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An additional dermoscopic clue in basal cell carcinoma of the lower limb: the purpura-like pattern

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Abstract

Background Dermoscopy is a critical tool for diagnosing basal cell carcinoma (BCC) and differentiating its histopathological subtypes. However, BCC on the lower limbs may present with atypical dermoscopic features, making its diagnosis challenging.

Objectives To identify specific dermoscopic patterns of BCC on the lower limbs, focusing on the newly observed purpura-like pattern, and to assess how these features differ from BCCs in other anatomical sites.

Methods A retrospective, single-centre study reviewed standardized polarized dermoscopic images of 478 BCCs collected between January 2011 and December 2022. Two independent dermatologists evaluated the dermoscopic images, blinded to histopathological diagnoses and anatomical sites. Statistical analysis was performed to determine correlations between dermoscopic features and BCC locations. A matched test set with dermoscopic images of skin conditions of the lower limb (control group) was then evaluated.

Results A new dermoscopic pattern, a purpura-like pattern, was identified in lower-limb BCCs, in addition to other features such as dotted-glomerular vessels, shiny-white structures and small erosions. The purpura-like pattern, which appeared as peripheral, out-of-focus dots or globules on a coppery red background, was significantly associated with lower-limb BCCs (odds ratio 7.13, 95% confidence interval 5.01–10.16, $P<0.001$). Dotted-glomerular vessels were also more frequent in lower-limb BCCs. In the control group, composed of 239 histologically confirmed non-BCC lower-limb lesions, the purpura-like pattern was identified in 3.8% (9/239) of lesions, including Kaposi sarcoma, acroangiodermatitis/stasis dermatitis, mycosis fungoides, viral wart and basosquamous carcinoma. Interrater agreement for pattern recognition was high (Cohen's kappa = 0.81, $P<0.001$).

Conclusions The purpura-like pattern is an additional dermoscopic feature significantly associated with BCC on the lower limbs. Although not exclusive to BCCs, its presence, especially if combined with other dermoscopic criteria, may enhance diagnostic accuracy in this diagnostically challenging anatomical site. Further validation in larger, prospective studies is warranted.

What is already known about this topic?

- Dermoscopic features of basal cell carcinoma (BCC) vary by anatomical site.
- Lower-limb BCCs often lack classic dermoscopic patterns, making diagnosis more challenging.

What does this study add?

- This study identifies the purpura-like pattern as a novel dermoscopic clue significantly associated with lower-limb BCCs.
- This finding will enhance diagnostic precision when combined with established dermoscopic criteria for BCCs.

Dermoscopy is a sensitive and specific noninvasive tool that aids in diagnosing basal cell carcinoma (BCC) and in differentiating different BCC subtypes.[1–5] It is well established that BCCs exhibit varying dermoscopic features based on the patient's age, sex and anatomical site.[6–8] Lower-limb BCC represents a unique diagnostic challenge owing to its relative rarity compared with BCCs occurring in more sun-exposed areas. The clinical and dermoscopic appearance of these lesions and their similarity to other skin conditions often lead to delayed or incorrect diagnoses. Factors

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such as past sun exposure, differences in skin thickness, and age-related skin changes are all interrelated and can influence the dermoscopic appearance of BCC.[6–9]

Previous studies have shown that BCC on the lower extremities may present vascular patterns not typically seen in classic BCC.[10,11] Furthermore, BCC on the lower limbs can clinically and dermoscopically resemble both benign and malignant skin lesions, with squamous cell carcinoma (SCC) representing the main differential diagnosis.[10]

Further investigation of the dermoscopic features of BCC on the lower extremities is essential to potentially distinguish it from other skin tumours. In this study, we aimed to explore the distribution of BCC subtypes and their associated dermoscopic features across different anatomical sites, with a particular focus on lesions located on the lower extremities. We also aimed to describe the frequency of the newly observed purpura-like pattern in BCC and other skin conditions of the lower limbs.

Materials and methods

This was a retrospective, single-centre, observational study that reviewed consecutive BCC images collected between January 2011 and December 2022. All patients were treated at the Skin Cancer Center of Arcispedale Santa Maria Nuova in Reggio Emilia, Italy. Standardized polarized dermoscopic images were captured using a DermLite Photo device (3Gen, San Juan Capistrano, CA, USA) mounted on a Canon G16 camera. The cases of all patients included in the image set had a histopathological diagnosis.

