Original Article

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The significance of blue color in dermatoscopy

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Summary

Background and objectives: Skin lesions with blue color are frequently excised to rule out malignancy. The objective of the present study was to investigate the significance of blue color.

Methods: We retrospectively scanned dermatoscopic images for blue color and classified them according to pattern analysis.

Results: Of 1,123 pigmented skin lesions, 144 (12.8 %) showed blue color, 92 of which (63.9 %) were malignant. Among lesions with blue color, the most common benign diagnoses were nevi (n = 35, 24.3 %) and seborrheic keratoses (n = 8, 5.6 %). Of 103 (71.5 %) lesions with a structureless blue pattern, eight (7.8 %) were entirely blue and 95 (92.2 %) were partly blue, of which 81 (78.6 %) showed peripheral or patchy and 14 (13.6 %) central blue color. Most lesions with peripheral or patchy blue color were melanomas (n = 47, 58 %), whereas most lesions with central blue color were nevi (n = 9, 64.3 %). Of 28 lesions with blue clods, 17 (60.7 %) were basal cell carcinomas. With respect to malignancy, the positive predictive value of blue color was 63.9 % (95 % CI: 56.0–71.8 %).

Conclusions: Among malignant lesions with blue color, structureless peripheral or patchy blue color is a clue for melanoma, while blue clods point to basal cell carcinoma. Pitfalls include seborrheic keratoses, which may show blue color, as well as some nevi, especially combined nevi.

Introduction

The assessment of colors in dermatoscopy is essential [1, 2]. Colors depend on the type of chromophores (melanin, hemoglobin) and the anatomic level of the skin they are located in. Blue color corresponds to melanin or hemoglobin in the reticular dermis or hemoglobin poorly saturated with oxygen. Less frequently, blue color corresponds to melanin within an acanthotic epidermis with overlying compact orthokeratosis [3]. Various diagnostic algorithms for dermatoscopy include blue color as a clue for melanoma [4–7]. Blue color is also an essential part of the 3-point checklist and the "chaos and clues" algorithm [8, 9]. Both algorithms have been designed to detect malignancy in general, not just melanoma. Blue color may also be present in benign lesions including common diagnoses such as blue nevi, dermatofibroma, vascular lesions, and seborrheic keratoses (Table 1). Dermatoscopically, the extent of blue color, its distribution, and the patterns created by blue structures may help diagnose blue lesions with more specificity. The objective of this retrospective study was to identify patterns of blue color and to analyze their significance.

Material and methods

We selected lesions with blue color from a collection of dermatoscopic images consecutively taken at the Department of

Table 1 List of differential diagnoses with blue color on dermatoscopy.

Melanocytic proliferations		Non-melanocytic proliferations		
Benign	**Malignant**	**Benign**	**Malignant**	**Exogenous dermal color**
Nevus: blue, Spitz, combined, congenital, deep penetrating	Primary melanoma or melanoma metastasis	Seborrheic keratosis, dermatofibroma, vascular lesions (hemangioma, angiokeratoma) hemorrhage, spiradenoma, cylindroma, trichilemmal cyst, apocrine hidrocystoma, pilomatricoma	Basal cell carcinoma, Kaposi's sarcoma, angiosarcoma	Exogenous pigment (e. g. tattoos), traumatic penetration of pigmented foreign material

Dermatology of the Medical University of Vienna, between January 2006 and December 2015. All lesions were excised for diagnostic reasons and all images were taken with polarized dermatoscopy. We excluded lesions of the mucosa and nail apparatus. The dermatoscopic images were evaluated in random order in a darkened room. The presence or absence of blue color was established by consensus of two readers who were blinded to the final diagnosis. Classification of selected lesions was carried out separately by the authors according to pattern analysis. We categorized lesions with blue color according to the pattern (structureless or clods), extent, and distribution thereof. A structureless pattern was defined as a coherent area marked by the absence of a dominant basic structural element; clods were defined as any well-circumscribed, solid structure – of any shape – larger than dots [10]. Lesions with structureless blue were further divided into lesions that were entirely blue and those that were partly blue. Partly blue lesions were divided into those with a peripheral blue structureless area and those with a central blue structureless area. According to the aforementioned criteria, all cases were finally classified into five groups (Figure 1).

