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ORIGINAL ARTICLE

Dermoscopy of cutaneous melanoma metastases: A color-based pattern classification

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ABSTRACT

Dermoscopic studies about cutaneous metastases of malignant melanoma (CMMM) are few. Our objective was to analyze the dermoscopic features of CMMM and propose a new dermoscopic pattern classification based on color pigmentation and some specific dermoscopic features. A retrospective evaluation of 150 dermoscopic images of CMMM taken from 40 patients was performed. One hundred CMMM images were individually evaluated by six dermatologists in order to classify them according to four dermoscopic patterns: (i) blue pattern; (ii) pink pattern; (iii) brown pattern; and (iv) mixed pattern. One hundred and fifty dermoscopic images including 50 CMMM and 100 benign lesions were evaluated by five dermatologists to calculate the accuracy of these patterns in the recognition of CMMM. An intra- and interobserver reproducibility agreement study between all different dermoscopic pattern classifications was performed. Seventy-five percent of our cases of CMMM showed a monochromatic pattern. Light brown pigmented halo, peripheral gray spots and polymorphic atypical vessels were the most significant focal dermoscopic structures. The reproducibility of the color-based dermoscopic pattern classification was superior to previous dermoscopic pattern classification. In summary, a dermoscopic pattern classification based on color pigmentation and some specific dermoscopic features may be useful in recognizing early cutaneous melanoma metastasis. Multicentric studies are recommended in order to lower the impact of interobserver variability.

Key words: **cutaneous metastases of malignant melanoma, dermoscopy, interobserver agreement, melanoma, skin melanoma metastases.**

INTRODUCTION

Cutaneous metastases of malignant melanoma (CMMM) are relatively frequent in patients with melanoma, with a reported incidence ranging 2–20%.[1,2] CMMM can show a wide clinical and dermoscopic diversity[3] and may be the first clinical manifestation of disseminated melanoma in 2–8% of patients.[4] CMMM may also mimic benign lesions, so their identification is critical to patients' prognosis.

Dermoscopy is a non-invasive diagnostic technique that has proven to be a useful tool in the differential diagnosis of skin tumors.[5] However, the most limiting factor in dermoscopy is its interobserver variability.[6] To date, only a few studies of dermoscopic characteristics of CMMM have been reported.[7–10]

First, Bono *et al*.[8] described four dermoscopic global patterns of CMMM: (i) homogenous; (ii) amelanotic; (iii) saccular and multicomponent; or (iv) polymorphic. Years later, Costa *et al*.[9] proposed five new dermoscopic patterns of CMMM: (i) blue nevus-like; (ii) angioma-like; (iii) nevus-like; (iv) vascular; and (v) unspecific. No studies have compared these two different dermoscopic pattern classifications of CMMM so far.

In our experience, most CMMM show a monochromatic appearance, so we propose a new dermoscopic classification criteria based on color pigmentation and some specific dermoscopic features. The aim of this study was to describe dermoscopic structures of CMMM, analyze the reproducibility of this color-based dermoscopic classification and to compare its reproducibility with dermoscopic patterns of CMMM that had been previously published.

METHODS

A retrospective evaluation of 150 dermoscopic images of CMMM taken from 40 different patients who had attended our department between June 2007 and June 2016 was

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performed. This study was approved by the ethics review committee of our hospital.

Dermoscopic images of each lesion were obtained using a digital microscopy system (DermLite Foto© [3Gen, Dana Point, CA, USA] and Olympus E450© [Olympus, Tokyo, Japan]). Clinical data was obtained for each patient, including age at primary melanoma diagnosis, sex, anatomical location of the primary cutaneous malignant melanoma, histological type, Breslow tumor thickness, presence of ulceration, and average time delay between melanoma diagnosis and cutaneous metastases. All CMMM included in the study were confirmed by histopathology.

In the first part of the study, a list of the dermoscopic criteria established by all previous publications was evaluated in all 150 images of CMMM by one of the contributing investigators experienced in dermoscopy (J. A.). The following dermoscopic features were analyzed: main color pigmentation (blue, pink-red, brown and two or more colors), focal dermoscopic structures and vascular structures as described by Jaimes *et al*.[10]

A new dermoscopic classification of CMMM based on main color pigmentation and some specific dermoscopic features including four dermoscopic patterns (blue, pink, brown and mixed pattern) is defined in Table 1 (Fig. 1).

