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Original Research

Longitudinal melanonychia in an Iranian population: a study of 96 patients

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ABSTRACT

Background: Longitudinal melanonychia (LM) can be a challenging sign since it may be caused by a wide variety of benign and malignant conditions. Cutaneous melanoma is the most important cause of LM. **Objective:** We performed this study to examine different aspects of LM in Iran, where cutaneous melanoma is rare.

Methods: In this cross-sectional study, we reviewed medical records and pathology reports of a total of 96 patients presenting with LM. These patients had been visited and undergone nail biopsy in Razi Hospital, Tehran University of Medical Sciences, Tehran, Iran. Demographic, clinical, and pathological data were recorded.

Results: The most common diagnosis was junctional nevi in 28 patients (29.2%) followed by melanoma in 19 patients (19.8%). Patients had a mean age of 42.4 years (± 19.4). The mean ages in the groups with junctional nevi and melanoma were 33.3 (± 19.5) and 51.9 (± 17.8), respectively; their difference was statistically significant (P value = 0.001). Hutchinson's sign was present in 10 patients, 9 of which had melanoma. Also, melanoma was only observed in patients presenting with a solitary nail lesion. Nails mostly affected by melanoma were middle fingers of the hands (7 patients) and thumbs (6 patients). Out of 18 patients with nail dystrophy, 13 (72.2%) were diagnosed with melanoma.

Limitations: Only patients who have undergone biopsy were studied.

Conclusion: Melanoma is an important cause of LM in Iranian patients and should especially be suspected in older patients who present with a solitary nail lesion on their middle finger or thumb. Other findings that direct us toward melanoma are presence of Hutchinson's sign and nail dystrophy.

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Introduction

Longitudinal melanonychia (LM) refers to brown, black, or grayish bands on the long axis of the nail that run from the proximal nail fold to the distal free edge. Although pigmented bands on the nail can be caused by hemorrhage, infections, drugs, etc., the brown-black appearance in LM is commonly caused by melanin deposition in the nail plate (Baran and Kechijian, 1989; Di Chiacchio et al., 2013b; Sohn et al., 2015). Melanocytes of the nail are primarily located in the suprabasal layer of the matrix, and melanin is produced

by these melanocytes (Baran and de Berker, 2010; Dominguez-Cherit et al., 2008; Theunis et al., 2011).

From a histological perspective, longitudinal melanonychia can occur due to melanocytic activation (hypermelanosis), melanocytic hyperplasia (lentigo), melanocytic nevi, and nail apparatus melanoma (Baran and de Berker, 2010; Baran and Kechijian, 1989). In melanocytic activation, the number of melanocytes in the nail matrix is not increased, but the melanin content that is deposited in the nail plate is more than usual (Ruben, 2010). Racial melanonychia, a very common form of melanonychia, is mostly the result of this process and is seen commonly in blacks and Asians (Dominguez-Cherit, et al. 2008; Elder et al., 2008). Melanocytic hyperplasia is a benign process in which the number of nail melanocytes is moderately increased and the resulting lesion is a lentigo. Nail matrix nevi are usually junctional and comprise the major cause of melanonychia in children

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(Ruben, 2010). Nail apparatus melanoma is the most important cause of LM, but if diagnosed and treated early in the course of the disease, the survival rate increases dramatically (Baran and de Berker, 2010). Cutaneous melanoma is much rarer in Iran, compared to western countries (Noorbala et al., 2013).

Until now, no studies have been done on Iranian patients presenting with LM. In this study, we tried to evaluate different aspects of LM in Iranian patients to ascertain the causes of LM and their relative frequencies.

Methods

In this cross-sectional study, we reviewed the medical records and pathology reports of 96 patients with clinical diagnosis of LM who had undergone nail biopsy between September 2006 and September 2010 in Razi Hospital, Tehran University of Medical Sciences, Tehran, Iran. Our patients were Iranians who were mostly of skin phototypes III or IV. Clinical data including age, gender, number, and name of involved fingers, presence of nail dystrophy, and presence of the Hutchinson's sign and pathological diagnosis were collected. Pathological slides were reexamined by a dermatopathologist if previous reports were inconclusive or incomplete.

