Dermatoscopic and clinical features of congenital or congenital-type nail matrix nevi: A multicenter prospective cohort study by the International Dermoscopy Society

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Background: Congenital nail matrix nevi (NMN) are difficult to diagnose because they feature clinical characteristics suggestive of adult subungual melanoma. Nail matrix biopsy is difficult to perform, especially in children.

Objective: To describe the initial clinical and dermatoscopic features of NMN appearing at birth (congenital) or after birth but before the age of 5 years (congenital-type).

Methods: We conducted a prospective, international, and consecutive data collection in 102 hospitals or private medical offices across 30 countries from 2009 to 2019.

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Results: There were 69 congenital and 161 congenital-type NMNs. Congenital and congenital-type NMN predominantly displayed an irregular pattern of longitudinal microlines (n = 146, 64%), reminiscent of subungual melanoma in adults. The distal fibrillar ("brush-like") pattern, present in 63 patients (27.8%), was more frequently encountered in congenital NMN than in congenital-type NMN (P = .012). Moreover, congenital NMN more frequently displayed a periungual pigmentation (P = .029) and Hutchinson's sign (P = .027) than did congenital-type NMN.

Limitations: Lack of systematic biopsy-proven diagnosis and heterogeneity of clinical and dermatoscopic photographs.

Conclusion: Congenital and congenital-type NMN showed worrisome clinical and dermatoscopic features similar to those observed in adulthood subungual melanoma. The distal fibrillar ("brush-like") pattern is a suggestive feature of congenital and congenital-type NMN. (J Am Acad Dermatol 2022;87:551-8.)

Key words: children; congenital; congenital nail matrix nevus; dermatoscopy; longitudinal melanonychia; melanonychia striata; nevus of the nail unit; pediatric; subungual melanoma.

INTRODUCTION

Nail matrix nevi (NMN) are a common differential diagnosis of subungual melanoma (SUM). Melanonychia is the common feature of both diagnoses. Most NMN acquired during adulthood are usually easy to differentiate from SUM on the basis of clinical and dermatoscopic features.[1-3] However, as observed on other cutaneous sites, childhood NMN frequently combine semiologic features of irregularity and asymmetry with a multicomponent pigmentation of the nail plate and surrounding tissue that could suggest malignancy.[4,5]

Nail matrix biopsy, an invasive procedure associated with emotional distress and the risk of permanent nail scarring, is difficult to propose in cases with a low-level of suspicion, especially in newborns or very young children. Moreover, large series of biopsied melanonychia in children have shown that

CAPSULE SUMMARY

- Congenital nail matrix nevi are difficult to diagnose and little is known about their initial clinical and dermatoscopic features.
- Congenital nail matrix nevi most often display an irregular dermatoscopic pattern of longitudinal microlines like adult subungual melanoma. The distal fibrillar ("brush-like") pattern is a suggestive feature of benignity.

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Abbreviations used:

IDS: International Dermoscopy Society
LM: longitudinal melanonychia
NMN: nail matrix nevus
SD: Standard deviation
SUM: subungual melanoma

the vast majority were benign NMN and very rare reported cases of SUM in children younger than 5 are often considered "questionable" nowadays in terms of false-positive diagnoses by nail pathology experts and pediatric dermatologists.[6]

No consensus is available to manage these rather rare but difficult cases. The International Dermoscopy Society (IDS) decided to open an observational, international, prospective registry of melanonychia observed before the age of 5 to describe their clinical, dermatoscopic, and, if applicable, pathologic features.

This first report about this international registry of congenital and congenital-type NMN aims to describe the initial features of all included cases to date.

MATERIAL AND METHODS

The International Dermoscopy Society congenital NMN registry

The IDS congenital NMN registry prospectively collected clinical and dermatoscopic images of melanonychia arising in children before the age of 5 that were voluntarily submitted by physicians around the world. The registry, located in Lyons France, is coordinated by L.T. and has been promoted by the IDS website since 2009. It has been approved by the institutional ethical board (N°20-63; May 15, 2020) and its use for the present study was approved by the French Data Protection Authority (N° 20_009; June 11, 2020). Its activities were funded in part by Lyon1-Claude-Bernard-University, by the Hospices Civils de Lyon and by the "Foundation Vaincre le Mélanome."

There are no widely acknowledged clinical, dermatoscopic, or pathologic criteria to accurately distinguish so-called acquired nevi from so-called congenital ones either on skin or on nails. However, recent research on nevogenesis showed that embryogenetically determined lesions could become clinically observable after birth.[7] Thus, we considered that including only patients with melanonychia present at birth was too stringent. Accordingly, the executive board of the IDS decided also to include postnatal lesions acquired until a cutoff age, with the assumption that they mostly share the same pathogenesis as congenital ones.