In the second part of the study, the 150 dermoscopic images of CMMM were divided into two groups following a chronological diagnostic criteria: the first 100 images were selected for an inter- and intraobserver reproducibility study and the latest 50 images for a case–control study. The first set were individually evaluated by six investigators (J. A., C. C., E. R., A. S., A. M., L. N.) in order to classify these images according to the two previous dermoscopic CMMM pattern classifications[8,9] and the color-based criteria proposed in this study. Interobserver reproducibility of these patterns was assessed with Fleiss kappa statistics with a 95% confidence interval.

Intraobserver reproducibility of all dermoscopic pattern criteria performed individually by two dermatologists (J. A. = κ1, E. R. = κ2) was assessed with Cohen's kappa statistics. Mean Kappa agreement between these two intraobserver analyses was calculated (κ1 + κ2/2).

Table 1. Definitions of dermoscopic patterns of cutaneous metastases of malignant melanoma based on main color pigmentation and specific dermoscopic features

Blue pattern	Homogeneous diffuse monochromatic blue, blue-black or blue-gray pigmentation without any other dermoscopic structures
Pink pattern	Homogeneous diffuse monochromatic pink or reddish pigmentation with irregular/polymorphous vessels in asymmetrical arrangement and/or false red lacunae
Brown pattern	Homogeneous diffuse monochromatic brown pigmentation with brown dot/globules in asymmetrical arrangement.
Mixed pattern	Pigmented areas with two or more different colors and any dermoscopic structures, especially peripheral gray spots and/or crystalline structures

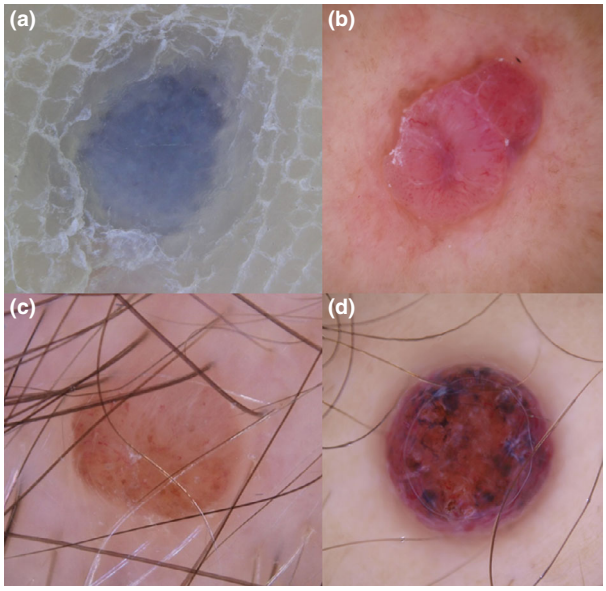

Figure 1. Color pattern classification of cutaneous metastases of malignant melanoma based on main color pigmentation and specific dermoscopic features: (a) blue pattern, (b) pink-red pattern, (c) brown pattern and (d) mixed pattern.

Table 2. Frequencies of the predominant dermoscopic structures in cutaneous metastases of malignant melanoma

Dermoscopic features	*n* = 150 (%)
Main color pigmentation	
Blue	34 (22)
Pink-red	42 (28)
Brown	37 (25)
Two or more colors	37 (25)
Focal dermoscopic structures	
Light brown halo	53 (35)
Peripheral gray spots	51 (34)
Crystalline structures	48 (32)
Brown/black dots or globules	37 (25)
Perilesional erythema	15 (10)
Microhemorrhages	15 (10)
Lacunae-like areas	13 (9)
Streaks	6 (4)
Vascular structures	
Lineal irregular	40 (27)
Glomerular	18 (12)
Dotted	15 (10)
Serpentine	9 (6)
Milky red areas	7 (5)
Hairpin	6 (4)
Corkscrew	3 (2)
Arborizing	3 (2)
Two or more vascular patterns	50 (33)