Quantitative variables were presented as mean \pm standard deviation (SD), and qualitative variables as frequency and percentage. Chi-square test and student t-test were used whenever appropriate. P value less than 0.05 was considered significant.

Results

A total of 96 patient records were reviewed in this study. Fifty-eight of our patients were female (60.4%) and 38 were male (39.6%). The mean age of the patients was 42.4 years old (\pm 19.4), and their age range was between 5 and 86 years. The most frequent histopathological diagnosis among them was junctional nevus observed in 28 patients (29.2%). Melanoma was diagnosed in 19 patients (19.8%). The frequencies of different pathological diagnoses of melanonychia based on the patients' gender and age have been summarized in Table 1. There was no significant difference between the two genders in regard to the frequencies of any of the diagnoses (P value = 0.37).

Hutchinson's sign was recorded in a total of 10 patients (10.4%). Nine were diagnosed with melanoma, and one patient had a junctional nevus.

Eighteen patients had dystrophic nails (18.7%); 13 were in the group with the diagnosis of melanoma.

In 88 patients, only one nail was affected with melanonychia (91.6%); in one patient, all 20 nails were affected (1%), and the rest of the patients had melanonychia in multiple nails but not all of them. Melanoma was only found in patients presenting with a single nail lesion. In 25 patients, the affected nail was the thumb (26%); in 24 patients, the big toe (25%) was affected; in 18 patients, the index finger of the hand was involved (18.75%).

Table 1
Frequency of different types of longitudinal melanonychia (LM) based on patients' gender and age.

Diagnosis	Mean age (SD)(year)	Male	Female	Total
Junctional nevi	33.3 (19.5)	12 (42.9%)	16 (57.1%)	28 (29.2%)
Melanoma	51.9 (17.8)	5 (26.3%)	14 (73.7%)	19 (19.8%)
Hemorrhage	46.8 (20.9)	10 (58.8%)	7 (41.2%)	17 (17.7%)
Racial LM	42.9 (14.8)	4 (26.7%)	11 (73.3%)	15 (15.6%)
Inflammation	43.3 (19.2)	5 (38.5%)	8 (61.5%)	13 (13.5%)
Lentigo	37.0 (17.9)	2 (50%)	2 (50%)	4 (4.2%)
Total	42.4 (19.4)	38 (39.6%)	58 (60.4%)	96 (100%)

After histopathological examination, in 14 patients' specimens, a pagetoid spread was observed, all of whom were diagnosed with melanoma.

The mean age in the group with the diagnosis of junctional nevi was 33.3 years (\pm 19.5), 16 of them were female (57.1%), and the other 12 were male (42.9%). Only 3 patients in this group had multiple affected nails while the rest had presented with a single nail lesion. We had a total of 33 nail biopsies with the diagnosis of nevi; seven of these were in thumbs, and another 7 were in index fingers. Another 5 biopsies were from the middle fingers of the hands, and 4 were taken from the big toes.

Among all 19 patients who had melanoma, the mean age was 51.9 years old (\pm 17.8), 5 of them were male (26.3%), and the other 14 were female (73.7%). The most frequently involved nails were middle fingers of the hand (7 patients) and thumbs (6 patients), and all of the lesions were solitary.

The mean age of patients with melanoma (51.9 years old) was significantly higher than patients with junctional nevi (33.3 years old) (P value = 0.001).

Nine patients were in the pediatric age group (18 years old or younger). In 6 patients, junctional nevi were the cause of LM. Inflammation was seen in two patients, and the remaining one was due to hemorrhage. No melanoma was found.