Since we knew from data about pediatric melanomas that the biologic behavior and clinical presentation of prepubertal melanomas clearly differed from those of postpubertal, an arbitrary cutoff age of 5 was chosen to ensure no patient with a melanonychia acquired around puberty was included.[8] To statistically verify the hypothesis of a shared pathogenesis, we differentiated true congenital lesions visible at birth (congenital NMN) from cases in which lesions were acquired after birth but before 5 (congenital-type NMN).

For each submitted case, volunteer physicians declared they had obtained the patient's oral parental consent and were invited to provide clinical data using a standardized questionnaire detailing age at presentation, age at discovery (as remembered by parents), sex, topography, and, whenever available, the result of a nail matrix biopsy. No management instruction was given, and responsible clinicians retained their choice as to whether or not to perform surgical biopsy or excision of the lesion and to decide the follow-up schedule. No standardized photography or photodermatoscopy tools were required, yet volunteer participants were invited to send clinical close-up images as well as dermatoscopic images of the nail plate and of the distal free edge of the nail.

Patient population

All patients included in the IDS congenital NMN registry until October 2019 (data lock) were analyzed. Exclusion criteria for this study were unknown date of the appearance of the melanonychia, melanonychia onset after the age of 5, and absence of dermatoscopic images.

Primary objective and data collection

The primary objective was to describe the clinical and dermatoscopic characteristics of congenital and congenital-type NMN. A resident (F.P.) created an Excel 2016 (Microsoft) form containing 6 clinical items (width of bands, longitudinal melanonychia (LM), erythronychia, xanthonychia, nail dystrophy, true Hutchinson's sign (true periungual pigmentation of the proximal and lateral aspect of the nailfold or hyponychium)) and 21 dermatoscopy items based on the 2016 IDS dermatoscopic terminology consensus[9] (color of background, pattern and color of longitudinal microlines, triangular shape, lateral borders of bands, black or brown dots, microscopic sign of Hutchinson (invisible to the naked eye but only observable by dermatoscopy),[1] localization and pattern of the periungual

pigmentation, distal fibrillar ("brush-like") pattern, pseudo sign of Hutchinson, proximal blue spot, splinter hemorrhages, blood spots, and pigmentation of the nail plate free edge).

All the clinical and dermatoscopic photographs were anonymously included in a slideshow using PowerPoint 2016 (Microsoft) Photographs were independently reviewed by 4 dermatologists with different levels of expertise in nail dermatoscopy: 1 expert (L.T.), 2 experienced (A.B. and N.P.), and 1 beginner (F.P.). The 4 dermatologists scored each criterion as present or absent.

For each criterion, we reached consensus when at least 3 among the 4 investigators agreed on the same answer. Any disagreements were resolved through group discussion.

Statistical analysis

We then compared each criterion between patients with congenital and patients with congenital-type NMN, assuming the null hypothesis that the distribution of each criterion were the same in the 2 groups. Quantitative variables were compared using a Student *t* test and qualitative variables were compared using a chi-square test or a Fisher's exact test. A statistical significance threshold of 5% was taken. Statistic test was performed using Statistical Package for the Social Sciences (SPSS) Statistics for Windows v.19.0 (IBM Corp, 2011).

In our study, there were 4 unique raters who independently rated 27 nominal variables in each of 230 patients. As it was a fully crossed study, we measured the inter-rater reliability by using Light's average kappa.[10,11] Scores ranged between−1 and 1, in which 1 indicated perfect agreement and−1 indicated no agreement. We used predefined and widely accepted thresholds for kappa values: <0 (poor agreement), 0-0.20 (slight agreement), 0.21-0.40 (fair agreement), 0.41-0.60 (moderate agreement), 0.61-0.80 (substantial agreement), and 0.81-1 representing almost perfect agreement.[12] Statistic test was performed using R version 4.1.1 (R Foundation for Statistical Computing).

RESULTS

Cohort characteristics

From 2009 until 2019, 114 physicians from 102 hospitals or private medical offices across 30 countries have submitted cases for the IDS registry. A total of 243 potential lesions from 243 patients were included in the registry; 13 patients were excluded (missing age of appearance of melanonychia in 5 cases, first appearance of melanonychia after age of 5 in 6 cases, and missing dermatoscopic images in 2 cases). The final dataset included 230 lesions in 230 patients. Of the 175 (75.7%) of the cases recruited from European countries, 139 were submitted from France; the remaining 56 (24.3%) cases were from the rest of the world. Demographic data of congenital or congenital-type NMN are summarized in Table I.

