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CLINICAL REPORT

Polarized Light-surface Microscopy for Description and Classification of Small and Medium-sized Congenital Melanocytic Naevi

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Owing to a lack of well-defined clinical criteria for identifying congenital lesions, the diagnosis of small and medium-sized congenital melanocytic naevi is always uncertain. Our aim was to describe the features of small congenital melanocytic naevi, as observed by digital videomicroscopy, with the purpose of identifying single patterns characteristic of small congenital melanocytic naevi or different morphological subgroups. We could then perform a classification based on their macroscopic and surface microscopic aspects. Digital images referring to 154 small congenital melanocytic naevi and to 150 acquired naevi were examined for pattern analysis. New features characterizing small congenital melanocytic naevi, such as target network, target globules, target vessels and focal thickening of network lines, were identified, and a subdivision of small congenital melanocytic naevi into different subgroups was performed. Discriminant analysis enabled the distinction between congenital and common naevi with a sensitivity of 82.5% and a specificity of 64%. Small congenital melanocytic naevi can be described and classified by digital videomicroscopy and pattern analysis. The most important discriminant features are target network, small globules, follicles and vessels. This classification may represent a useful tool in the follow-up of small congenital melanocytic naevi. *Key words: epiluminescence microscopy; pattern analysis; videomicroscopy.*

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Congenital melanocytic naevi (CMN) are pigmented lesions that are present at birth. At least 2.5% of white newborn infants are noted to have some type of pigmented lesion, and 1% have biopsy-confirmed naevocellular naevi (1–3). CMN are commonly classified as small (<1.5 cm), medium-sized (1.5 to 19.9 cm) and large (20 cm or greater) (4). Small and medium-sized CMN are considerably more common than large ones, and are therefore of potentially greater epidemiological significance if they represent precursors of melanoma. Whereas a range of probable lifetime risk for the occurrence of melanoma is quoted between 5% and 15% for giant naevi (4–9), the risks in small and medium-sized CMN are still a matter of debate (3, 4, 10–15). Although unreliability of anamnesis regarding the congenital nature of the lesion cannot always be excluded, a careful history is often more useful than histology in diagnosing a naevus as congenital, owing to a lack of specificity and sensitivity of histologic criteria. This low diagnostic accuracy may markedly influence any estimate of relative risk. Moreover, routine prophylactic removal of all small CMN has been suggested by some authors (6, 8, 12), and it is necessary to balance the cost and risk of surgery with any possible risk of malignant change.

The introduction of instrumental devices allowing observation of subsurface structures has enabled the identification of morphological features characterizing different pigmented skin lesions (16–21). The aim of this study was to describe the features of small and medium-sized CMN, as observed by digital videomicroscopy, to identify parameters suitable for the diagnosis of congenicity, and to perform a classification based on their surface microscope aspects.

MATERIALS AND METHODS

Patients and lesions

One-hundred-and-fifty-four patients with 154 congenital naevi, 83 male and 71 female, aged 1 to 78 (mean age = 22.4 ± 15.4), undergoing clinical examination at the Department of Dermatology of the University of Modena, Italy, were considered during a period of one year. Lesions were selected as congenital only in the case of a convincing clinical history. Mean diameter of the lesions was 18.8 ± 17.5 mm. One-hundred-and-twenty were small (<1.5 cm) and 34 medium-sized (>1.5 cm). CMN were located on the chest and abdomen in 32 cases, on the back in 51 cases, on the head in 9 cases, on the upper limbs in 16 cases, and on the lower limbs in 46 cases. No lesion involved the palms or the soles. As a control group, 150 consecutively acquired melanocytic lesions in 150 patients undergoing dermatological examination were considered. Control naevi were matched for anatomic site and patient age. Lesion size ranged from 2 to 7 mm. No atypical naevi were studied.