Statistical analysis

Frequencies were described in absolute and relative numbers. Comparisons of proportions were performed with chi-square or Fisher's exact tests, as appropriate. The positive predictive value was calculated by dividing the true positives (malignancies with blue color) by the sum of the true positives and false positives (benign lesions with blue color). All given P values are 2-tailed and a P value < 0.05 indicates statistical significance.

Results

General data

Of a series of 1,123 excised pigmented lesions, 144 (12.8 %) showed blue color. The latter were obtained from 139 patients (85 men, 61.2 %; and 54 women, 38.8 %), with a mean age of 57 years (range: 10–95 years). Of the 144 lesions, 92 (63.9 %) were malignant, 52 (36.1 %) were benign. With regard to the detection of malignancy, the positive predictive value of blue color was 63.9 % (95 % confidence interval [CI]: 56.0–71.8 %). The distribution of histopathological diagnoses is shown in Table 2. A structureless blue pattern was found in 103 lesions (71.5 %) and a pattern of blue clods in 28 samples (19.5 %). A combination of structureless blue and blue clods was present in 13 lesions (9.0 %) (Table 3). Of the 103 lesions with a structureless pattern, eight (7.8 %) showed blue color of the entire lesion; 14 (9.7 %), central blue color; and 81 (78.6 %), peripheral or patchy blue color.

Significance of patterns

Structureless blue color: The distribution of malignant diagnoses varied among patterns. For structureless blue

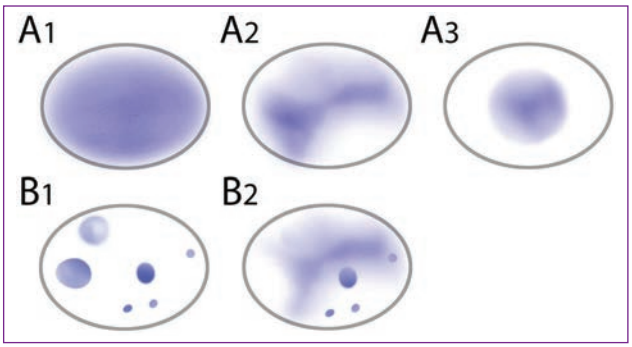

Figure 1 Classification of lesions according to pattern, distribution, and extent of blue color. *First row:* structureless blue color. Structureless blue covering the entire lesion (A1); structureless blue with peripheral or patchy blue color (A2); structureless blue with central blue color (A3). *Second row:* clods. Blue clods (B1); combination of clods and structureless areas (B2).

Table 2 Distribution of blue lesions according to histopathological diagnoses.

Diagnosis	N = 144	%
Primary Melanoma	57	39.6
Nevus	35	24.3
Basal cell carcinoma	31	21.5
Seborrheic keratosis/solar lentigo	8	5.6
Vascular benign lesion	5	3.5
Melanoma metastasis	3	2.1
Cylindroma	1	0.7
Pilomatricoma	1	0.7
Trichoepithelioma	1	0.7
Viral acanthoma	1	0.7
Kaposi's sarcoma	1	0.7

lesions, we found the highest frequency of malignant diagnoses in the subgroup of peripheral and patchy blue structureless color (n = 81). In this group, 72.8 % (n = 59) of cases were malignant (47 melanomas, 11 basal cell carcinomas (BCCs), and one Kaposi's sarcoma). Of the 14 lesions with central blue structureless color, four (28.6 %) were malignant. Most benign lesions in this group were nevi (n = 9, 64.3 %). Eight lesions were entirely structureless and blue, with three of them (37.5 %) being malignant. Compared to the two other subgroups of structureless lesions, the odds ratio for malignancy of peripheral and patchy blue color was 4.9 (95 % CI: 1.5–16.6, p = 0.01); the odds ratio for melanoma (including metastases) was 4.1 (95 % CI: 1.5–10.9, p = 0.005).

