoscopic examination in terms of morphological structures, pigmentation, and vessels. Dermoscopic evaluation showed the overall pattern of an absent pigment network (144/151; 95.3%) and the presence of one or

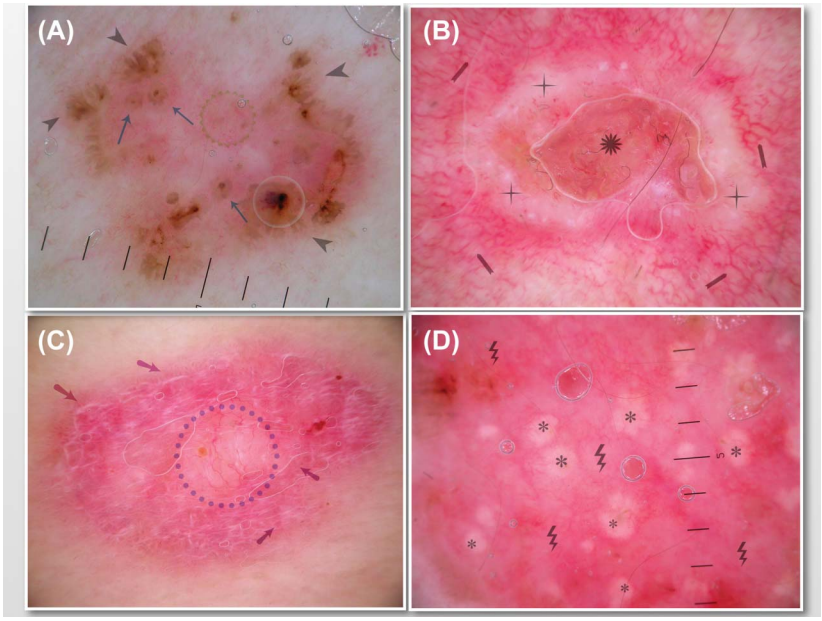

Figure 1. Dermoscopic features: (A) maple leaf-like areas (gray arrows), spoke-wheel areas (blue arrows), erosion (white circle), and SFT (green circle); (B) annular hypopigmentation (purple cross), ulceration (purple star), and arborizing telangiectasias (purple arrows); (C) shiny white lines (pink arrows) and arborizing microvessels (blue circle); (D) milky-red background (lightning-like lines) and white rosettes (stars).

TABLE 2. Standard Formulas for Calculation Sn, Sp, PPV, and NPV

	Dermoscopic Feature in BCCs	*Dermoscopic Feature in Control Group*	*Total*
Positive	A (true positive)	B (false positive)	Positive
Negative	C (false negative)	D (true negative)	Negative
Total	151	27	178

more positive feature. In total, 21 dermoscopic features were scored for every lesion. Distribution of dermoscopic features in BCCs is reported in Figure 2. Milky-red background was the most common feature found (Sn = 85%) in this study, but with low specificity (Sp = 48%) and lower diagnostic value (PPV = 90%) for BCC.

Typical large vessels were found less frequently (Sn = 35.1%) than arborizing microvessels (Sn = 49%) with total sensitivity of 84.1%. Both caliber of telangiectatic vessels had high diagnostic value (vessels PPV = 98%; microvessels PPV = 97%) for BCC. Short fine telangiectasias (SFTs) were the least frequent (Sn = 19.9%) vascular feature of this study but with the highest value for diagnosis of BCC (PPV = 100%).

Multiple blue–gray globules was the most frequent (Sn = 35.8%) type of pigmentation seen in this study followed by blue–gray ovoid nests (Sn = 28.5%), leaf-like areas (Sn = 19.2%), and spoke-wheel (Sn = 14.6%) areas. The highest diagnostic value for BCC among pigmented features had the spoke-wheel areas (PPV = 100%) followed by multiple blue–gray globules (PPV = 95%), leaf-like areas (PPV = 91%), and large blue–gray ovoid nests (PPV = 86%).

Multiple erosions were found more frequently (Sn = 39.1%) than ulceration (Sn = 23.2%). Presence of both features were strongly spoke (PPV = 100%) in favor of BCC. Translucency was found in 25.8% of evaluated BCCs, with high diagnostic value (PPV = 95%) for this tumor.

According to frequency, in this study, white shiny areas were more frequently (Sn = 51.7%) observed than white shiny lines (Sn = 31.8%). Furthermore, their presence did not strongly support the diagnosis of BCC (areas PPV = 90%; lines PPV = 81%). White shiny rosettes were the least frequent (Sn = 2.6%) of all evaluated features in this study, but with high significance for BCCs (PPV = 100%).

