Eur. J. Pediat. Dermatol.
27, 215-23, 2017

Longitudinal melanonychia in childhood.

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Summary There are in the literature 11 cases of primary melanoma of the nail matrix presenting as longitudinal melanonychia (LM) in children. Asian or South American children with a dark phototype were mainly affected - 8 cases -, more rarely - 3 cases - Caucasian children with a fair-skinned phototype were involved and all of them were Italian. The fingers were involved in 8 cases, with prevalence of the 5th finger - 3/8 cases -, whereas the big toe was affected in 3 cases. In all cases the histological diagnosis was melanoma in situ; however, the differential diagnosis from benign melanocytic hyperplasia was almost always difficult. The clinical and dermoscopic signs allowing the differential diagnosis between malignant and benign LM in the adult are less valid in children. Moreover, also due to the anatomical and physiological peculiarities of the melanocytes of the nail matrix, there are no reliable histological criteria for this differential diagnosis. This is why longitudinal melanonychia in childhood should be very carefully monitored clinically, performing a biopsy of the nail matrix in case of rapid and persistent evolution of the lesion.

Key words Longitudinal melanonychia, melanoma in situ, nail matrix.

Longitudinal melanonychia (LM) is a dark band that affects the nail plate from its proximal portion up to the distal margin. The LM is due to a hyperproduction of melanin by the melanocytes of the nail matrix and can occur for a benign – such as hyperfunction, simple lentigo and melanocytic nevus – or a malignant disorder as melanoma. The differentiation between benign and malignant hyperproduction of melanin, which is not always easy on the skin, is even more difficult at the level of the nail due to some particular anatomical and physiological characteristics of the matrix melanocytes.

Anatomical and-physiological characteristics of the matrix melanocytes. The melanocytes of the nail matrix, which are 6.5 per millimeter of basement membrane, are present in the lower three layers of the epidermis and not only in the basal layer as in the epidermis of any other site: this anatomical peculiarity can create difficulty in the differential diagnosis between benign lesions and melanoma at the level of the nail matrix.

Furthermore, the melanocytes of the matrix, especially in the Caucasians, do not usually produce melanin; the production of melanin by the melanocytes of the matrix can be observed in white people only in the particular benign and malignant already mentioned conditions and usually manifests itself in the form of longitudinal melanonychia with a more or less large band.

The histological examination allows to distinguish the different conditions responsible for longitudinal melanonychia, from the hyperfunction,

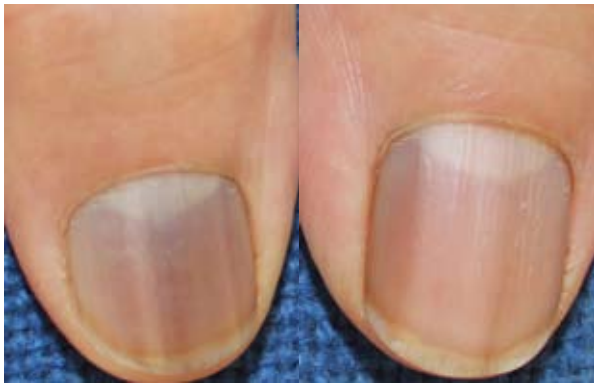


Fig. 1

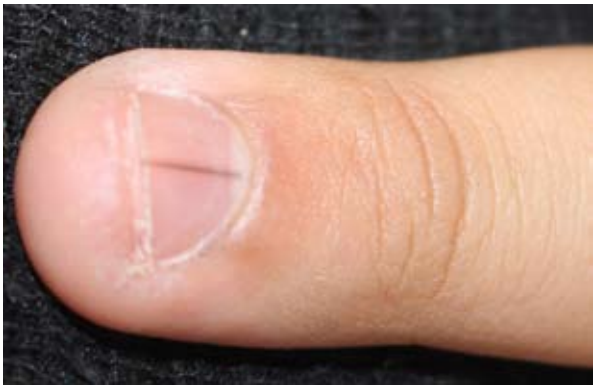
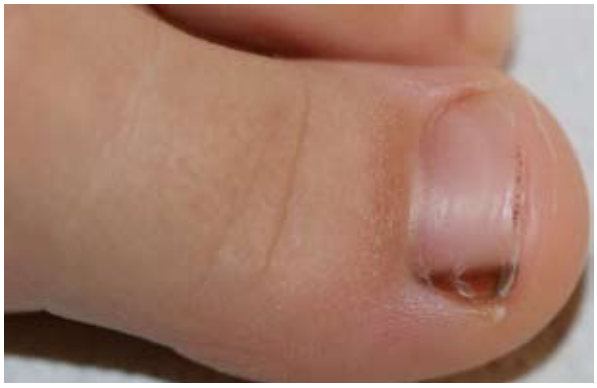