Instrumentation and image database

The instrument, an NTSC VMS-110A videomicroscope (Scalar Mitsubishi, Tama-shi, Tokyo, Japan), which has already been described elsewhere (22), consists of a camera probe, a processing unit and a colour monitor. Twenty-fold magnified images for global detection of the lesions and 50-fold

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magnified images for pattern description were acquired by means of the Videocap 8.0 program (DS Medica, Milan, Italy); 223 twenty-fold and 526 fifty-fold magnified images of 154 congenital naevi and 150 twenty-fold and 204 fifty-fold magnified images of acquired naevi were evaluated.

Image examination

Subsequently, digital images were retrieved and examined blindly in random order by three examiners to assess "classic" (23) and new morphological features. Following a first inspection, a form of image description was prepared and the lesions were evaluated again in order to record the frequency of these features.

Statistics

A statistical evaluation was carried out employing the SPSS statistical package (release 10.0.6, 1999; SPSS Inc., Chicago, Ill., USA). As basic statistical analysis, frequencies of each surface microscopic criterion were calculated in the two groups. In a univariate approach, significant differences between congenital and acquired naevi were evaluated using the chi-square test of independence (Fisher's exact test was applied if any expected cell value in the 2×2 table was less than 5). The positive predictive value (considered as the probability that a lesion presenting that feature is a congenital naevus rather than a common naevus) was calculated for each feature.

In a multivariate approach, the data referring to the most powerful non-correlated features, i.e. target network, small globules, follicles and vessels, underwent elaboration by means of multivariate discriminant analysis. Discriminant analysis enables the identification of variables that are important for distinguishing among groups and develops a procedure for group classification based on a score attribution. In order to test the effectiveness of the discriminant equation in distinguishing between congenital and common naevi, the leave-one-out method was used.

The Spearman test was employed to check the correlation between different features. A $p < 0.05$ was considered statistically significant.

RESULTS

Morphological descriptors, selected for image evaluation, are listed in Table I. The definition of the patterns refers to the recent consensus net meeting on dermoscopy (23); however, some new features have been described as suitable for the description of small and medium-sized CMN: light-brown globules with a central dot were defined as target globules (Fig. 1a), network meshes centred by a dot were named target network (Fig. 1b), whereas target vessels appeared in faintly pigmented lesions as a network mesh centred by a vessel (Fig. 1c). Focal thickening of network lines, sometimes also showing small dot-like eversions (Fig. 1d), and skin furrow- and perifollicular hypopigmentation were also recorded as possible characteristic features of small and medium-sized CMN. Because of a possible different biologic meaning, a distinction between big and small globules was introduced. As measured on the magnified image, the diameter of big globules is larger than 0.25 mm (corresponding to 30 pixels in our system using a 50-fold magnification) and the diameter of small globules ranges