Blue clods: A pattern of blue clods was found in 28 of the 144 lesions (19.5 %), 18 (64.3 %) of which were malignant. Seventeen of the 18 malignant neoplasms with this pattern were BCCs. When blue clods were present, the positive predictive value for BCC was 60.1 % (95 % CI: 40.6–78.5 %). Benign lesions with blue clods included nevi (n = 4, 14.3 %), seborrheic keratoses (n = 2, 7.14 %), as well as one angioma (3.57 %).

Combination of patterns: A combination of blue clods and blue structureless areas was found in 13 (9.0 %) lesions with blue color; here, eight (61.5 %) tumors were malignant and five (38.5 %) benign. Most malignant lesions in this group were melanomas (n = 6, 46.2 %), with the remaining two being BCCs (15.4 %).

Benign lesions with blue structures

Of the 52 benign lesions with blue structures, 35 (67.3 %) were nevi, including 11 combined nevi, 11 congenital nevi, five blue nevi, three Clark nevi, two acral nevi, two Spitz nevi, and one Reed nevus. Most combined nevi presented with central structureless blue color (n = 5). The other combined nevi showed either a peripheral structureless (n = 3) or one of the other patterns (n = 3). In the eight seborrheic keratoses with blue structures, structureless blue was the most common pattern (n = 5). There was also one seborrheic keratosis exhibiting a combination of structureless areas and clods, as well as two seborrheic keratoses with blue clods; one of the latter was histopathologically diagnosed as clonal seborrheic keratosis. Four of the eight seborrheic keratoses had no specific dermatoscopic clues such as "milia-like cysts"

Table 3 Distribution of blue color according to basic pattern.

	Structureless blue color: entire lesion (n = 8)	Structureless blue color: central (n = 14)	Structureless blue color: peripheral or patchy (n = 81)	Pattern of clods (n = 28)	Combination of structureless areas and clods (n = 13)
All malignancies (n = 92)	3 (37.5 %)	4 (28.6 %)	59 (72.8 %)	18 (64.3 %)	8 (61.5 %)
Melanoma or melanoma metastasis (n = 60)	2 (25 %)	4 (28.6 %)	47 (58 %)	1 (3.6 %)	6 (46.2 %)
Basal cell carcinoma (n = 31)	1 (12.5 %)		11 (13.6 %)	17 (60.7 %)	2 (15.4 %)
Kaposi's sarcoma (n = 1)			1 (1.24 %)		
All benign lesions (n = 52)	5 (62.5 %)	10 (71.4 %)	22 (27.2 %)	10 (35.7 %)	5 (38.5 %)
Nevus (n = 35)	5 (62.5 %)	9 (64.3 %)	14 (17.3 %)	4 (14.3 %)	3 (23.1 %)
Seborrheic keratosis/solar lentigo (n = 8)		1 (7.2 %)	4 (4.9 %)	2 (7.14 %)	1 (7.7 %)
Vascular lesion (n = 5)			3 (3.7 %)	1 (3.57 %)	1 (7.7 %)
Other (n = 4)			1 (1.23 %)	3 (10.7 %)	

or "comedo-like openings". All five vascular lesions that showed blue structures provided the additional clue of red clods (lacunes).