Clinical and dermatoscopic features

We confirmed the predominant localization of LM at the thumb or the hallux.[6,4,13] The main clinical and dermatoscopy features of congenital and congenital-type NMN are presented and compared in Table II. Inter-rater reliability is presented in Supplementary Table SI (available via https://data.mendeley.com/datasets/t7by98f6pp/1). We subclassified congenital and congenital-type NMN cases into 5 different dermatoscopic patterns. The irregular pattern (n = 146, 64%) was defined by longitudinal microlines irregular in width/space/color with interrupted lines/disruption of parallelism, triangular shape, polychromia, onychodystrophy, irregular periungual pigmentation). Regular pattern (n = 48, 21%) was defined by a regular pattern of longitudinal microlines without prevalent features of irregular pattern. The remaining patterns were homogeneous (n = 26, 11%); exclusively periungual pigmentation (n = 7, 3%), which was defined by periungual pigmentation without any LM; and LM associated with a medium-sized cutaneous congenital nevus of the periungual skin (n = 3, 1%; Supplemental Fig 1, available via https://data.mendeley.com/datasets/t7by98f6pp/1).

The most prevalent dermatoscopic pattern of the periungual pigmentation was the distal fibrillar ("brush-like") pattern (n = 64, 27.8%; Supplemental Fig 2). No case displayed the parallel ridge pattern or the diffuse irregular pattern of the periungual skin.

Dermatoscopic photographs of the nail-free edge were provided in only 58 cases, of which, the pigment was localized at the bottom of the free edge in 28 cases, and localized both at the upper and the bottom portion of the free edge in 27 cases, and not visible in 3 cases.

Histopathologic analysis

Results of nail matrix biopsies were available in 12 patients and histopathology revealed junctional NMN in 11 cases and functional melanocytic activation in 1 case. At the time of writing, no melanoma has been confirmed or reported in any included patient. However, further observation and formal follow up is required.

DISCUSSION

We conducted a multicenter, international, prospective registry study that included 230 patients

Table I. Demographic data and anatomic sites of congenital or congenital-type NMN

Characteristics	All lesions (n = 230)	Congenital NMN (n = 69)	Congenital-type NMN (n = 161)	*P* value
Age at diagnosis, y, mean ± SD	5.3 ± 4.1	5.1 ± 3.7	5.3 ± 4.2	.310
Age at onset, y, mean ± SD	1.9 ± 1.8	0 ± 0	2.8 ± 1.6	<.001
Sex, n (%)				.441
Female	92 (40.0)	26 (37.7)	66 (41.0)	
Male	135 (58.7)	43 (62.3)	92 (57.1)	
Unspecified	3 (1.3)	0 (0)	3 (1.9)	
Continent of origin, n (%)				N/A
Europe	174 (75.7)	59 (85.5)	115 (71.4)	
Asia	30 (13.0)	5 (7.2)	25 (15.5)	
Central and South America	9 (3.9)	1 (1.4)	8 (5.0)	
Oceania	7 (3.0)	3 (4.3)	4 (2.5)	
Africa	7 (3.0)	1 (1.4)	6 (3.7)	
North America	3 (1.3)	0 (0)	3 (1.9)	
Affected nail location, n (%)				
Right	119 (51.7)	34 (49.3)	85 (52.8)	.568
Left	106 (46.1)	34 (49.3)	72 (44.7)	
Digit	160 (69.6)	50 (72.5)	110 (68.3)	.139
Toe	67 (29.1)	19 (27.5)	25 (15.5)	
Thumb	85 (37)	27 (39.1)	58 (36.0)	
Hallux	34 (14.8)	9 (13.0)	25 (15.5)	

N/A, Not available; *NMN*, nail matrix nevus; *SD*, standard deviation; *y*, years.

with congenital and congenital-type NMN. We described the most prevalent clinical and dermatoscopic features of the largest case series of LM arising in children before the age of 5.

We confirmed that a high proportion of the congenital or congenital-type NMN displayed worrisome clinical and dermatoscopic features very similar to those observed in SUM: broad band, nail dystrophy, triangular shape, polychromia, microscopic Hutchinson's sign, blurred border of bands, and, above all, longitudinal microlines irregular in their thickness, spacing, and coloration. These criteria for the diagnosis of adulthood SUM are therefore not applicable to children.