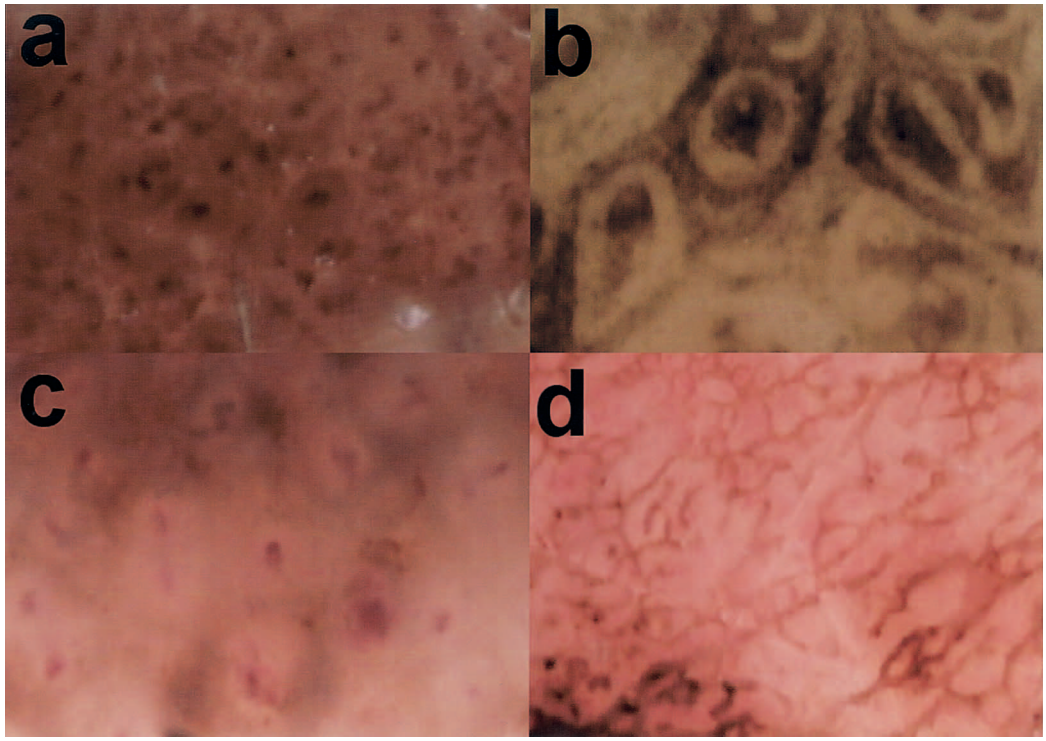

Fig. 1. (a) Target globules: light-brown globules with a central dot (50×). (b) Target network: network meshes centred by a dot (200×). (c) Target vessel: network meshes centred by a vessel (200×). (d) Focal thickening of network lines, sometimes showing small dot-like eversions (50×).

Table I. *Morphologic aspects of 154 small and medium-sized congenital melanocytic naevi (CMN) and 150 acquired nevi, as assessed by videomicroscopy. Parameters for discrimination between CMN and common naevi in italics. Focal network thickening was compared to the number of lesions with a network (n=82), and perifollicular hypopigmentation to the number of observed follicles (n=115)*

	No. (%) of observations in SCMN	No. (%) of observations in acquired nevi	PPV %	Discriminant analysis coefficients
Asymmetry	9 (5.8)	12 (8.0)	42.9	
Surface microscopic structures				
Network	82 (53.2)	109 (72.7)	42.9	
Target network	31* (20.1)	3 (2.0)	91.2	1.572
Focal thickening of network lines/network	17/82* (20.7)	7/109 (6.4)	70.8	
Parallel network	5 (3.2)	0 (0.0)	100	
Small globules	79* (51.3)	17 (11.3)	82.3	1.438
Big globules	59* (38.3)	30 (20.0)	66.3	
Target globules	13 (8.4)	4 (2.7)	76.5	
Dots	105* (68.2)	54 (36.0)	66.0	
Peripheral structures				
Peripheral globules	23* (14.9)	7 (4.7)	76.7	
Peripheral dots	17 (11.0)	16 (10.7)	51.5	
Peripheral streaks	7 (4.5)	13 (8.7)	35.0	
Diffuse pigmentation				
Homogeneous diffuse pigment	111 (72.1)	143 (95.3)	43.7	
Blotches	36* (23.4)	59 (39.3)	37.9	
Hyperpigmented areas	10* (6.5)	0 (0.0)	100	
Satellite areas	6* (3.9)	0 (0.0)	100	
Hypopigmented structures				
Focal hypopigmentation	30 (19.5)	22 (14.7)	57.7	
Skin furrow hypopigmentation	27* (17.5)	11 (7.3)	71.1	
Follicles	115* (74.7)	40 (26.7)	74.2	1.463
Perifollicular hypopigmentation/follicles	82/115 (71.3)	35/40 (87.5)	70.1	
Pseudofollicles	11* (7.1)	28 (18.7)	28.2	
Veil	2 (1.3)	2 (1.3)	50.0	
Blood vessels				
Vessels	13* (8.4)	0 (0.0)	100	1.742
Target vessels	6* (3.9)	0 (0.0)	100	
No. of features per lesion	5.55±1.94*	4.14±1.51		

*$p<0.05$ with respect to acquired naevi.
PPV = Positive predictive value.

from 0.08 to 0.25 mm, whereas the diameter of dots is less than 0.08 mm.