Structureless hyperpigmented areas were noted in 40.4% of evaluated BCCs, whereas structureless hypopigmented areas were less frequent (Sn = 31.1%). These structureless areas had lower diagnostic

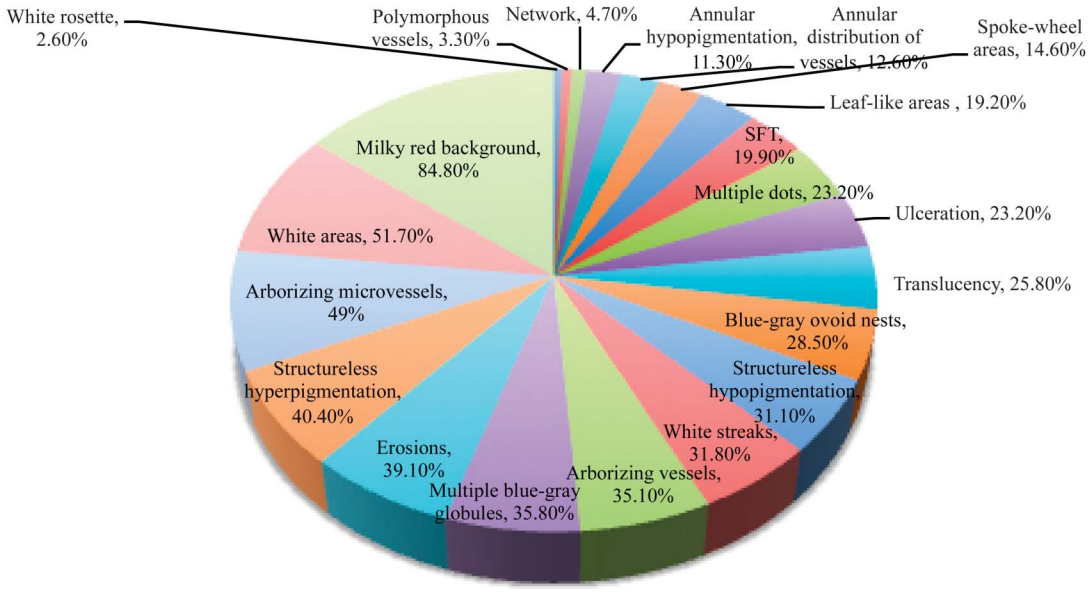

Figure 2. Distribution of dermoscopic features in BCCs.

significance (hyperpigmented areas PPV = 88%; hypopigmented areas PPV = 80%) for BCC.

Ulcerous BCCs of this study were found to have annular (around the ulcer) distribution of telangiectatic vessels (Sn = 12.6%) and hypopigmentation (Sn = 11.3). This study established that both features had high diagnostic value (annular hypopigmentation PPV = 100%; annular telangiectasias PPV = 95%) for BCC.

Of the dermoscopic features characteristic for melanocytic lesions, multiple dots (Sn = 23.2%) were the most common, followed by pigment network (Sn = 4.7%) and polymorphous vessels (Sn = 3.3%). None of these 3 features had high diagnostic value (dots PPV = 85%; network PPV = 78%; vessels PPV = 50%) for BCC. Sensitivity, specificity, PPV, and NPV of evaluated dermoscopic features are reported in the Table 3.

TABLE 3. Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of Evaluated Dermoscopic Features for BCCs

Dermoscopic Features	*PPV, %*	*Sp, %*	*Sn, %*	*NPV, %*
Spoke-wheel areas	100	100	15	17
SFT	100	100	20	18
White rosette	100	100	3	16
Annular hypopigmentation	100	100	11	18
Ulceration	100	100	23	19
Multiple erosions	100	100	39	23
Arborizing vessels	98	96	35	21
Arborizing microvessels	97	93	49	25
Multiple blue–gray globules	95	89	36	20
Annular distribution of vessels	95	96	13	16
Translucency	95	93	26	18
Leaf-like areas	91	89	19	16
White areas	90	67	52	20
Milky-red background	90	48	85	36
Structureless hyperpigmentation	88	70	40	17
Large blue–gray ovoid nests	86	74	28	16
Multiple dots	85	78	23	15
White streaks	81	59	32	13
Structureless hypopigmentation	80	56	31	13
Pigment network	78	93	5	15
Polymorphous vessels	50	81	3	13

Discussion

Pigmented BCCs make ~7% of the total BCCs, and using dermoscopy represents the most evaluated type of BCC, despite the fact that most BCCs are overall nonpigmented lesions.[1,2] Therefore, the conducted study included different morphological types of BCCs with different amounts of pigmentation where most tumors were nonpigmented. In poorly pigmented tumors, findings in blood vessels may provide complementary information important for diagnosis. Prominent vasculature situated parallel to the surface, varying amounts and degree of fibromucinous stroma, and epithelial aggregations that vary in size comprise the common histopathologic findings of a nonpigmented BCC.[3]

Because of general lack of pigments in BCCs, it is not surprising that milky-red background and arborizing vessels were the most common features found in this study. However, despite their frequent presence, these 2 features had completely different contribution in making diagnosis of BCCs. Dermoscopic feature that had the highest sensitivity value was milky-red background. Presence of this dermoscopic structure correlate with the vascularization of the lesions, and with dermoscopy, this feature was seen in several non-BCCs lesions of control group including Bowen disease, actinic keratosis, squamous cell carcinoma, seborrheic keratoses, and angiomas. Therefore, despite the highest sensitivity, milky-red background had low specificity (48%) for BCC in the conducted study and presence of this feature did not have significant diagnostic value for BCC.