Fig. 2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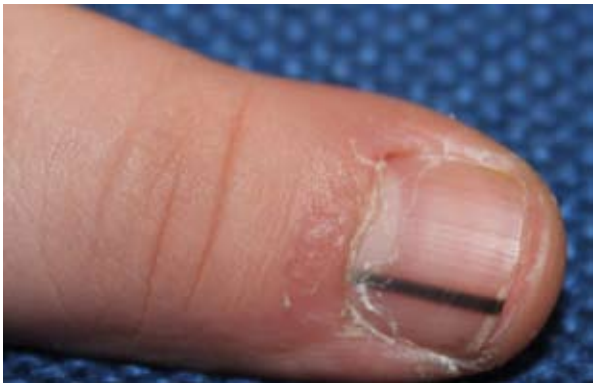


Fig. 4

Fig. 1, 2, 3, 4: A longitudinal melanonychia affecting several nails is usually benign and more frequent in subjects with dark phototype (Fig. 1). Longitudinal melanonychia can affect any site othe matrix (Fig. 2, 3, 4). Sometimes longitudinal melanonychia is attributed by the parents to trauma, in this case (Fig. 4) to repetitive biting of the matrix.

characterized by a normal number of typical melanocytes, to simple lentigo with an increased number of melanocytes and possible elongation of the epidermal ridges, to the nevus with the presence of nevus cell nests up to melanoma characterized by the presence of atypia and high mitotic index.

Melanin production in different ethnic groups. However, it must be remembered that all these conditions, from benign longitudinal melanonychia (BLM) to melanoma starting from the nail matrix (MSNM) and finally to acral melanoma in a broader sense are more frequent in the dark-skinned ethnic groups: BLM would be present in almost all blacks over the age of 50, in 10-20% of the Japanese (14) and more frequently in the peoples of the Mediterranean area than in northern Europe (5).

Nail melanoma is also much more common in black – more than 20% of all cases of melanoma – than in white people – 1.5-2% – (24). However, even considering the latter percentage Haneke (8) points out that nail melanoma in white people is overrepresented compared to the melanoma of other sites, since the surface occupied by the 20 nails is less than 1% of the body surface.

Benign and malignant melanonychia. Most cases of longitudinal melanonychia are nevi; nail melanoma has an incidence of between 0.7% (6) and 7% (4) of all cases of melanoma. According to Theunis et Al. (25) in the adult 6% of LM are melanomas, while in the child there are currently only 11 cases of nail melanoma in situ in the literature (Table 1).

In the current report we will consider the differential diagnosis between benign melanonychia,

usually due to the presence of a nevus of the matrix, and malignant melanonychia caused by melanoma.

Regarding malignant melanonychia we will only consider the melanoma starting from the nail matrix (MSNM) which begins with longitudinal melanonychia and may secondarily affect the periungual skin, omitting melanoma that starts from periungual skin and can only later affect the nail matrix causing the appearance of longitudinal melanonychia (16), and even more so the acral melanoma affecting the palmar-plantar region, because only MSNM should be differentiated from benign melanonychia.

Differential diagnosis of LM. Age is even more important for nail melanoma than for cutaneous melanoma. Subjects with nail melanoma are more advanced than those with skin melanoma (8, 16); there seemed to be a slight prevalence of male sex in Asian populations, but the difference is now attenuating (8, 23).

While the acral melanoma is more frequent on the feet, the nail melanoma prevails in the fingers and the big toe is the most affected toe (8). As the actinic rays are not able to stimulate the production of melanin in the melanocytes of the nail matrix they have no role on the onset of the nail melanoma.

LM is the most common mode of presentation of the nail melanoma, so that every melanonychia arising after 30 years must be looked at with suspicion, even more so when the band is wider than 5 mm (8).