Table I indicates the frequency of microscopic features in small and medium-sized CMN and in acquired lesions in our image database. Major differences were observed for target network, focal network thickening, small globules, skin furrow hypopigmentation and hair follicles. Vessels, target vessels and satellite areas were observed in congenital lesions alone. In small and medium-sized CMN a higher number of features per lesion was observed with respect to common naevi. Target network, small globules, follicles and vessels were employed for the distinction between the two groups by the discriminant analysis function, which was able to distinguish small and medium-sized CMN with a sensitivity of 82.5% and a specificity of 64%. A positive predictive value of 100% was found for parallel network, hyperpigmented areas, satellite areas, vessels and target vessels. A direct correlation was observed between network, target network and focal thickening of network lines, between small globules, big globules, target globules, peripheral globules and dots, between follicles, pseudofollicles, and perifollicular and skin furrow hypopigmentation. An inverse correlation was observed between network, small globules, big globules, dots and follicles.

Table II gives the classification of small and medium-sized CMN based on the predominant surface microscopy pattern and on the macroscopic aspect of the lesion. Depending on their microscopic appearance, lesions fall into three main categories (the "diffuse pigmentation" type, the "globular" type and the "network" type). Eighty-nine lesions belonged to the diffuse pigmentation group. Diffuse pigmentation appeared either as an isolated feature, or, more often, was associated with globules, dots or the network. It was either homogeneously or irregularly distributed, appearing as blotches. Lesions

Table II. *Classification of 154 small- and medium-sized congenital melanocytic naevi according to their surface-microscopic and macroscopic aspect*

	Total no. of lesions 154 (100%)	Light brown 40 (26%)	Dark brown/black 66 (42.8%)	Variegated 48 (31.2%)
Diffuse pigmentation	89 (57.8%)	24 (60)	38 (58)	27 (56)
Homogeneous diffuse pigmentation	5 (3.2%)	1 (3)	2 (3)	2 (4)
Inhomogeneous diffuse pigmentation (blotches)	30 (19.5%)	1 (3)	18 (27)	11 (23)
Diffuse pigmentation + small globules	18 (11.7%)	6 (15)	6 (9)	6 (13)
Diffuse pigmentation + dots	10 (6.5%)	5 (13)	3 (5)	2 (4)
Diffuse pigmentation + small peripheral globules	5 (3.2%)	2 (5)	1 (1)	2 (4)
Diffuse pigmentation + peripheral network	21 (13.6%)	9 (22)	8 (12)	4 (8)
Globular	36 (23.4%)	10 (25)	22 (33)	4 (8)
Globules	23 (14.9%)	5 (12)	16 (24)	2 (4)
Cobble-stone pattern	13 (8.4%)	5 (12)	6 (9)	2 (4)
Network	29 (18.8%)	6 (15)	6 (9)	17 (35)
Network with diffuse pigmentation	6 (3.9%)	1 (3)	2 (3)	3 (6)
Network with focal line thickening	18 (11.7%)	3 (7)	3 (5)	12 (25)
Network with dots	5 (3.2%)	2 (5)	1 (1)	2 (4)

with small or big globules or polygonal areas were grouped together forming the globular-type category. Among network lesions, a thickening of the mesh lines, sometimes presenting dot-like eversions, was the main characteristic in 18 cases.

Lesions were subdivided into three groups in accordance with the clinical examination: light brown, dark brown-black and variegated. The light-brown naevus type was present mainly in fair-skinned patients, and included 40 lesions. In most of these lesions (24 cases), diffuse pigmentation prevailed, either alone or associated with the presence of globules, dots or network. Sixty-six lesions in our image database belonged to the dark-brown to black-coloured type. One-third of dark small and medium-sized CMN showed globular structures, whereas in 18 lesions pigmentation was irregularly distributed. In variegated lesions the darker parts of the lesion were due to the presence of globules, to un-homogeneous diffuse pigmentation, or to broadened network lines. Discontinuous thickening of network lines sometimes superimposed by dots was the most characteristic aspect of the variegated naevus type.