Telangiectatic vessels were the second frequent feature of this study and had almost the same sensitivity (84%) as milky-red background. The only non-BCC lesion where these vessels were seen in this study was cyst. But here, telangiectatic vessels were without sharp demarcation and not in the focus as they are in BCC. Therefore, both the caliber of telangiectatic vessels had high PPV (this value reflects the probability of a lesion with these features being BCC) for BCC and strongly supported the diagnosis of BCC. Therefore, sharply focused, superficial, typical telangiectatic vessels should be considered as the

most reliable diagnostic feature for BCC.[1,2,4–7] The most specific features with the highest diagnostic value were multiple erosions, ulceration, SFT, and spoke-wheel areas listed by decreasing order of sensitivity.

The BCCs have tendency to ulcerate early in contrast to melanoma or SCC, where the ulcer is developing later in their advance stage of development. Multiple small erosions are considered to be initial stage in development of ulcer. In this study, two thirds of the included BCCs had early or late stage in destruction of tumor tissue. The presence of any of these 2 features were strongly spoke in favor of BCC and should be considered as reliable features for diagnosis of BCC.

Among vascular features, SFT were the least frequent but with the highest value for diagnosis of BCC. Therefore, if this feature is present, the diagnosis of BCC should be strongly considered.

Spoke-wheel areas are described as the rare but the most specific feature for pigmented BCCs. The same results were obtained in this study, which included predominantly nonpigmented BCCs. The probability of a lesion with this feature to be a BCC was 100%. Therefore, presence of this uncommon dermoscopic feature strongly pointed toward diagnosis of BCCs.

Among the pigmented features, multiple blue–gray globules were the most common type of pigmentation seen in this study. Pigmented features (except spoke-wheel areas) were a frequent dermoscopic finding in other lesions with partial pigmentation, especially SK. Therefore, the specificity of multiple globules was lower than the spoke-wheel areas with probability of BCC diagnosis, if this feature is present, of 95%. Leaf-like areas that were found to be the most specific feature in pigmented BCC in this study was a rare finding with lower specificity and diagnostic value for BCC. Large blue–gray ovoid nest was the second frequent feature among the pigmented ones and did not show high specificity or high diagnostic significance for BCC.

The translucency observed by dermoscopy may be subtle to obvious, depending on the size and location of the neoplastic epithelial aggregations and the amount of fibromucionous stroma.[8] Translucency is more prevalent in nodular BCCs compared with the flatter BCCs. This dermoscopic feature was found in 26% of the included BCCs with high diagnostic value for this tumor.

The other evaluated dermoscopic features (white shiny structures, areas of dispigmentation, and some dermoscopic features that are characteristic for melanocytic lesions) did not have high importance for diagnosis of BCCs. However, they could be noted in BCCs and may narrow the diagnostic possibilities for the clinician but only in concept with clinical examination and anamnestic data.

In conclusion, the most reliable features for diagnosis of BCC were telangiectatic vessels (both calibers) and multiple small erosions. Presence of spoke-wheel areas, multiple blue–gray globules, SFT, ulceration, and translucency presented further important clues in detection of BCC.

References

1. Menzies SW, Westerhoff K, Rabinovitz H, Kopf AW, et al. Surface microscopy of pigmented basal cell carcinoma. Arch Dermatol 2000;136:1012–6.
2. Menzies SW. Dermoscopy of pigmented basal cell carcinoma. Clin Dermatol 2002;20:268–9.
3. Zalaudek I, Kreusch J, Giacomel J, Ferrara G, et al. How to diagnose nonpigmented skin tumors: a review of vascular structures seen with dermoscopy: part II. Nonmelanocytic skin tumors. J Am Acad Dermatol 2010;63:377–86.
4. Neale RE, Davis M, Pandeya N, Whiteman DC, et al. Basal cell carcinoma on the trunk is associated with excessive sun exposure. J Am Acad Dermatol 2007;56:380–6.
5. Felder S, Rabinovitz H, Oliviero M, Kopf A. Dermoscopic differentiation of a superficial basal cell carcinoma and squamous cell carcinoma in citu. Dermatol Surg 2006;32:423–5.
6. Puspok-Schwarz M, Steiner A, Binder M, Partsch B, et al. Statistical evaluation of epiluminescence microscopy criteria in the differential diagnosis of malignant melanoma and pigmented basal cell carcinoma. Melanoma Res 1997;7:307–11.
7. Argenziano G, Zalaudek I, Corona R, Sera F, et al. Vascular structures in skin tumors: a dermoscopic study. Arch Dermatol 2004;140:1485–89.
8. Altamura D, Menzies SW, Argenziano G, Zalaudek I, et al. Dermatoscopy of basal cell carcinoma: morphologic variability of global and local features and accuracy of diagnosis. J Am Acad Dermatol 2010;62:67–75.

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