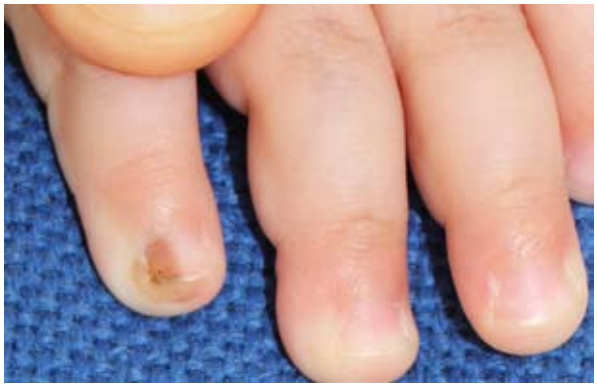
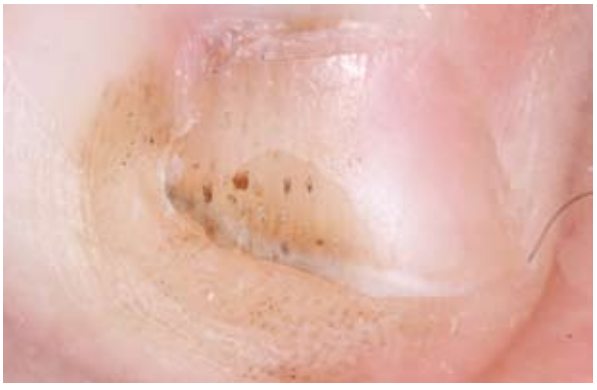


Fig. 5



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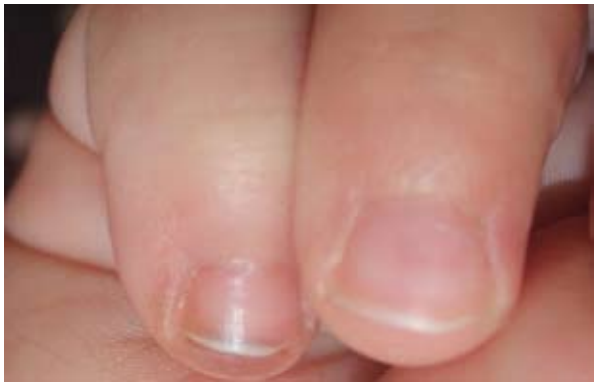

Fig. 7

Fig. 8

Fig. 5, 6, 7, 8: Periungual congenital melanocytic nevus of the fifth finger with longitudinal melanonychia (Fig. 5); dermoscopy examination (Fig. 6) showed irregular globules on the nail and regular pigmentation along the dermatoglyphics on the skin reminiscent of Hutchinton's sign; after 2 years longitudinal melanonychia is no more evident (Fig. 7); in Fig. 8 you can see the triangle sign with pseudoHutchinson in a 2-year-old child with longitutinal melanonychia arisen from 1 month.

Since both the nevus of the matrix and melanoma have an initial phase of growth, in assessing the significance of the width of the band physicians must consider both the age and the history of the lesion. When a 5 mm band is present from the earliest years of life and has stopped growing, it is more likely a congenital or early acquired nevus; when the bands of LM involve more than one finger (Fig. 1) we are more probably facing BLM, especially if the subject has a very dark phototype; when a 5 mm band starts after 30 years and continues to grow, it is more likely melanoma.

The melanonychia band is generally wider in the child (16); however, at this age the different width of the bands (Fig. 2, 3, 4) is less important than in the adult. The presence of a triangular melanonychia with a proximal base is a sign of rapid growth and is suspected for melanoma (triangle sign); however, this sign can also be found in the child's BLM (Fig. 8).

A dark subungual stain unrelated to the matrix may instead be the expression of melanoma arisen from the nail bed (8).

The intensity of the pigmentation does not matter for the differential diagnosis; moreover, about 30% of nail melanomas are amelanotic or poorly pigmented (8); more important is an irregular pigmentation, that can be better highlighted with the help of the dermoscope.

Very important is the presence of melanin pigmentation on periungual skin (Hutchinson's sign) especially when irregularly distributed (12). Important is also the presence of nail dystrophy, linked to the presence of aggregates of suprabasal melanocytes that disturb the production of melanin.

Some Authors (17) wrote an alphabet of nail melanoma with the different aspects to be taken into account in the diagnosis: A Age (50-70 years), African-American, Native American, Asian; B nail Band, Brown-Black, Breadth > 3 mm, irregular Border; C Change (rapid increase in diameter), absence of Change (absence of improvement of nail dystrophy in spite of an appropriate treatment); D single digit (thumb > frequent than allux > more frequent than index finger); E Extension of the pigment to affect the proximal or lateral folds of the nail.