Discussion

The presence of LM is a helpful clue in the diagnosis of melanoma, a disease that may be associated with a high mortality rate. Early diagnosis and treatment of melanoma can affect prognosis and increase patients' 5-year survival rate; therefore, it is important to determine clinical and histopathological characteristics of melanoma in patients with LM (Baran and de Berker, 2010; Carreño et al., 2013). Features that suggest a possible malignant melanoma of the nail include the presence of LM on the thumb, index finger, or big toe confined to only one finger or toe, sudden appearance of LM in an adult, irregular shape and color variation of the band, rapid changes in the shape and color of the lesion, presence of Hutchinson's sign (extension of pigmentation to adjacent nail folds or to the hyponychium), and nail dystrophy (Baran and de Berker, 2010). A triangular band that is broader proximally is cause for concern (Di Chiacchio et al., 2013a, 2013b). Based on these features, if melanoma is suspected, a nail biopsy and subsequent histopathological examination of the lesion should be performed (Baran and de Berker, 2010; Di Chiacchio et al., 2013b). Levit et al. (2000) developed an acronym (the ABCDEF rule) for the diagnosis of subungual melanoma which stands for Age; Band, Breadth, and Border; Change; Digit involved, Dominant hand; Extension; Family or personal history. However, neither this rule nor dermoscopy improved the overall diagnostic accuracy of dermatologists in the diagnosis of nail matrix melanoma in situ (Di Chiacchio et al., 2010).

In our study, the most common cause of LM was junctional nevi, followed by melanoma. Melanoma was only observed in patients who presented with a solitary lesion in one finger. In addition, the presence of Hutchinson's sign and nail dystrophy were strong indicators of melanoma. Also, observing a pagetoid spread on microscopy seemed to be an exclusive finding in melanoma.

Up until this time, not many large-scale studies have been carried out on the causes of LM (Table 2).

The rate of melanoma as a cause of LM seems to be higher in our patients compared with most other studies. This can reflect a selection bias since biopsy is not performed routinely in all cases of LM; only patients in whom there was a higher suspicion of an underlying melanoma were biopsied. As expected and in accordance to most previous studies, melanoma presented exclusively as a single band (Baran and de Berker, 2010; Carreño et al., 2013; Molina and Sanchez,

Table 2
Studies on longitudinal melanonychia.

Authors	Number of patients	Country	Causes	Comments
Dominguez-Cherit et al. (2008)	68 Hispanics	Mexico	48 (68.7%) racial melanonychia; 3 (4.3%) melanoma	Two melanoma cases had LM on more than one finger.
Molina and Sanchez (1995)	18 Hispanics	Puerto Rico	10 racial melanonychia, one case of melanoma in situ and one case of keratinocytic proliferation with focal atypia	
Sobjanek et al. (2014)	36	Poland	21 lentigo, 10 nevi, and 2 melanoma. Two racial melanonychia	Melanonychia was observed more commonly in people with III and IV phototypes.
Theunis et al. (2011)	40	Belgium	19 acral lentiginous melanoma, 10 racial LM, and 7 junctional nevi.	
Goettmann-Bonvallet et al. (1999)	40 children less than 16 years of age	France and Belgium	Nevi in 19 patients, lentigo in 12 and functional longitudinal melanonychia in 9. No melanoma.	
Astur et al. (2016)	352 (58 were biopsied)	Brazil	Hypermelanosis in all 58 patients (racial melanonychia)	Even with brown or black coloration of the background by dermoscopy
Sawada et al. (2014)	137 (18 were biopsied)	Japan	122 functional melanonychia (nevus/lentigo), 15 melanoma in situ	
Cooper et al. (2015)	30 children (18 years old or younger)	United States	No cases of melanoma. Twenty had lentigo, 5 were diagnosed with nevi, and the remaining 5 had atypical melanocytic hyperplasia.	
Ronger et al. (2002)	148 consecutive cases	France	Melanoma, 20; melanocytic nevus, 37; drug induced, 16; lentigo, 45; ethnic type, 8; hemorrhage, 22.	
Jin et al. (2016)	275 cases (35 biopsy)	Korea	Subungual hemorrhage (29.1%), nevus (21.8%), trauma-induced pigmentation (14.5%), lentigo (11.6%), ethnic-type pigmentation (8.0%), and melanoma (6.2%)	

1995; Perrin, 2013; Ruben, 2010; Tosti et al., 2012). Interestingly, two out of three melanoma cases reported by Dominguez-Cherit et al. (2008) had LM in more than one finger (Dominguez-Cherit et al., 2008). This suggests that the presence of racial melanonychia in multiple nails does not rule out melanoma and that all lesions need to be properly investigated.