Discussion

Blue color on dermatoscopy is considered a clue for malignancy (Figure 2), and represents a crucial factor in the decision to excise a given lesion [10]. Blue color is part of many short algorithms, including the 7-point checklist, the 3-point checklist, and the "chaos and clues" algorithm [4–9]. In melanoma, blue color is frequently present in the form of a blue structureless zone classically referred to as "blue whitish veil" in dermatoscopic terminology [11]. In basal cell carcinoma, blue clods (blue ovoid nests) are the most common presentation of blue color [12, 13]. Blue color, however, may also be found in benign lesions. In our study, 36.1 % of lesions with blue color were benign (Figure 3). Not surprisingly, the most common nevi with blue color were combined nevi and congenital nevi. While blue nevi usually do not pose a major diagnostic problem, combined nevi may present a challenge. In our series, most combined nevi exhibited a central structureless blue color. On the other hand, the blue structureless color of melanomas was commonly distributed in a peripheral or patchy fashion. Seborrheic keratoses may also show areas that appear blue and structureless. Previously also observed by Braun et al. [14], the latter finding contradicts the doctrine that melanin appearing blue on dermatoscopy has to be located in the reticular dermis. Usually, there is no pigment in the reticular dermis in seborrheic keratoses. If, however, acanthosis is prominent and the color of the basal epidermal layers is dense, melanin may appear blue on dermatoscopy, even if it is located in the epidermis and not in the dermis.

We confirmed that blue clods (blue ovoid nests) are a clue for BCC [12, 13]. Angiomas or angiokeratomas may sometimes have blue clods. Usually, this is not a diagnostic dilemma because there are other clues available to differentiate an angioma from BCC. If other clues are missing, it may be useful to remember that the blue clods in angiokeratoma are pigmented by hemoglobin and the blue clods in BCC are pigmented by melanin. As also observed in the present study, the blue clods in angioma and angiokeratoma lesions are usually admixed with red clods (lacunes). In BCC on the other hand, the blue clods are combined with brown structures, usually clods as well. We also confirmed that blue nevi and melanoma metastases may be indistinguishable [15, 16]. Both may show a blue structureless pattern without any other clues. In such cases, information beyond dermatoscopy, such as a history of melanoma as well as the sudden onset and growth may point in the right direction. Argenziano et al. demonstrated that pigmented nodular melanomas can be distinguished from nevi by the blue-black rule [17]. Given that our sample collection only contained five genuine nodular melanomas, we can neither confirm nor refute this observation.

In summary, we confirmed that blue structures are a clue for malignancy. The positive predictive value for any type of malignancy was 63.9 %. In other words, nearly two-thirds of lesions with blue structures will turn out to be malignant.

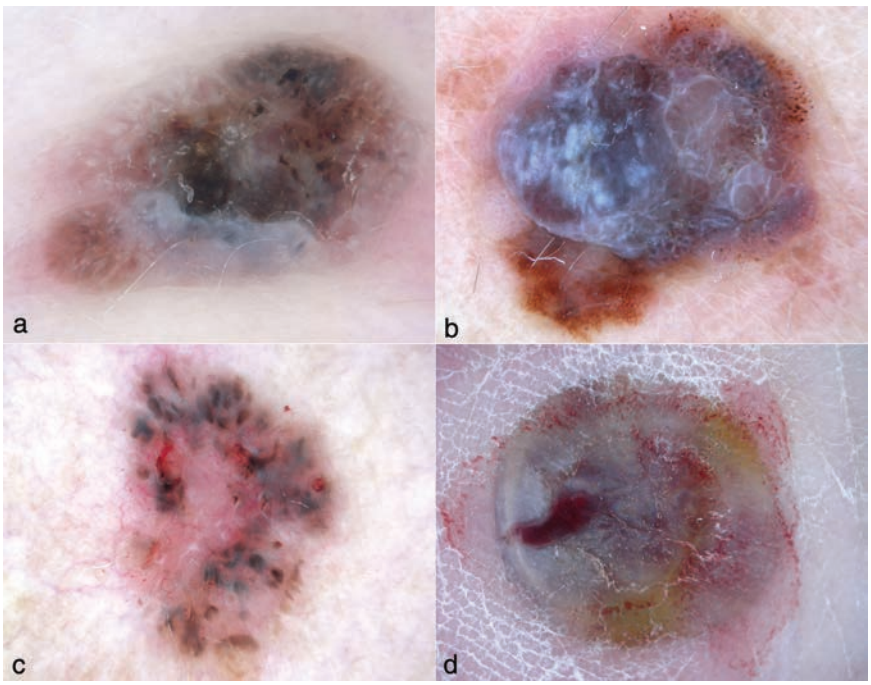

Figure 2 Malignant lesions with blue color. Melanoma with peripheral blue structureless color (blue veil) (a); melanoma with Peripheral blue structureless color (blue veil) (b); BCC with blue clods (c); Kaposi's sarcoma with peripheral blue structureless color (d).