The first image sets were randomly presented and evaluated by two investigators: one dermatologist with advanced dermoscopy expertise (M.S.) and one dermatologist with intermediate expertise (A.S.), both blinded to histopathological subtypes and anatomical sites. No clinical images were provided to prevent the identification of anatomical locations. Images were analysed for the presence of specific dermoscopic criteria (Table S1; see Supporting Information).[12–17] Evaluators were asked to classify the BCC subtype based on dermoscopic findings. Clinical data (age at diagnosis, sex, histopathological diagnosis when available, anatomical location, BCC histopathological subtype) were retrieved from the hospital clinical database.

A second test set (control group) was then created to further assess the presence of the purpura-like pattern in lower-limb lesions. Given the limited number of biopsied lower-limb lesions initially suspected to be BCC but diagnosed as non-BCC in the final histopathological examination, we included all benign and malignant biopsied lesions of the lower limbs from our Skin Cancer Center, matched for age and sex with the first test set (Table S2; see Supporting Information). This broader inclusion approach better reflects the real-world clinical practice of a tertiary centre and allows for a more comprehensive assessment of whether, and where, the purpura-like pattern is also present in skin conditions other than BCC. The test set included cutaneous lesions, with clinical and dermoscopic images, surgically excised in the same timeframe as the first test set, and a complete histopathological report. Two independent dermatologists (M.S. and A.S.), blinded to the histopathological diagnoses, were asked to assess the presence of the purpura-like pattern within the lesional skin under dermoscopy. This evaluation was conducted only after the purpura-like pattern had been defined based on the prior analysis of BCC images in the first part of this study.

Statistical analysis

To balance the groups of patients with lower-limb lesions vs. those with lesions in other anatomical locations, the propensity score matching technique was employed. Statistical analysis was performed using Stata software version 17 (StataCorp. 2021, Stata Statistical Software, Release 17; College Station, TX, USA: StataCorp LLC). Descriptive statistics were presented for baseline demographic clinical characteristics for all patients. Continuous variables were presented as the number of patients, mean, SD and range and compared between subgroups using an unpaired Student's *t*-test, while categorical variables were presented as frequency (*n*, %) and compared using Pearson's χ^2 test.

Univariate and multivariate logistic regression models used a stepwise selection method to identify the prognostic factors between lower limbs and other sites. In the first step, the intercept-only model was fitted and individual score statistics for the potential variables were evaluated. A significance level of $P<0.05$ was used to allow a variable into the model. In stepwise selection, an attempt was made to remove any insignificant variables from the model before adding a significant variable to the model. Hosmer and Lemeshow tests were used to evaluate 'goodness of fit' in the selection model. Data from the univariate and multivariate logistic regression analyses were expressed as odds ratio (OR) and 95% confidence interval (CI). Descriptive and inferential statistical analyses were conducted to evaluate the agreement between independent raters for the identification of the purpura-like dermoscopic pattern. Interrater agreement was assessed using Cohen's Kappa statistic, which measures the degree of concordance between two raters while accounting for agreement occurring by chance. Kappa values were interpreted as follows: 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; > 0.80, almost perfect agreement. All statistical tests were two-tailed, and a *P*-value < 0.05 was considered statistically significant. Analyses were performed using Stata software version 17.

Results

Population

The study included 478 BCCs from 478 patients (156 females, 32.6%; mean age 71.3 years, SD 12.5), of which 403 had a BCC histopathological diagnosis with a defined subtype on the histopathological report. Demographic data and histopathological BCC subtypes are presented in Table 1.

Patients with infiltrative BCC (iBCC) (mean 75.3, SD 12.1 years) and nodular BCC (nBCC) (mean 72.6, SD 11.7 years) were significantly older than those with superficial BCC (sBCC) (mean 65.9, SD 12.6 years, $P<0.001$).

Data on the anatomical distribution of BCC subtypes ($P<0.001$) showed a prevalence of nBCC (53.9%) and iBCC

Table 1 Demographic data and histopathological basal cell carcinoma (BCC) subtypes

Characteristics		BCC				
	Total (*N* = 478)	Superficial (*n* = 123, 25.7%)	Nodular (*n* = 150, 31.4%)	Infiltrative (*n* = 130, 27.2%)	Missing subtype (*n* = 75, 15.7%)	*P*-value
Sex						
Female	156 (32.6)	50 (40.7)	40 (26.7)	39 (30.0)	27 (36)	0.08
Male	322 (67.4)	73 (59.3)	110 (73.3)	91 (70.0)	48 (64)	
Age on visit, mean (SD), range	71.3 (12.5) 34–97	65.9 (12.6) 34–91	72.6 (11.7) 38–97	75.3 (12.1) 43–97	70.6 (11.3) 37–96	**< 0.001**

Data are *n* (%) unless otherwise specified. *P*-value in bold is significant.