In addition to BLM and MSNM, brownish longitudinal bands can be caused by basal cell carcinoma, Bowen's disease, Peutz-Jeghers and Laugier-Hunziker syndromes, cytostatic drugs, malnutrition, malabsorption, adrenal insufficiency and vitamin B12 deficiency (8).

Differential diagnosis of LM in the child. Benign longitudinal melanonychia in pediatric age may presents many of the characteristics of the primary melanoma of the nail matrix we have already discussed. Some Authors (21) comparing 58 BLM in the child (mean age 5.7 years) and 35 BLM in the adult (mean age 42.4 years) showed that in the child are statistically more frequent some dermoscopic signs like bands of diferent color (Fig. 9, 10, 11, 12), pseudo-Hutchinson (Fig. 15), triangle sign (Fig. 8), points and globules (Fig. 6, 16); other signs such as the width of the bands and their irregularities are more frequent but with a borderline statistical significance.

Other Authors (16) compared the clinical, dermoscopic and histological characteristics of 20 children and 8 adults with BLM due to nevi of the nail matrix. The mean width of LM was on average 3.5 times larger in children than in adults and total melanonychia was observed only in children; nail dystrophy (Fig. 12) and periungual pigmentation (Fig. 5, 6 Hutchinson's sign) was significantly more frequent from a statistical point of view in the child. In 40% of cases the punch-biopsy of the matrix was responsible for subsequent nail dystrophy. Haneke (8) suggested the optimal technique for the complete removal of small lesions of the matrix.

To the clinical and dermatoscopic diagnostic difficulties should be added histological difficulties because as already mentioned in the epidermis of the matrix the melanocytes are physiologically found also outside the basal layer and may show slight dysplasia and nuclear atypia (3, 7, 15, 27); it does not seem a casual coincidence that the 11 primary melanomas of the nail matrix in children described up to now in the literature are all in situ (1, 2, 10, 27) and it is not by chance that the diagnosis has often been problematic according to the Authors themselves (11, 13).

Some Authors (26) argue that the clinical and dermoscopic criteria are not sufficient to resol-

ve the doubt about the benignness or malignancy of a melanonychia; other Authors (3) argue that some of the cases labeled as in situ melanomas have histological characteristics superimposable to those diagnosed as atypical melanocytic hyperplasia.

The examination of Table 1 shows how the primary melanoma of the nail matrix in the child affects 8 Asian children or in any case children with a dark phototype; only 3 cases of MSNM were diagnosed in white children with a light phototype and in all three cases they were Italian