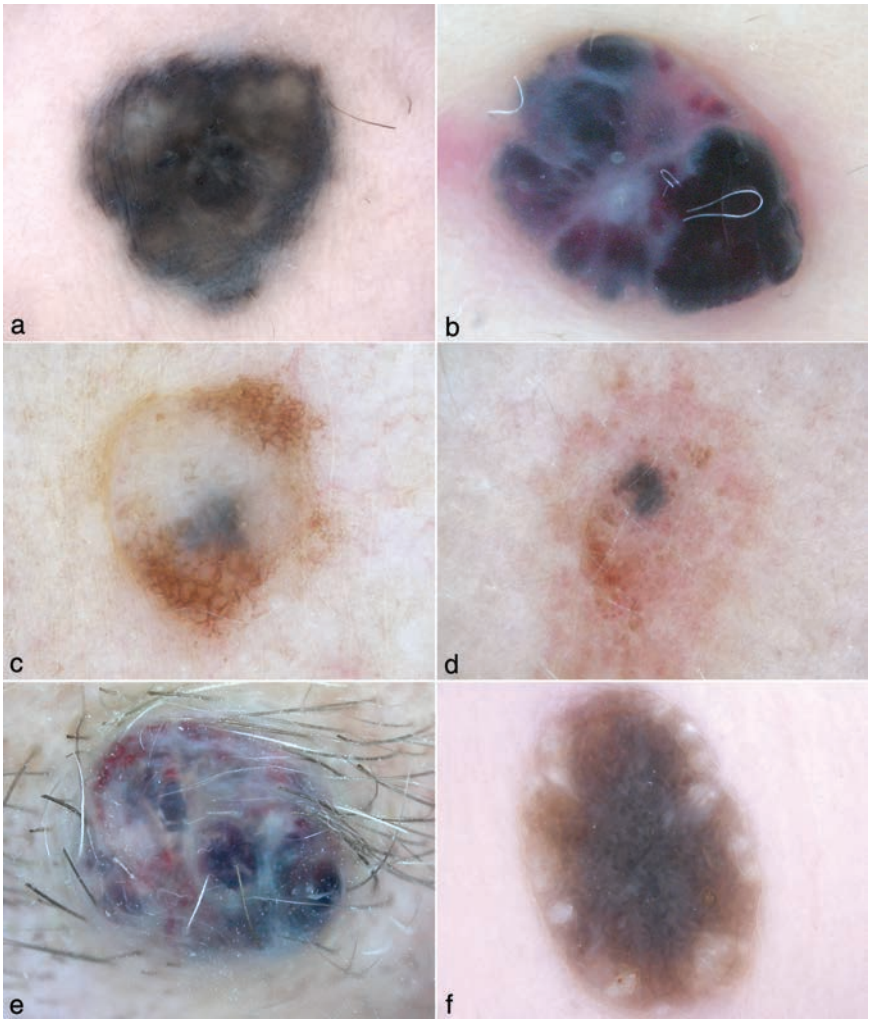

Figure 3 Benign lesions with blue color. Blue nevus with structureless blue color of the entire lesion (a); angioma with blue clods (b); combined nevi with central blue structureless color (c, d); pilomatricoma with blue clods (e); seborrheic keratosis with central blue structureless color (e).

We also showed that the kind of pattern of blue color bears diagnostic significance, with some patterns more likely to indicate a malignant diagnosis than others. A major limitation of our study is its retrospective design. All included lesions had been scheduled for excision, creating a bias that leads to overestimation of the positive predictive value because unequivocally benign blue lesions (for example, some blue nevi) were not included in this sample.

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