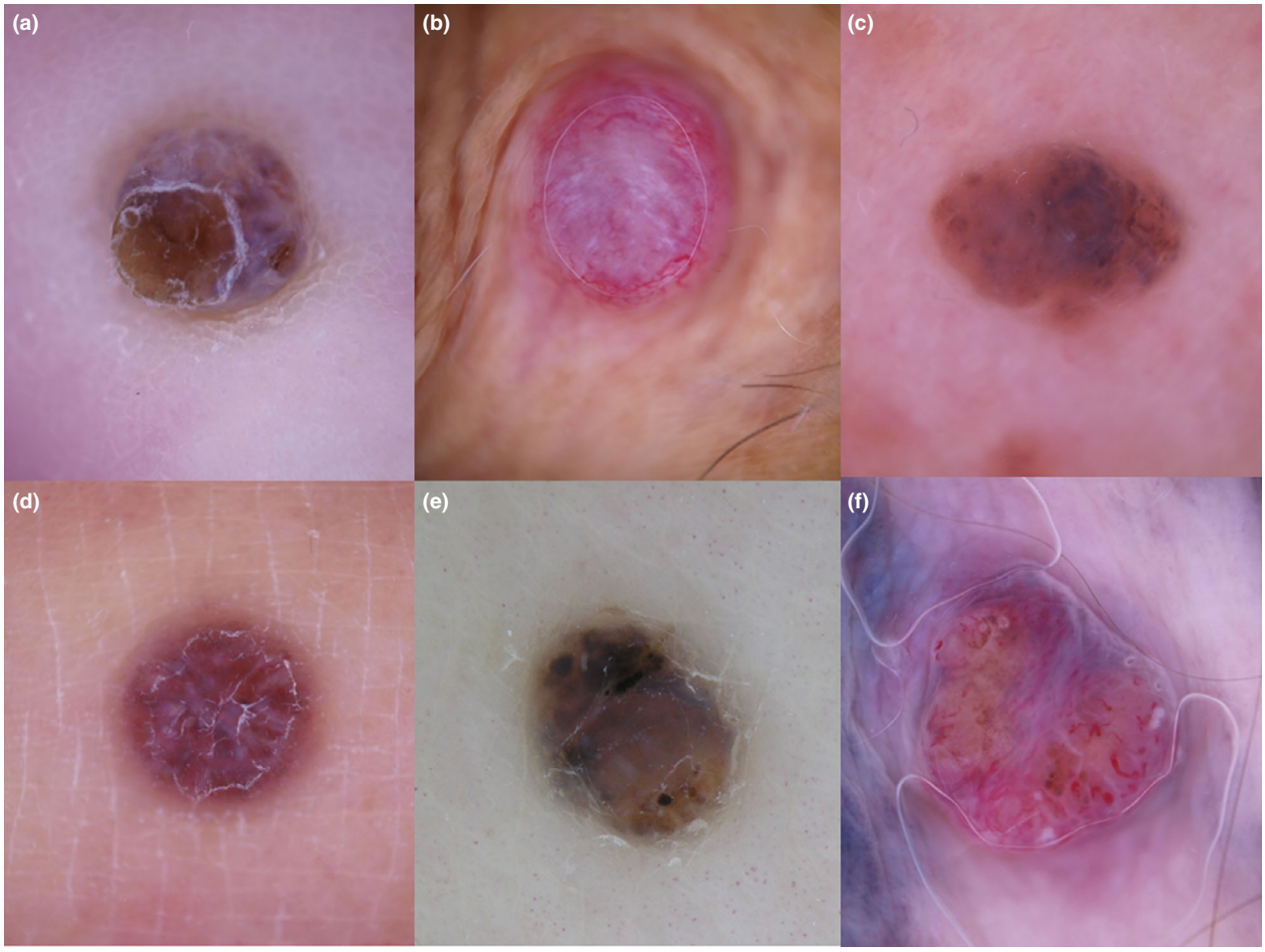

Figure 2. Focal dermoscopic structures commonly observed in cutaneous metastases of malignant melanomas: (a) light brown halo, (b) crystalline structures, (c) brown globules, (d) peripheral erythema, (e) peripheral gray spots and (f) pseudo-lacunae.