Table 2 Data on the anatomical distribution of basal cell carcinoma (BCC) subtypes

BCC subtype[a]	Anatomical site, *n* (%)			
	Head and neck (*n* = 126)	Upper limb (*n* = 10)	Trunk (*n* = 53)	Lower limb (*n* = 204)
Superficial BCC	10 (7.9)	3 (30)	22 (41.5)	88 (43.1)
Nodular BCC	68 (54.0)	6 (60)	19 (35.8)	57 (27.9)
Infiltrative BCC	58 (46.0)	1 (10)	12 (22.6)	59 (28.9)

[a]Histopathological diagnosis.

Table 3 Dermoscopic features of basal cell carcinomas across different anatomical sites

Features		Anatomical site, *n* (%)				
	Total (*N* = 956)	Head and neck (*n* = 322, 33.7%)	Upper limb (*n* = 22, 2.3%)	Trunk (*n* = 134, 14.0%)	Lower limb (*n* = 478, 50.0%)	*P*-value
Multiple blue–grey dots	361 (37.8)	111 (34.5)	8 (36)	75 (56.0)	167 (34.9)	**< 0.001**
Blue–grey ovoid nests/ globules	299 (31.3)	93 (28.9)	1 (5)	55 (41.0)	150 (31.4)	**0.003**
Leaf-like areas	59 (6.2)	15 (4.7)	2 (9)	15 (11.2)	27 (5.6)	0.05
Concentric/spoke-wheel structures	108 (11.3)	23 (7.1)	5 (23)	29 (21.6)	51 (10.7)	**< 0.001**
Arborizing vessels	334 (34.9)	169 (52.5)	8 (36)	48 (35.8)	109 (22.8)	**< 0.001**
Short fine telangiectasia	488 (51.0)	174 (54.0)	15 (68)	95 (70.9)	205 (42.9)	**< 0.001**
Milky pink background	503 (52.6)	158 (49.1)	14 (64)	77 (57.5)	254 (53.1)	0.26
Shiny-white structures	409 (42.8)	127 (39.4)	8 (36)	38 (28.4)	236 (49.4)	**< 0.001**
Ulceration	286 (29.9)	103 (32.0)	1 (5)	26 (19.4)	156 (32.6)	**0.001**
Multiple small erosions	365 (38.2)	94 (29.2)	13 (59)	48 (35.8)	210 (43.9)	**< 0.001**
Scales/crust	150 (15.7)	55 (17.1)	3 (14)	11 (8.2)	81 (16.9)	0.08
MAY globules	124 (13.0)	66 (20.5)	2 (9)	17 (12.7)	39 (8.2)	**< 0.001**
Purpura-like pattern	252 (26.4)	28 (8.7)	2 (9)	16 (11.9)	206 (43.1)	**< 0.001**
Dotted-glomerular vessels	182 (19.0)	11 (3.4)	4 (18)	20 (14.9)	147 (30.8)	**< 0.001**

MAY, multiple aggregated yellow–white. *P*-values in bold are significant.

(46.0%) on the head and neck. On the upper limbs, nBCC was the most common BCC subtype. On the trunk, the most prevalent BCC subtype was sBCC (41.5%), followed by nBCC (35.8%) and iBCC (22.6%). On the lower limbs, the most frequently observed BCC subtype was sBCC (43.1%) (Table 2).

Moderate agreement was found between the two evaluators for dermoscopic diagnosis of BCC subtypes ($\kappa = 42.8$). For 10 out of 14 dermoscopic criteria, there was moderate to high agreement (κ ranging from 43.5 to 81.0).

Table 3 summarizes the dermoscopic features of BCC across different anatomical sites. On the head and neck, the most frequently observed significant criteria were arborizing vessels (52.5%, $P < 0.001$), short fine telangiectasia (54.0%, $P < 0.001$), shiny-white structures (39.4%, $P < 0.001$), ulceration (32.0%, $P = 0.001$) and multiple blue-grey dots (34.5%, $P < 0.001$). On the trunk, multiple blue-grey dots (56.0%, $P < 0.001$), blue-grey ovoid nests (41.0%, $P = 0.003$) and short fine telangiectasia (70.9%, $P < 0.001$) were commonly found significant features. On the upper limbs, short fine telangiectasia (68%, $P < 0.001$) and multiple small erosions (59%, $P < 0.001$) were frequently observed significant features. On the lower limbs, shiny-white structures (49.4%, $P < 0.001$), multiple small erosions (43.9%, $P < 0.001$), purpura-like patterns (43.1%, $P < 0.001$) and short fine telangiectasia (42.9%, $P < 0.001$) were the most common significant features (Figures 1–3). Interrater agreement for pattern recognition was high (Cohen's kappa = 0.81, $P < 0.001$).