Fig. 9

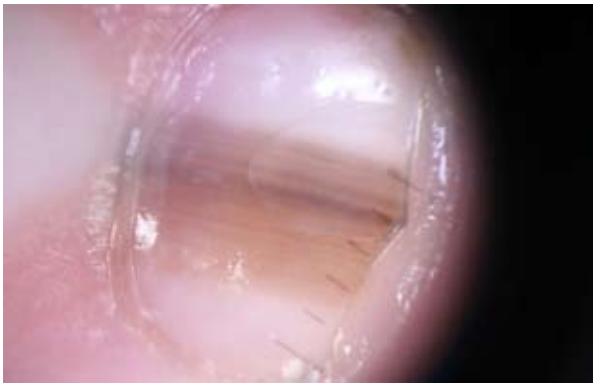
Fig. 10

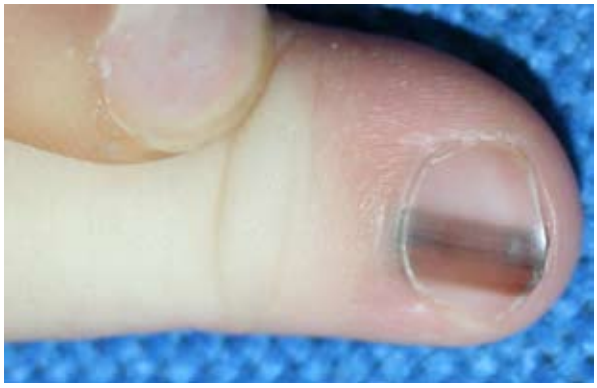
Fig. 11

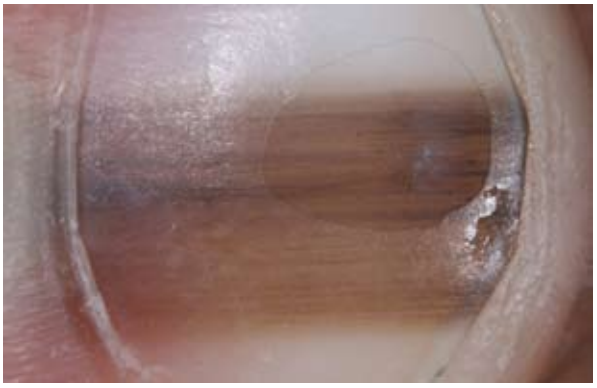
Fig. 12

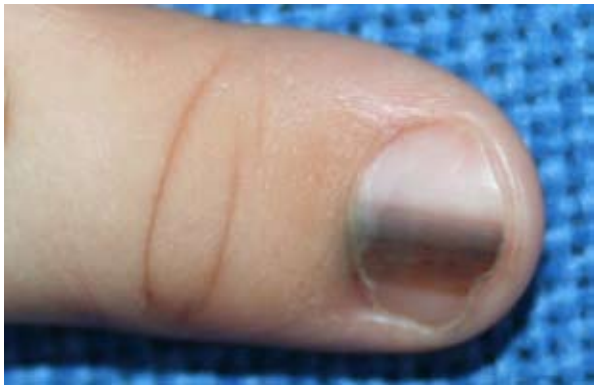
Fig. 13


Fig. 14

Fig. 9, 10, 11, 12, 13, 14: The three clinical images (Fig. 9, 11, 13) with the relevant dermoscopy findings (Fig. 10, 12, 14) were taken at an interval of 1 year from each other; you can see the changes with time more evident in the dermoscopy images (bands of different color, onychodystrophy in Fig. 12, irregular pigmentation in Fig. 14).

Fig. 15

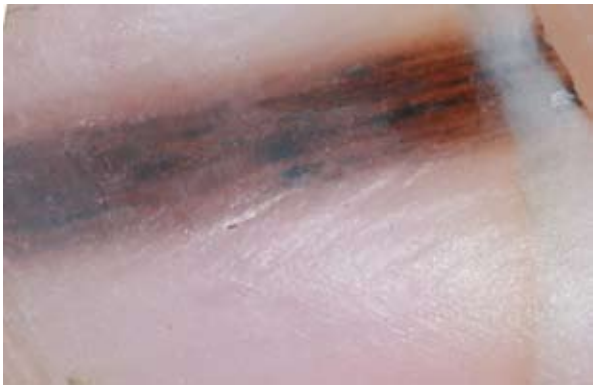

Fig. 16

Fig. 17

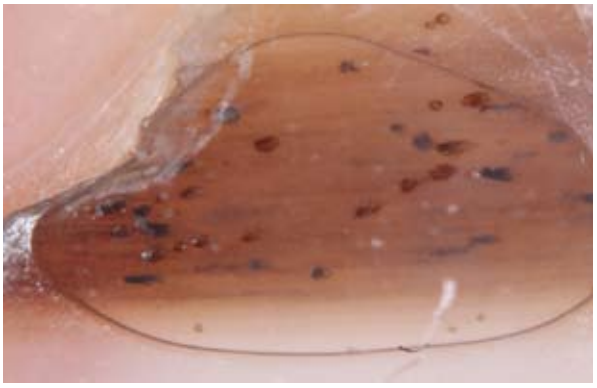

Fig. 18

Fig. 15, 16, 17, 18: Pseudo-Hutchinson in longitudinal melanonychia of Fig. 15 that on dermoscopy (Fig. 16) shows irregularly pigmented bands. In Fig. 17 marginal longitudinal melanonychia that on dermoscopy (Fig. 18) shows globules of different size and color.

TABLE 1: Primary melanoma of the nail matrix in children.

Author reference	*Sex*	*Country*	*Age of onset (years)*	*Site*	*Pathology*
Hori et Al. 9	F	Japan	?	5th finger	in situ
Kato et Al. 11	M	Japan	1	3rd finger	in situ
Kato et Al. 11	F	Japan	1½	2nd finger	in situ
Kato et Al. 11	F	Japan	½	Hallux	in situ
Kyriu 13	F	Japan	3	5th finger	in situ
Antonovich et Al. 1	F	Philippines	1	4th finger	in situ
Iorizzo et Al. 10	F	Argentine	1	3rd finger	in situ
Iorizzo et Al. 10	M	Brazil	6	Hallux-	in situ
Tosti et Al. 26	M	Italy	½	Hallux	in situ
Tosti et Al. 26	F	Italy	1	2nd finger	in situ
Bonamonte et Al. 2	M	Italy	2	5th finger	in situ