Other studies of pediatric NMN reported lower proportions of the irregular pattern but were limited by fewer included patients and the description of only 2 dermatoscopic patterns (regular or irregular). We introduced 3 supplementary patterns, among which the homogeneous pattern was probably counted as a regular pattern.[5,13,14]

Regarding differences between characteristics of congenital and congenital-type NMN, congenital NMN more frequently displayed periungual pigmentation, Hutchinson's sign, and the distal fibrillar ("brush-like") pattern than did congenital-type NMN. Apart from these differences, congenital and congenital-type NMN mostly shared common initial features. We hypothesize that the sooner the congenital NMN appears during the embryonic development, the more it would be expected to be extended beyond the nail matrix into the nailfolds. Another explanation may be that a few included postnatal lesions in the study were rather acquired NMN or lentigos with different characteristics than congenital NMN.

Unlike SUM, no congenital or congenital-type NMN displayed a parallel ridge pattern or a diffuse irregular pattern of the periungual skin. Rather, the distal fibrillar ("brush-like") pattern was observed in about a third of cases with a substantial inter-rater reliability. Its frequency might yet be underestimated, as not all observers provided dermatoscopic images of a freshly trimmed nail plate. This sign has been first coined as "linear brushy pattern" by Kawabata et al[15] in a 2-year-old boy with biopsy-proven NMN and was later reported as "longitudinal brushy pattern" by Lee et al[5,16] in a similar proportion (25%). It consists of a dense fibrillar pigmentation pattern beneath the hyponychium composed of multiple thin parallel lines that cross both the furrows and ridges and is considered as a benign nevus pattern variant on soles.[17] Therefore, we believe that its location distally from the hyponychium should be called "distal fibrillar pattern" for the sake of homogenization. Indeed, the IDS recommended avoiding metaphoric terms to describe dermatoscopic features and to use

Table II. Clinical and dermatoscopic characteristics of congenital and congenital-type NMN

Characteristics, n (%)	All lesions (n = 230)	Congenital NMN (n = 69)	Congenital-type NMN (n = 161)	*P* value
Width of melanonychia				.227
None	5 (2.2)	0 (0)	5 (3.1)	
Less than one-third of the nail plate	109 (47.4)	30 (43.5)	79 (49.1)	
One-third to two-thirds of the nail plate	52 (22.6)	15 (21.7)	37 (23.0)	
More than two-thirds of the nail plate	31 (13.5)	9 (13.0)	22 (13.7)	
Totality of the nail plate	33 (14.4)	15 (21.7)	18 (11.2)	
Longitudinal melanonychia	223 (97)	69 (100)	154 (95.7)	.106
Nail dystrophy	35 (15.2)	11 (15.9)	24 (14.9)	.841
Color of background				N/A
None	9 (3.9)	0 (0)	9 (5.6)	
Gray	6 (2.6)	0 (0)	6 (3.7)	
Light brown	159 (69.1)	49 (71)	110 (68.3)	
Dark brown	40 (17.4)	13 (18.8)	27 (16.8)	
Black	17 (7.4)	7 (10.1)	10 (6.2)	
Pattern of longitudinal microlines				.971
No streak	37 (16.1)	11 (15.9)	26 (16.1)	
Regular pattern	51 (22.2)	16 (23.2)	35 (21.7)	
Irregular pattern	142 (61.7)	42 (60.9)	100 (62.1)	
Color of longitudinal microlines				.839
Yellow	0 (0)	0 (0)	0 (0)	
Gray	78 (33.9)	20 (30)	58 (36)	
Light brown	144 (62.6)	39 (56.5)	105 (65.2)	
Dark brown	176 (76.5)	52 (75.4)	124 (77)	
Black	60 (26.0)	19 (27.5)	41 (25.5)	
Number of colors of longitudinal microlines				.479
1 color	25 (10.9)	9 (13.0)	16 (9.9)	
2 different colors	92 (40.0)	31 (44.9)	61 (37.9)	
3 different colors	54 (23.5)	13 (18.8)	41 (25.5)	
4 different colors (polychromia)	22 (9.6)	5 (7.2)	17 (10.6)	
Lateral border of bands				.289
Not visible	33 (14.4)	14 (20.3)	19 (11.8)	
Blurred	78 (33.9)	23 (33.3)	55 (34.2)	
Sharpen	113 (49.1)	32 (46.4)	81 (50.3)	
Missing data	6 (2.6)	0 (0)	6 (3.7)	
Triangular shape	30 (13)	10 (14.5)	20 (12.4)	.669
Black or brown dots	87 (37.8)	28 (40.6)	59 (36.7)	.573
Periungual pigmentation	86 (37.4)	32 (46,4)	54 (33.5)	**.029***
Hyponychium ± other folds	67 (29.1)	29 (42.0)	38 (23.6)	
Proximal and/or lateral folds	19 (8.3)	3 (4.4)	16 (9.9)	
Hutchinson's sign	48 (20.9)	21 (30.4)	27 (16.8)	**.027***
Missing data	5 (2.2)	0 (0)	5 (3.1)	
Microscopic sign of Hutchinson only	36 (15.7)	8 (11,6)	28 (17,4)	.268
Distal fibrillar (''brush-like'') pattern	64 (27.8)	27 (39.1)	37 (23.0)	**.012***
Pseudo sign of Hutchinson	114 (49,6)	33 (47.8)	81 (50.3)	.730