From univariate analysis (Table 4), dermoscopic criteria significantly associated with lower-limb BCC compared with other anatomical sites were shiny-white structures (OR 1.71, 95% CI 1.33–2.23, $P < 0.001$), multiple small erosions (OR 1.64, 95% CI 1.25–2.13, $P < 0.001$), purpura-like patterns (OR 7.13, 95% CI 5.01–10.16, $P < 0.001$) and glomerular vessels (OR 5.63, 95% CI 3.79–8.37, $P < 0.001$). Negative predictors for lower-limb BCC included arborizing vessels (OR 0.33, 95% CI 0.25–0.44, $P < 0.001$), short fine telangiectasia (OR 0.51, 95% CI 0.39–0.66, $P < 0.001$) and multiple

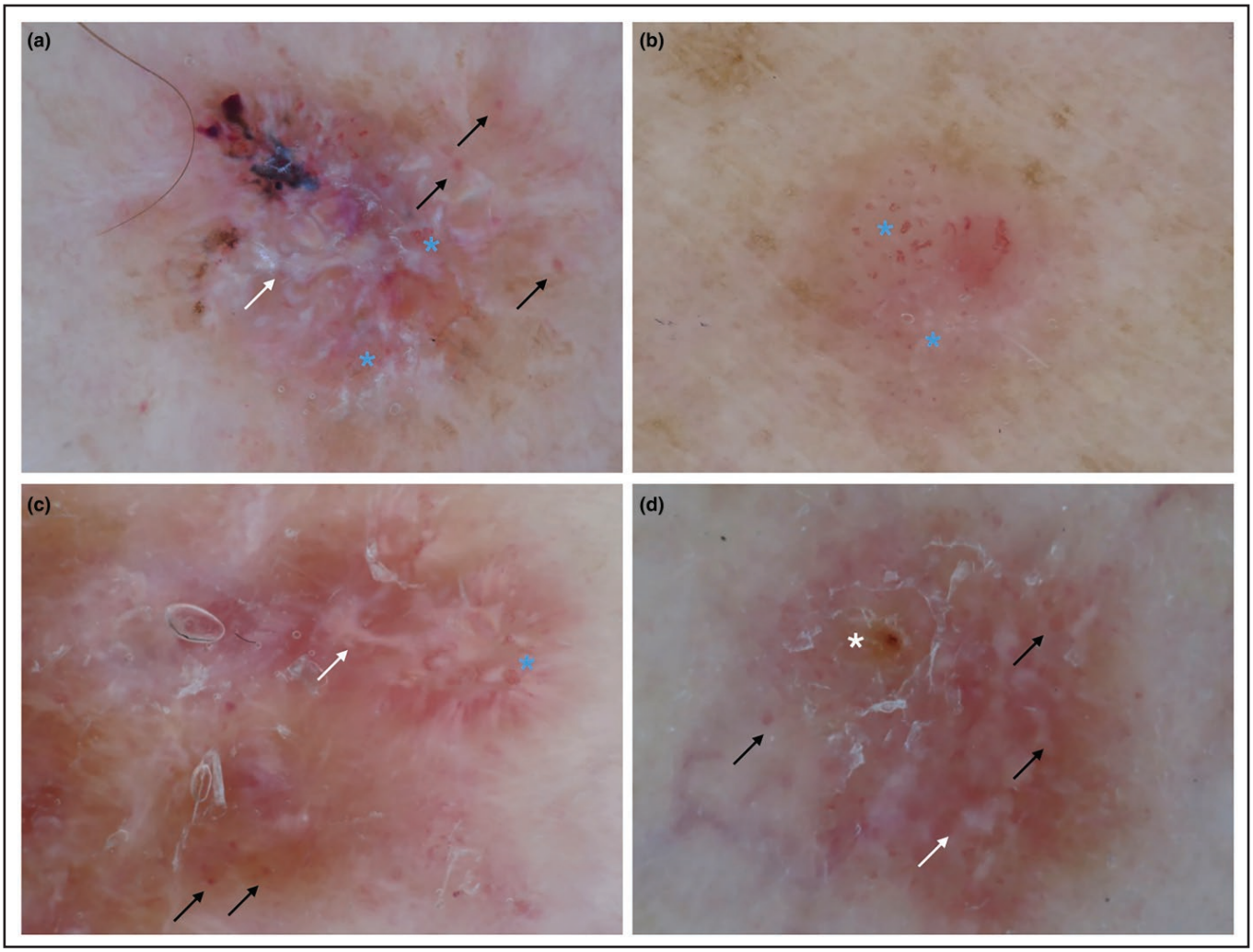

Figure 1 Dermoscopic images of lower-limb basal cell carcinomas (BCCs, × 10 magnification). (a) A dermoscopic image showing out-of-focus purpuric dots–globules at the periphery of the lesion (purpura-like pattern; black arrows), dotted-glomerular vessels (blue asterisks) and shiny-white structures (white arrow). (b) A dermoscopic image showing dotted-glomerular vessels (blue asterisks) with no other specific dermoscopic clues for BCC. (c) A dermoscopic image showing out-of-focus purpuric dots–globules on a coppery red background (purpura-like pattern; black arrows), dotted-glomerular vessels (blue asterisk) and shiny-white structures (white arrow). (d) A dermoscopic image showing out-of-focus purpuric dots–globules on a coppery red background (purpura-like pattern; black arrows), shiny-white structures (white arrow) and superficial erosion (white asterisk).

aggregated yellow–white (MAY) globules (OR 0.41, 95% CI 0.27–0.61, $P<0.001$).