Finally, a case–control set of 150 dermoscopic images including 50 CMMM and 100 benign lesions was individually evaluated by three investigators (C. C., E. R., L. N.) in order to identify which images were CMMM or not. The three investigators had no additional clinical information about these images. For the case–control study, two different investigators (J. A., A. S.) selected 100 dermoscopic images from benign lesions from patients with melanoma who had attended our department during the same period (from June 2007 to June 2016). Criteria to select them were: (i) lesions with a combination of monochromatic pigmentations (blue, pink, brown) and any dermoscopic structures similar to the proposed color-based dermoscopic patterns showed in Table 1; and (ii) lesions with an unspecific dermatoscopic pattern so that CMMM should be ruled out. All of these benign lesions were histologically confirmed. We included 20 hemangiomas, 20 blue nevi, 20 melanocytic nevi, 20 seborrheic keratoses and 20 pink lesions with a vascular pattern such as psoriasis, lichen planus, adnexal benign tumors, molluscum contagiosum, Spitz nevi and sarcoidosis. Fifty CMMM cases were located on the head (n = 11, 22%), trunk (n = 10, 20%), upper limbs (n = 4, 8%) and lower limbs (n = 25, 50%) and their largest diameter's mean size was 4.14 mm. One hundred control cases were located on the head (12%), trunk (28%), upper limb (12%) and lower limb (48%) and their largest diameter's mean size was 4.33 mm.

Sensitivity, specificity, predictive positivity value (PPV) and predictive negativity value (PNV) were determined to analyze the significance of CMMM color-based dermoscopic patterns. Statistical analysis was performed with SPSS version 22.0 (Chicago, IL, USA). Regarding the interpretation of statistics, a value of 1.00 indicated perfect agreement, values of more than 0.80 were considered excellent, 0.61–0.80 were good, 0.40–0.60 were fair and values of less than 0.40 were poor.

RESULTS

Description of clinical and histological characteristics of patients

The images were obtained from 40 patients, 21 (52%) men and 19 (48%) women, ranging 45–90 years of age (median,