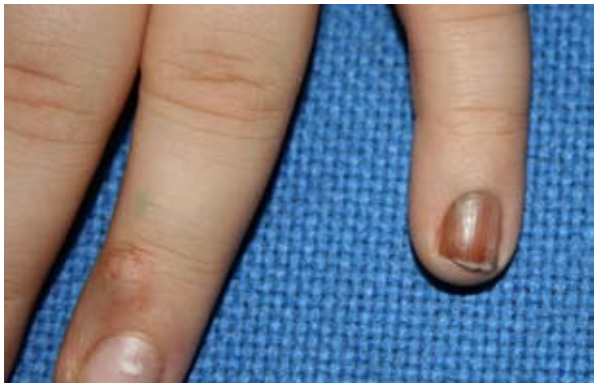

Fig. 19

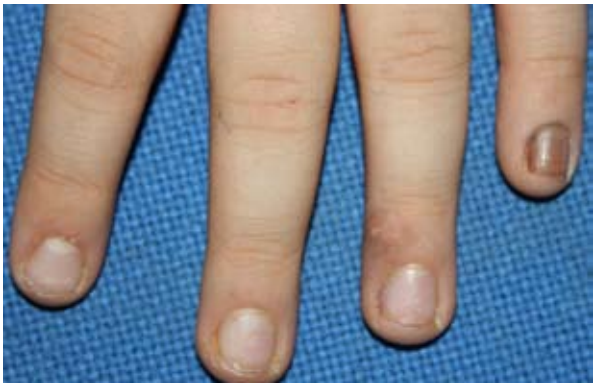

Fig. 20

Fig. 19, 20: Last case of Table 1 (ref. 2). Total melanonychia of the left fifth finger with pseudo-Hutchinson sign of the nail cuticle in a -5-year-old child (Fig. 19) started at the age of 2; at the age of 7 (Fig. 20) there were no significant changes. After two more years a biopsy of the matrix led to diagnose melanoma in situ and to radically remove the nail apparatus.

children; as far as the affected sites are concerned, the involvement of the fingers prevails – 8/11 cases – and the most frequently affected finger is the 5th finger – 3/8 cases –; the 3 cases affecting the toes are all localized to the hallux.

How to behave when facing a LM in children. The School of Pediatric Dermatology in Bordeaux (15), after having followed 8 cases of LM of the child on average for 5.5 years, after having done in 5 cases biopsies that ascertained the benign nature of LM although leaving dystrophic outcomes, stated that the LM in pediatric age should be bioptized following the same criteria for which a biopsy is performed in the common acquired or congenital melanocytic nevi of the skin in pediatric age.

Other Authors (7) performed biopsy in 40 children (mean age 8 years) with LM diagnosing nevus in 19 cases, simple lentigo in 12 and functional LM in 9 cases. In many cases they found dysplasia, nuclear atypia, transepidermal melanocytic migration, stating that these findings are non-exceptional in common melanocytic nevi in the pediatric age. The Authors believed that some cases of the literature labeled as melanoma in situ (11) were actually BLM because they were similar to those ones examined by themselves; the Authors concluded that a LM biopsy in the child should be performed only in the event of rapid evolutiont of the lesion.

Iorizzo et Al. (10) stated that all cases of the literature including their cases are melanoma in situ and the diagnosis of melanoma was long discussed; they questionned the case of melanoma in situ of Lyall (18) and stated that when facing a child's LM the best attitude is wait and see especially when clinical and dermoscopic signs indicate a low risk of melanoma and particularly in the absence of modifications over time.

In conclusion, the current report reviewed the 11 cases of primary melanoma of the nail matrix clinically characterized by longitudinal melanonychia described in the relevant literature. 8/11 children were Asian or South American with dark skin phototype; the only 3 white children with fair skin phototype were Italian. In all cases the histological diagnosis talked about melanoma in situ.

The clinical criteria that must raise the suspicion of primary melanoma of the nail matrix in the adult are the involvement of periungual skin, ulceration, nail dystrophy, the presence of a longitudinal band more than 3 mm wide and above all the rapid enlargement of a melanocytic band.

These criteria are less valid in the child. The only alarming sign in children is the rapid and continuous enlargement of a longitudinal melanonychia. Due to the scarcity of cases of primary melanoma of the nail matrix in children, there are no reliable clinical, dermoscopic and histological criteria of diagnosis.

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