A subanalysis for the purpura-like pattern showed no difference according to patient age at diagnosis. A mean age of 71.2 years (SD 12.4) was observed in patients with no evidence of a purpura-like pattern whereas a mean age of 71.5 years (SD 12.7) was described in patients with a purpura-like pattern under dermoscopy. Moreover, a purpura-like pattern was more frequently observed in sBCC ($n=91/214$, 42.5%) and in iBCC ($n=69/214$, 32.2%, $P<0.001$) (Table S3; see Supporting Information).

In the control group analysis, 239 lesions were included. The interrater agreement was high, with an overall agreement of 98.3% and a Cohen's kappa of 0.80, indicating substantial agreement ($P<0.001$). The expert evaluator identified the purpura-like pattern in 9 of 239 lesions (3.8%). It was reported in the following skin conditions: Kaposi sarcoma ($n=3$), acroangiodermatitis/stasis dermatitis ($n=3$), mycosis fungoides ($n=1$), viral wart ($n=1$) and basosquamous carcinoma ($n=1$).

Discussion

In this study, including 478 BCCs from different anatomical locations, we found a distinct distribution of BCC subtypes across different anatomical regions, confirming previous findings while introducing new insights. In the study, patients with iBCC and nBCC were significantly older than those with sBCC, confirming previous observations.[18] The different age distributions may reflect the cumulative effects of ultraviolet radiation and age-related decline in immune function, contributing to the development of more aggressive BCC subtypes in older patients.

Our data confirmed a peculiar anatomical distribution of different BCC subtypes.[6,7] BCC in chronically sun-exposed