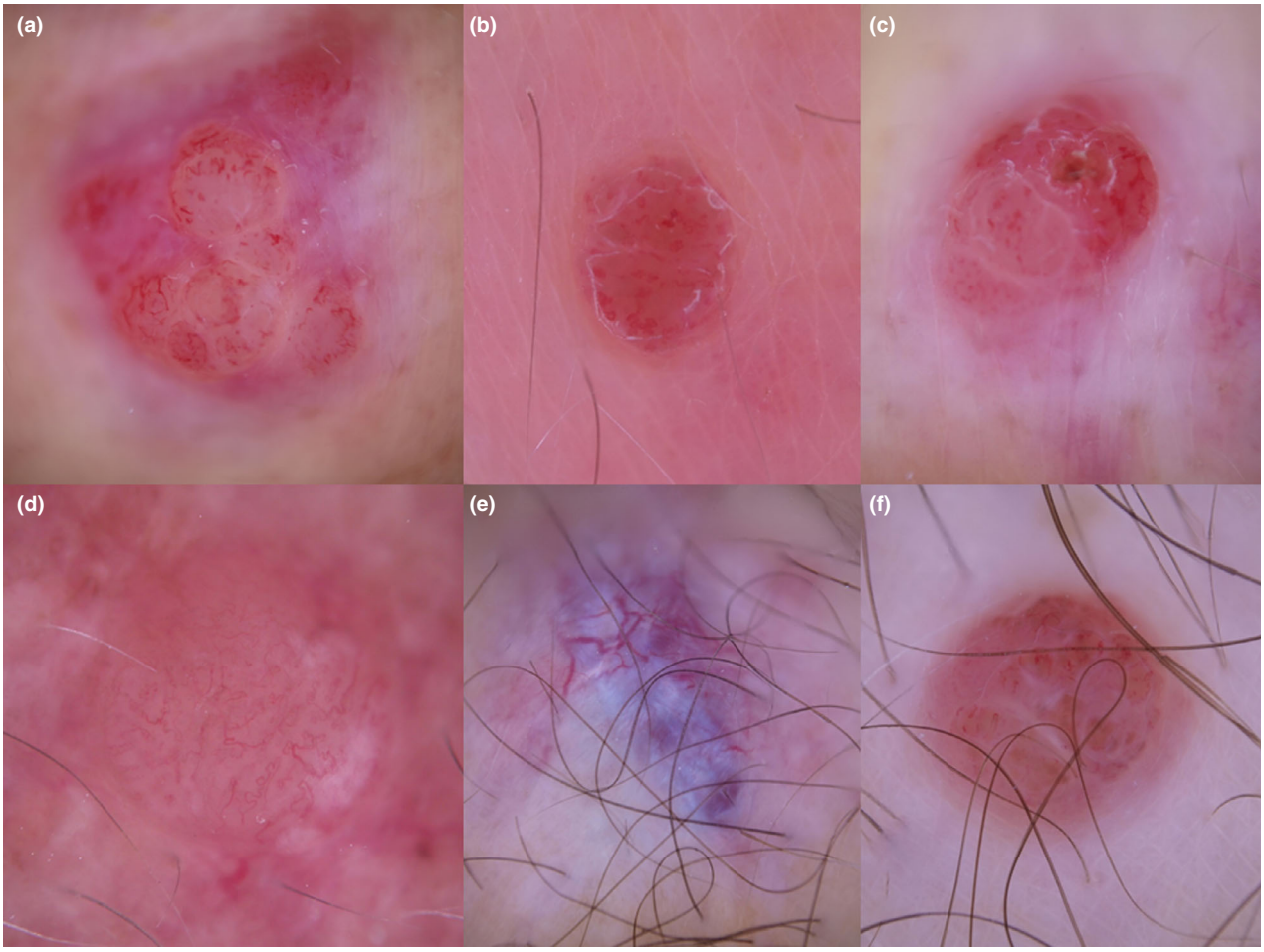

Figure 3. Vascular structures identified in our case series of cutaneous metastases of malignant melanomas: (a) linear irregular vessels, (b) glomerular vessels, (c) dotted vessels, (d) serpentine vessels, (e) arborizing vessels and (f) hairpin vessels.

62.6) at diagnosis of the primary melanoma. The location of primary melanoma was more common in the lower limbs (15 patients, 37.5%), followed by the sole (10 patients, 25%), scalp (six, 15%), trunk (five, 12.5%), face (two, 5%) and upper limbs (two, 5%). Histological type of primary melanoma was superficial spreading melanoma (n = 20, 50%), acral lentiginous melanomas (n = 10, 25%), nodular melanomas (n = 5, 12.5%), lentigo maligna melanomas (n = 3, 7.5%) and animal-type melanomas (n = 2, 5%).

The mean Breslow thickness of primary melanomas was 3.7 mm, ranging 1.3–15 mm. Half of them were ulcerated. No patient had nodal metastases at the time of melanoma diagnosis. On average, the time delay between primary melanoma diagnosis and CMMM onset was 24 months (ranging from 2 months to 13 years).

The skin metastases were classified as follows: 42 lesions of satellitosis (28%), 98 cases of in-transit disease (65%) and only 10 distant cutaneous metastases (7%).

Dermoscopic patterns of cutaneous metastases of malignant melanoma

Dermoscopic structures in CMMM from our study are presented in Table 2. Thirty-seven (25%) lesions had two or more colors. The most frequent focal dermoscopic structures (Fig. 2) were light brown halo (n = 53, 35%), peripheral gray spots (n = 51, 34%), crystalline structures (n = 48, 32%) and brown/black dots or globules (n = 37, 25%). The most frequent vascular structures (Fig. 3) were linear irregular vessels (n = 40, 27%), glomerular vessels (n = 18, 12%) and dotted vessels (n = 15, 10%); however, 33% of CMMM had vessels with two or more different morphologies.

Interobserver and intraobserver agreement of all dermoscopic patterns described in CMMM are shown in Table 3. Overall, the Fleiss kappa coefficient agreement was higher in the color-based dermoscopic classification, with an excellent agreement ($\kappa > 0.80$) in blue pattern and pink patterns. Average intraobserver agreement was higher in color-based

Table 3. Inter- and intraobserver agreement between dermoscopic patterns described in cutaneous metastases of malignant melanoma