DISCUSSION

True CMN, melanocytic naevi present at birth, are not rare, and are encountered in approximately 1% of newborns (24). Large CMN are more at risk in the development of melanoma (4–9). On the contrary, the risk associated with small and medium-sized CMN is still much debated (3, 4, 10–15). However, until congenital lesions can be precisely diagnosed, their melanoma risk cannot be evaluated. In fact, relevant studies assessing the melanoma risk for a small and medium-sized CMN have been hampered by methodological problems concerning the lack of specificity in the clinical aspect, the frequent unreliability of patient history regarding the congenital nature of the lesion, and the lack of fully specific histologic criteria for the identification of CMN.

It is therefore necessary to identify parameters to be used in prospective studies, enabling the distinction between congenital lesions and acquired ones, and also to more accurately characterize those naevi that possess neoplastic potential and thus clearly warrant early surgical intervention.

Surface microscopy enables the observation of subsurface structures characterizing pigmented skin lesions, leading to an improvement in diagnostic accuracy of melanoma (25). Features specific for malignant and benign lesions have been identified and represent the basis for pattern analysis and semi-quantitative scoring systems (16–21). Braun et al. (26) investigated the morphologic modification of CMN in a follow-up study performed by digital dermoscopy. However, to the best of our knowledge the surface microscopic features of congenital naevi have not so far been described in detail and systematically. The aim of our study was first to identify surface microscopic morphological features specific for congenital naevi, which may enable their identification in the absence of a convincing clinical history. Second, we propose a classification of congenital naevi, based on their morphological pattern, to be used in prospective studies assessing the neoplastic risk of small and medium-sized CMN and correlating a certain naevus subgroup, or one or more specific patterns, to the evolution of the lesions.

For description of congenital pigmented skin lesions, we used both traditional patterns and others (such as target network, target vessels, skin furrow hypopigmentation and focal network line thickening) that have never been applied so far. In fact we observed that the frequency of the different features in congenital and acquired naevi significantly differed in most cases. A high positive predictive Value (PPV) was shown by target network and vessels, although they were present in only 20.1% and

8.4% of cases, respectively. Small globules and follicles were observed more frequently, but their presence was less powerful (PPV = 82.3% and 74.2%, respectively). Dots were often present in both small and medium-sized CMN and acquired naevi, showing a low PPV (66%). Homogeneous diffuse pigmentation was only useful if other features were also present, since this was frequently observed both in small and medium-sized CMN and acquired naevi (PPV = 43.7%). Pseudofollicles were infrequent both in acquired naevi and in small and medium-sized CMN, and had a low PPV (28.2%). In the discriminant analysis equation, parameters positively associated with small and medium-sized CMN were target network, small globules, follicles and vessels. In spite of the unavoidable clinical selection of our lesions possibly introducing some biases and of the limited number of lesions examined, the results of our study are promising: the multivariate approach enabled the identification of CMN with a sensitivity of 82.5% and a specificity of 64%. We are also proposing a classification of CMN based on their prevalent surface-microscopic appearance and on their macroscopic aspect, as regards the intensity of pigmentation. Owing to their composite arrangement, it is not always easy to classify CMN. Very often diffuse pigmentation, globules and network coexist in the same lesion. Moreover, the size of globular structures is often variable and we can observe at the same time, dots, small and big globules. The most typical and frequent subgroups consisted of: 1) light-brown lesions with diffuse pigmentation associated with small globules or dots or peripheral network, 2) a dark brown to black type consisting of globules or polygonal areas arranged in a cobblestone pattern, and 3) a variegated type, where the darker part of the lesion was due to the presence of aggregated globules or blotches or a thickened network with dots.

Surface microscopy has enabled a dramatic improvement in diagnostic accuracy for melanoma (25). However, although the patterns specific for melanomas have been well established (16–21), there is no agreement on surface microscopic features characterizing benign lesions with an increased risk of malignant transformation. To date, also for congenital naevi, we do not have any indications as regards possible surface-microscopic features indicating biologic behaviour at risk. We are proposing a simple classification which may represent a basis for prospective studies assessing the risk of CMN. The identification of particular subtypes of CMN with different prognostic implications or the association of a specific morphologic pattern with an increased risk of malignancy could enable a selective surgical prophylaxis as an alternative to routine removal of all congenital lesions or life-long follow-up.

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