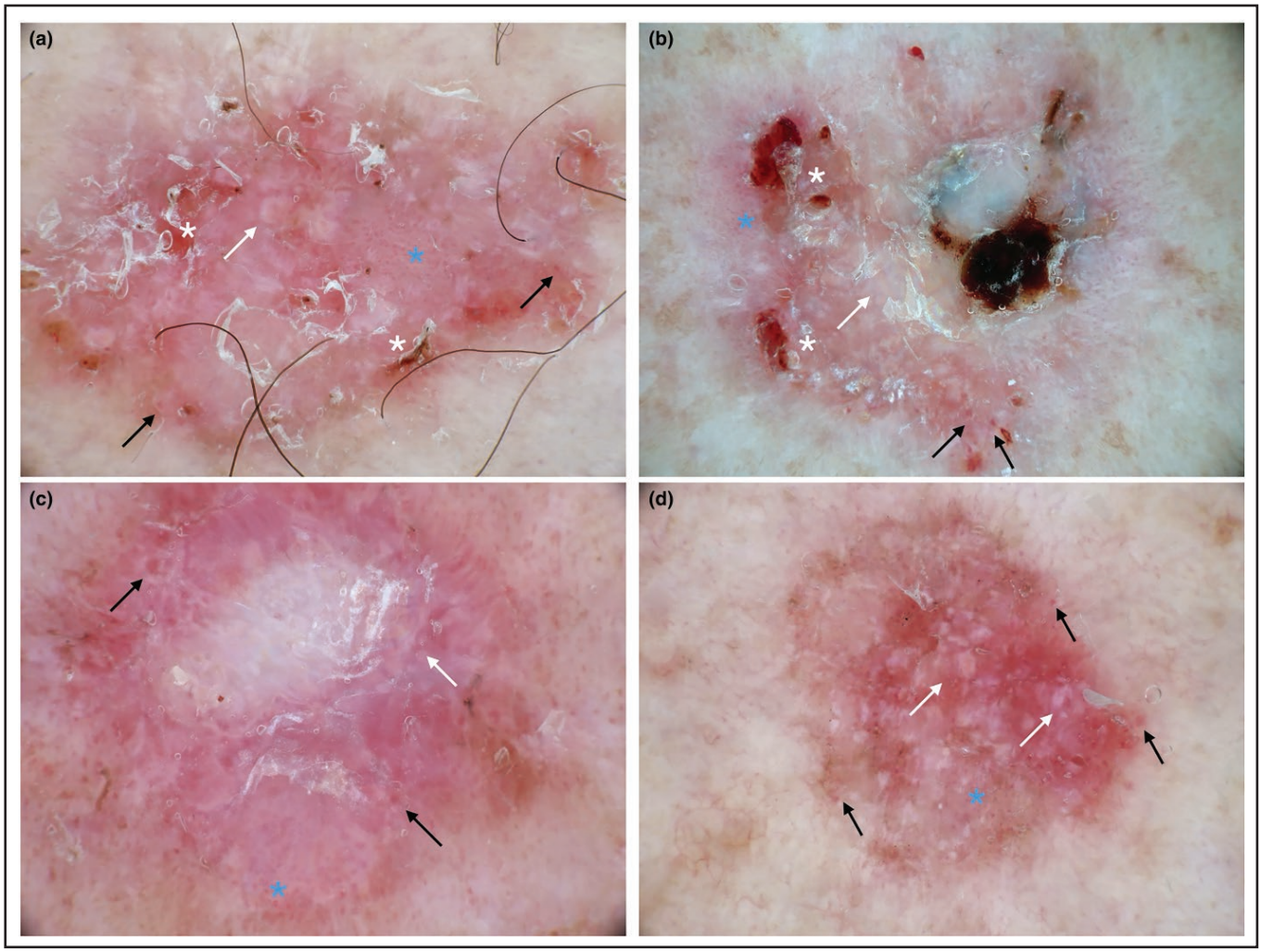

Figure 2 Dermoscopic images of lower-limb basal cell carcinomas (× 10 magnification). (a) A dermoscopic image showing out-of-focus purpuric dots–globules at the periphery of the lesion (purpura-like pattern; black arrows), dotted-glomerular vessels (blue asterisks), superficial erosions (white asterisk) and shiny-white structures (white arrow). (b) A dermoscopic image showing dotted-glomerular vessels (blue asterisks) and shiny-white structures (white arrow), a peripheric purpura-like pattern (black arrows) and superficial erosions (white asterisks). (c) A dermoscopic image showing out-of-focus purpuric dots–globules (purpura-like pattern; black arrows), dotted-glomerular vessels (blue asterisk) and shiny-white structures (white arrow). (d) A dermoscopic image showing out-of-focus purpuric dots–globules on a coppery red background (purpura-like pattern; black arrows), shiny-white structures (white arrow) and dotted-glomerular vessels (blue asterisk).

areas, such as the head and neck, predominantly exhibited nodular and invasive forms, whereas BCC in nonchronically sun-exposed areas, such as the trunk and lower limbs, primarily manifested as sBCC. As suggested by Scrivener *et al.*,[18] BCC histological subtypes may not only be considered as architectural variations but as distinct entities with divergent biological behaviours and aetiological factors, reflecting the different pathways of carcinogenesis in sun-damaged vs. nonsun-damaged skin.

This study corroborated the presence of specific dermoscopic features according to BCC anatomical locations.[7,19] We decided to focus on the lower-limb area given the challenging dermoscopic features encountered in this area. These features typically overlap with other malignant (SCC, melanoma) and benign (lichen planus-like keratosis) neoplasms. The most frequently reported significant dermoscopic features were shiny-white structures, multiple small erosions and purpura-like patterns. Short fine telangiectasia, although often reported at this anatomical site, showed the lowest percentage compared with the other anatomical sites. Of particular interest was the occurrence of the purpura-like pattern, which we described as an additional dermoscopic clue frequently observed in lower-limb BCC, especially associated with the iBCC and sBCC subtypes.