Dermoscopic CMMM patterns	Interobserver agreement (κ [CI 95%])	Intraobserver agreement (κ)
Classic patterns (Bono *et al.*)[8]		
Homogenous	0.47 (0.43–0.53)	0.71
Amelanotic	0.78 (0.73–0.83)	0.76
Saccular	0.20 (0.15–0.25)	0.50
Polymorphic	0.28 (0.23–0.34)	0.49
Tumor-like pattern (Costa *et al.*)[9]		
Blue nevus-like	0.61 (0.55–0.67)	0.74
Nevus-like	0.52 (0.47–0.58)	0.66
Angioma-like	0.19 (0.15–0.25)	0.18
Vascular	0.80 (0.75–0.85)	0.76
Unspecific	0.29 (0.24–0.34)	0.41
Color-based pattern (current study)		
Blue pattern	0.81 (0.73–0.89)	86.5
Pink pattern	0.86 (078–0.94)	91.4
Brown pattern	0.60 (0.52–0.68)	81.7
Mixed pattern	0.43 (0.35–0.50)	78.8

CI, confidence interval; CMMM, cutaneous metastases of malignant melanoma.

dermoscopic patterns, with an excellent agreement ($\kappa > 0.80$) in blue, pink and brown patterns.

Regarding the accuracy of CMMM color-based dermoscopic patterns, overall sensitivity was 80.8% and overall specificity was 81% for the diagnosis of CMMM. Overall PPV was 68.4% and PNV was 89.5%.

DISCUSSION

Bono *et al.*[8] first described the dermoscopic features of CMMM. In their study, these authors highlighted light brown pigmented halo, peripheral gray spots and polymorphic atypical vessels as the most significant focal dermoscopic features suggestive of CMMM. Our results confirm the importance of these focal structures in the recognition of CMMM, and thus they were included in our dermoscopic patterns as additional clues to identify them. Perilesional erythema was observed in 12.3% of CMMM, but its specificity was high both in melanomas and blue nevi.[8] This fact could explain that in our case–control study we had many difficulties in distinguishing CMMM with blue pattern from blue nevi. Di Cesare *et al.*[11] described that 54.7% of blue nevi had a dichromatic combination of blue with other colors and 50.5% showed local dermatoscopic structures including whitish scar-like depigmentation, dots/globules, vascular pattern, streaks and network-like pattern. In our experience, CMMM with blue pattern were usually more homogeneous than blue nevi and they usually lacked any other dermoscopic focal structures. However, we must not forget that dermoscopy is a useful tool but can never replace clinical or histological information. Information such as personal melanoma background or change in size seems to be essential to help us differentiate between them.

While CMMM can present any vascular morphology in dermoscopy, certain subtypes such as irregular, glomerular and dotted vessels have been reported as the most frequent.[10,12] This particular finding was also observed in our cases. These vascular structures belong almost exclusively to forms of CMMM with pink pattern.

Costa *et al.*[9] described six dermoscopic patterns for CMMM based on tumor-like dermoscopic patterns with a good correlation among researchers. They obtained a sensitivity of 67.9% and specificity of 79.9%. In our study, we obtained a higher reproducibility and a superior intra- and interobserver agreement. We also think that these color-based dermoscopic patterns allow to identify CMMM more easily than with previous classifications, especially among less experienced dermatologists.

A marked variability in interobserver agreement concerning dermoscopic analysis has already been reported.[6] Other studies have focused on the diagnostic concordance using teledermoscopy, and their interobserver agreement ranged from poor to moderate as well.[13] The differences in dermoscopic experience between authors might have caused these findings, as agreement was poor especially among less experienced dermatologists.[14]

A few studies concerning intraobserver agreement in the identification of dermoscopic features have been reported with good reproducibility and satisfactory intra- and interobserver agreement.[15,16] However, many of these studies included analyses performed by only one investigator. In our study, intraobserver agreement was calculated from two different investigators, with an excellent correlation between them in almost all dermoscopic color-based patterns.

Limitations

In the first part of this study, only the most experienced investigator (J. A) examined the presence of the dermoscopic structures in order to avoid any other investigator having previous sight of the CMMM images. Also, our study was performed with patients from a single institution.

Conclusion

Dermoscopy may be useful in recognizing early cutaneous melanoma metastasis, facilitating an early excision and histopathological confirmation. We found a higher inter- and intraobserver agreement in dermoscopic color-based patterns compared with previous dermoscopic CMMM patterns. Multicentric studies performed on large populations are recommended to define more clearly the dermoscopic patterns of cutaneous melanoma metastases, in order to lower the impact of interobserver variability associated with experience in dermoscopy.

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CONFLICT OF INTEREST: None declared.

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