Xanthonychia (n = 0), erythronychia (n = 11), proximal blue spot (n = 11), splinter hemorrhages (n = 5), and blood spots (n = 0) were rarely or not encountered.

N/A, Not available; *NMN*, nail matrix nevus.

*Statistically significant.

descriptive terms instead.[9] However, to facilitate the transition from the former metaphoric to the descriptive terms, we propose to name this sign the distal fibrillar (“brush-like”) pattern.

We hypothesize that distal periungual pigmentation is more likely to be observed if the melanocytic hyperplasia seen in congenital NMN is present before the eighth week of gestation. Between the eighth and the tenth week, the primary nail field would progressively appear, dividing the congenital NMN into a proximal part across the proximal groove and a distal part across the distal groove (Supplemental Fig 3), similar to kissing nevus of the eyelids or of the penis.[18,19] The periungual pigmentation would depend on the initial location and on the size of melanocytic hyperplasia observed in NMN: the more distal its location in the developing nail organ, the more probable it would result in an exclusive pigmentation beneath of the hyponychium without LM; whereas, the more proximal its location in the developing nail organ, the more probable it would result in an exclusive pigmentation of the proximal nailfold with LM.

Another explanation for the distal fibrillar (“brush-like”) pattern associated with LM in our cohort would be the coincidence of a melanocytic hyperplasia on the same digit in both the matrix and the hyponychium, which seems unlikely. Nevertheless, we cannot exclude that true nevus on the hyponychium could account for the cases without proximal visible involvement, exhibiting the exclusive periungual pattern.[20] We consider the distal fibrillar (“brush-like”) pattern as a suggestive feature of congenital and congenital-type NMN in children with LM arising before the age of 5. That sign was commonly encountered in the present study cohort and has never been observed in adult patients we followed for SUM (personal observation, L.T.) where the periungual pigmentation is commonly a parallel ridge pattern. However, the diagnostic value of the distal fibrillar (“brush-like”) pattern should be prospectively confirmed in comparative studies with other nail pigmentation conditions.

The strengths of our study were its high number of included patients, its multicenter design, and the independent evaluation of cases by 4 dermatologists with different levels of expertise in onychoscopy. Dermatoscopy demonstrated a reliable tool for examination, as illustrated by a fair to substantiate inter-rater reliability for most of the evaluated dermatoscopic features.

There were some limitations to this study. First, the issue of absence of a control group of pediatric SUM could be raised. Yet, because of the extreme rarity of melanoma cases before the age of 5 on the skin as well as on nails, such a control group appeared elusive. Second, our diagnoses were not biopsy-proven for most cases. Indeed, similarly to the management of congenital cutaneous nevi, we considered that it was only required in cases with strong melanoma suspicion.[21] We acknowledge that pathology remains the gold standard for subungual melanocytic tumors so far and that some lentigos or functional LM have probably been included in the present study. Third, there was a lack of standardization of the clinical and dermatoscopic photographs, which was responsible for some missing data, but it is a weakness commonly encountered in large international registries. Finally, longer follow up is required to assess the natural history of congenital and congenital-type NMN, but this will be the subject of a future research project.

CONCLUSIONS

Congenital and congenital-type NMN most often show worrisome clinical and dermatoscopic features that are also commonly encountered in adult SUM with a predominant irregular pattern of longitudinal microlines. The distal fibrillar (“brush-like”) pattern is often present, and we consider it a suggestive feature of congenital and congenital-type NMN. Further studies of the cohort will focus on the evolutive characteristics of these lesions and hopefully will help us to better define management guidelines. To this end, the IDS continues to actively recruit new cases of melanonychia with onset before the age of 5 (https://dermoscopy-ids.org/wp-content/uploads/nail_study.pdf).

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Conflicts of interest

None disclosed.

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