In contrast to dotted-glomerular vessels – where both dotted and glomerular morphologies are generally considered the same vascular entity observed at different magnifications[20] – the purpura-like pattern was characterized by peripheral, out-of-focus dots or globules, often set against a coppery red background. This pattern resembles the dermoscopic findings in pigmented purpuric dermatosis, which histologically demonstrates extravasation of red blood cells and an increase in the number of dilated, swollen blood vessels.[21] The high incidence of this pattern in lower-limb BCC could be attributed to the thinner dermal layer in this region,

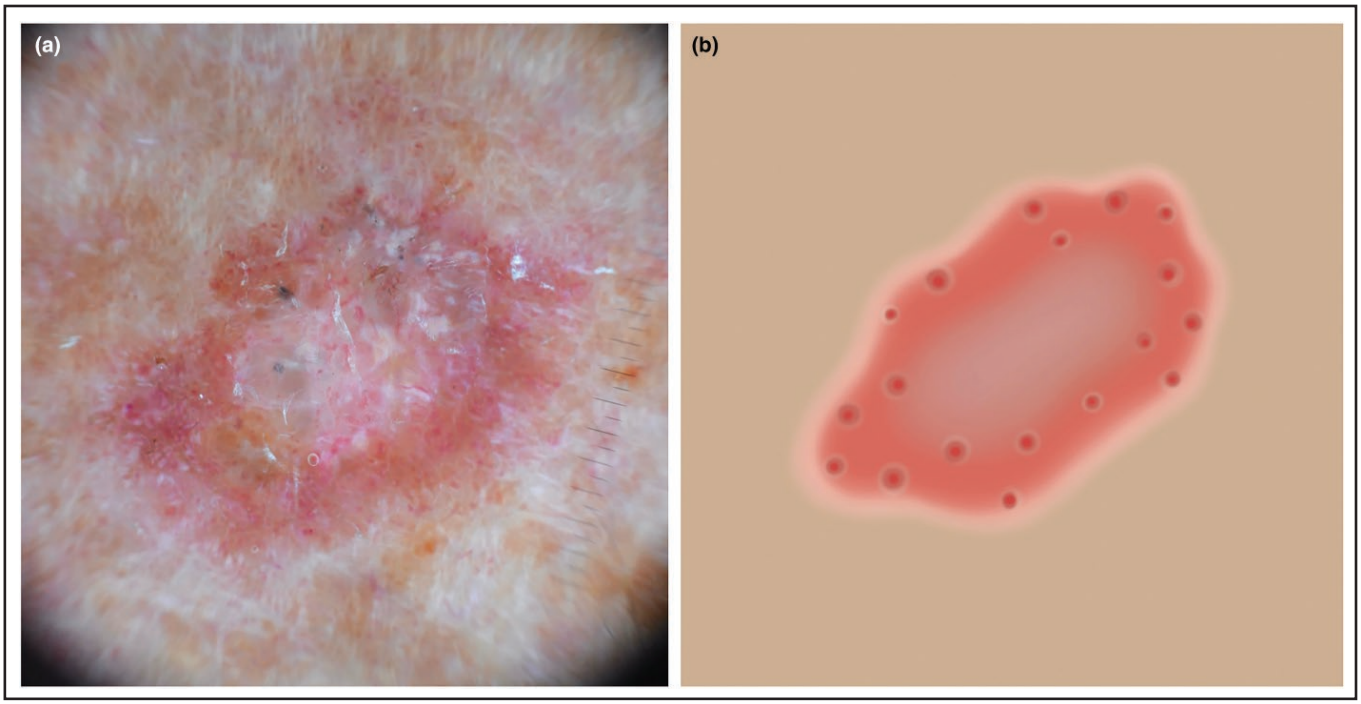

Figure 3 Lower-limb basal cell carcinoma, dermoscopy at×10 magnification. (a) A dermoscopic image showing out-of-focus purpuric dots and globules on a coppery red background at the periphery of the lesion (purpura-like pattern) and (b) a graphical representation of the novel purpura-like pattern.

Table 4 Univariate analysis for dermoscopic features of basal cell carcinoma (lower limb vs. other anatomical sites)

	Lower limbs vs. other anatomical sites	
Features	**OR (95% CI)**	***P*-value**
Multiple blue–grey dots	0.78 (0.60–1.02)	0.08
Blue–grey ovoid nests/globules	1.01 (0.77–1.33)	0.93
Leaf-like areas	0.83 (0.49–1.41)	0.51
Concentric/spoke-wheel structures	0.88 (0.59–1.32)	0.55
Arborizing vessels	0.33 (0.25–0.44)	**< 0.001**
Short fine telangiectasia	0.51 (0.39–0.66)	**< 0.001**
Milky pink background	1.04 (0.81–1.35)	0.72
Shiny-white structures	1.71 (1.33–2.23)	**< 0.001**
Ulceration	1.30 (0.98–1.71)	0.06
Multiple small erosions	1.64 (1.25–2.13)	**< 0.001**
Scales/crust	1.21 (0.85–1.72)	0.28
MAY globules	0.41 (0.27–0.61)	**< 0.001**
Purpura-like pattern	7.13 (5.01–10.16)	**< 0.001**
Dotted-glomerular vessels	5.63 (3.79–8.37)	**< 0.001**

CI, confidence level; MAY, multiple aggregated yellow–white; OR, odds ratio. *P*-values in bold are significant.

which may highlight vascular alterations under dermoscopy. Furthermore, the presence of venous stasis, particularly prominent in the lower limbs, might also contribute to the increased visibility of such vascular features.