We had 18 patients with nail dystrophy, 13 (72.2%) of which were eventually diagnosed with melanoma while in the study carried out by Dominguez-Cherit et al. (2008), and none of their three melanoma patients had nail dystrophy. This may be due to late diagnosis in some of our cases.

The mean age of our patients was 42.4 years while the mean age among the group that was diagnosed with melanoma was almost a decade more at 51.9 years. Also, patients who were in the group with the most common diagnosis, which was junctional nevi, had a mean age of 33.3 years, nearly two decades younger than our melanoma patients. These findings further suggest that the presence of LM in older adults is more alarming and requires more attention.

The nails that were most frequently affected were quite similar between the group with melanoma and the group with junctional nevi. In both groups, lesions had presented more frequently in thumbs. Index and middle fingers of the hands were also commonly affected in both groups. Interestingly, only fingers were involved in our melanoma cases.

Racial melanonychia was seen in 15.6% of our Iranian patients who are mostly of skin phototypes III and IV. Our findings differ from Hispanic studies (70%) (Astur et al., 2016; Dominguez-Cherit et al., 2008; Molina and Sanchez, 1995), and this may reflect that racial melanonychia is especially common in Hispanic and African-American populations.

In this study, we had 9 patients in the pediatric age range of 18 years old or younger, two-thirds of them were diagnosed with junctional nevi. No melanoma was found in our pediatric patients; a finding that is in accordance with previous studies. This suggests that the presence of LM in children is less likely to be due to melanoma, and

since invasive diagnostic procedures carry a risk for future dystrophy of the nails, more caution should be used in proceeding to aggressive procedures such as biopsies in children (Cooper et al., 2015; Goettmann-Bonvallet et al., 1999; Koga et al., 2016).

Dermoscopy is used increasingly as an adjunct, noninvasive tool in assessing LM (Haenssle et al., 2014). It is especially helpful in distinguishing blood from melanin (Di Chiacchio et al., 2013a, 2013b; Goettmann-Bonvallet et al., 2014). In general, thin gray lines on a homogenous background are mostly due to benign melanocytic activation while a brown background with lines that vary in shape, color, width, and spacing is more likely to be caused by melanoma though some benign lesions show the same features (Di Chiacchio et al., 2013a, 2013b). A diffusely dark background without any lines or with areas of different hue of pigmentation is also suggestive of melanoma (Di Chiacchio et al., 2013a, 2013b). According to a consensus on melanonychia nail plate dermatoscopy, it is always necessary to rely on clinical suspicion (history and physical examination) when deciding to perform a nail biopsy rather than dermoscopic pattern alone (Di Chiacchio et al., 2013a). On the other hand, intraoperative dermatoscopy had a higher sensitivity and specificity (Di Chiacchio et al., 2010; Göktay et al., 2015; Hirata et al., 2011).

The main limitation of the present study is that only patients who have undergone biopsy were studied. This study does not reflect the true frequency of different causes of LM as many less-suspicious lesions are not biopsied in routine clinical practice and melanoma cases are overrepresented.

Conclusion

Although melanoma is rare in Iran compared with western countries (Noorbala et al., 2013), in our study, performing biopsies on patients with LM led to the diagnosis of melanoma in almost one fifth of cases. Our study confirms that a high index of suspicion for melanoma is needed in every case of LM especially in older age groups, patients with Hutchinson's sign, and solitary nail involvement.

Conflict of interest

None.

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