In addition, the univariate analysis confirmed shiny-white structures, multiple small erosions, purpura-like patterns and dotted-glomerular vessels as positive predictors for lower-limb BCC. Conversely, arborizing vessels, short fine telangiectasia and MAY globules were identified as negative predictors of lower-limb BCC. In our series, vascular features differed from those classically described at other sites. Dotted-glomerular vessels emerged as a distinctive relevant feature in this anatomical region compared with the other locations. These findings are consistent with previous studies,[11,14] suggesting that vascular patterns in BCC can vary depending on the anatomical site, with lower-limb BCCs frequently showing dotted-glomerular vessels. This dermoscopic observation is even more evident in the study of nonpigmented BCC, which may closely resemble other cutaneous malignancies, such as SCC, that also present with vascular features similar to those seen in BCC. The overlap between BCC and other malignancies may lead to diagnostic pitfalls, especially in lesions where BCC is nonpigmented or exhibits minimal clinical features.[22,23]

In our control group, the presence of out-of-focus purpuric dots and globules typical of the purpuric-like pattern was not an exclusive finding for lower-limb BCC, as it could also be described in skin conditions with prominent vascular and/or petechial components. We described three patients with Kaposi sarcoma and three with acroangiodermatitis/stasis dermatitis showing a petechial component similar to the purpura-like pattern under dermoscopy.[24,25] Further, the pattern was also reported in a single case of mycosis fungoides, a condition where the presence of purpuric dots has been previously demonstrated.[26] Additionally, viral warts under dermoscopy have already been described with thrombosed vessels, possibly appearing as red dots.[27] Finally, the only case of a patient with basosquamous carcinoma in our dataset showed the purpura-like pattern, probably attributable to its basaloid tumour components.

As expected, the purpura-like pattern was not an exclusive finding of BCC and it should not be interpreted as pathognomonic for BCC. Rather, its diagnostic value increases when

observed alongside other BCC-associated dermoscopic criteria, such as shiny-white structures, multiple small erosions and glomerular vessels, as demonstrated in our univariate analysis. Therefore, the purpura-like pattern should be considered an additional clue aiding in the recognition of BCC in the diagnostic approach of equivocal lower-limb lesions.

Although this study provides important insights into the dermoscopic features of BCC and their anatomical distribution, there are some limitations that must be addressed in future research. First, its retrospective and single-centre design may limit the generalizability of the findings. Second, the lack of data on sun exposure, skin type, history of venous insufficiency and environmental factors that may influence both the regional distribution of BCC subtypes and their dermoscopic characteristics. Finally, the relatively small number or absence of certain control lesions in our dataset may have affected the statistical power of some subgroup analyses. Prospective, multicentre studies with larger and more heterogeneous cohorts are warranted to validate the diagnostic utility and reproducibility of the purpura-like pattern.

In conclusion, awareness of the unique dermoscopic features in the diagnosis of lower-limb BCC will aid clinicians in providing optimal care for patients, ensuring early detection and management of this common malignancy. The purpura-like pattern is an additional dermoscopic clue that could significantly enhance the diagnostic precision of dermoscopy for BCC recognition on the lower limbs, particularly when observed alongside other well-established dermoscopic criteria.

Author contributions

Marco Spadafora (Data curation, Formal analysis, Investigation, Methodology, Project administration, Writing—original draft [equal]), Alberto Sticchi (Data curation, Formal analysis [equal]), Cristian Navarrete-Dechent (Validation, Writing—review & editing [equal]), Shaniko Kaleci (Data curation, Formal analysis [equal]), Giovanni Pellacani (Supervision, Writing—review & editing [equal]), and Caterina Longo (Conceptualization, Supervision, Writing—review & editing [equal]).

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Conflicts of interest

The authors declare no conflicts of interest.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Ethics statement

This study was approved by the Institutional Review Board of Azienda Unità Sanitaria Locale – IRCCS di Reggio Emilia, Italy (CE: 875/2020/OSS/IRCCSRE).

Patient consent

The patients gave written informed consent for publication.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website.

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