The correlation between clinical and pathologic manifestations in nail disorders in Razi Hospital

Behzad Khodaei, MD [1,2]
Simin Seyedpour, MD [1,2]
Bahareh Gholami, MD [1]
Kambiz Kamyab Hesari, MD [3]
Seyed Ahmad Seyed Alinaghi, MD, M.Phil, PhD [4]
Maryam Nasimi, MD [5*]

1. Tehran University of Medical Sciences, Tehran, Iran
2. Nanomedicine Research Association, Universal Scientific Education and Research Network (USERN), Tehran, Iran
3. Department of Dermatopathology, Razi Hospital, Tehran University of Medical Sciences, Tehran, Iran
4. Iranian Research Center for HIV/AIDS, Iranian Institute for Reduction of High-Risk Behaviors, Tehran University of Medical Sciences, Tehran, Iran
5. Department of Dermatology, Razi Hospital, Tehran University of Medical Sciences, Tehran, Iran

*Corresponding author:
Maryam Nasimi, MD
Department of Dermatology, Razi Hospital, Tehran University of Medical Sciences, Tehran, Iran
Email: Nsm.maryam@gmail.com

Received: 01 January 2021
Accepted: 25 April 2021

Background: Nail disorders present with a wide range of manifestations. The problems associated with nail biopsies make the diagnosis even more challenging. Identifying the most common features of each nail disorder can prevent unnecessary biopsies and facilitate early diagnosis.

Methods: We conducted a cross-sectional study on 528 pathology reports, documented from March 2018 to March 2019 in the Razi Dermatopathology Hospital, Tehran, Iran. We extracted the demographic data and the nails' clinical and pathologic presentations. We used Fisher's exact test to determine the nail features' clinicopathological correlations.

Results: The mean age of the 359 included patients was 38.81 ± 18.11 years, and 50.81% were male. Benign melanonychia (12.82%), traumatic nail (11.96%), and junctional nevus (11.11%) were the most prevalent disorders. Onycholysis ($P < 0.001$), longitudinal ridges ($P < 0.001$), subungual hyperkeratosis ($P = 0.003$), dystrophy ($P = 0.017$), discoloration ($P = 0.052$), and pitting ($P < 0.001$) correlated significantly with nail psoriasis. The presence of subungual hyperkeratosis, onycholysis, and longitudinal ridges significantly increased the odds of nail lichen planus. Only 6.79% of patients with longitudinal melanonychia had malignant melanoma, while most (26.54%) correlated with benign melanonychia.

Conclusions: A detailed examination can narrow the differential diagnosis and avert unnecessary biopsies. However, in high-risk cases, physicians should regularly monitor the nails' changes and response to treatment.

Keywords: nail diseases, pathology, biopsy

Iran J Dermatol 2022; 25: 41-45

DOI: 10.22034/ijd.2021.265058.1301

INTRODUCTION

Nail disorders account for 10% of dermatology visits [1]. Diagnosing nail diseases is challenging. On the one hand, a specific nail lesion resembles a broad spectrum of differential diagnoses as most nail diseases share the same characteristics. On the other hand, unlike other dermatologic conditions, a biopsy is not indicated in initial nail disorder assessments because of subsequent iatrogenic nail dystrophy [2]. Other disadvantages of the nail biopsy include pain, functional impairment, and a poor cosmetic appearance. However, it is essential to quickly diagnose life-threatening disorders such as malignancies timely [3]. Therefore, identifying the most common features of each disorder can

facilitate a proper diagnosis. Only a few studies have investigated the association of clinical and pathology findings in nail lesions. We aimed to determine the frequency of nail manifestations and their association with the pathologic diagnosis in our dermatopathology department.

PARTICIPANTS AND METHODS

In this cross-sectional study, we reviewed 528 medical documents in the dermatopathology department of Razi Hospital, Tehran, Iran. A dermatologist provided a detailed report of the clinical history and physical examination of the patients, who referred to the clinic of Razi Hospital from March 2018 to March 2019. A detailed explanation of the nails' clinical features was also attached to the final pathology report in the patients' medical documents. Documents with missing/incomplete or vague clinical data and biopsy reports from unrelated sites (samples that did not contain nail tissue) were excluded. We extracted demographic data (age and gender), clinical history, nail characteristics, and pathology reports retrospectively from the patients' medical documents. We used Fisher's exact test to discover the association between the pathological diagnosis and the nail presentations. Odds ratios with respective 95%CI were shown for these associations. We also presented descriptive data as mean, range, and percentage. This study received approval from the local institutional ethics committee (IR.TUMS.MEDICINE.REC.1397.583).

RESULTS

Of 528 reviewed reports, we excluded 38 documents due to incomplete records or unrelated biopsy sites. Of 490 included documents, 131 reported normal or inconclusive pathology findings. The mean age of patients was 38.81 ± 18.11 years (range 3 to 84 years), and 50.81% were male.

The most frequent diagnoses of nail disorders were as follows: pigmented lesions in 123 patients (including benign melanonychia, junctional nevus, lentigo melanotic macule, and malignant melanoma), infections in 59 (including onychomycosis, paronychia, and wart), benign neoplasm in 46 (fibrokeratoma, glomus tumor, myxoid cyst, neurofibroma, onychomatricoma, pyogenic granuloma, subungual osteochondroma, subungual epidermoid cyst, subungual keratoacanthoma, superficial acralfibromyxoma), psoriasis in 32, lichen planus in 24, and non-melanocytic skin cancers in 10 patients.

Benign melanonychia (12.82%), traumatic nail (11.96%), and junctional nevus (11.11%) were the most prevalent disorders. Table 1 summarizes the association between various nail features and their pathological diagnosis. Nail psoriasis manifested with various presentations, of which pitting (40.63%), onycholysis (40.63%), and subungual hyperkeratosis (25%) were most prevalent (Table 1). Significant correlations were seen with onycholysis ($P < 0.001$), longitudinal ridges ($P < 0.001$), subungual hyperkeratosis ($P = 0.003$), dystrophy ($P = 0.017$), discoloration ($P = 0.052$), and pitting ($P < 0.001$) (Table 1). The presence of subungual hyperkeratosis (OR = 13.49, 95%CI: 5.37-33.91), onycholysis (OR = 5.38, 95%CI: 2.19-13.22), and longitudinal ridges (OR = 23.71, 95%CI: 7.64-73.53) significantly increased the odds of a pathological diagnosis of lichen planus. Also, nail dystrophy and distal and lateral subungual hyperkeratosis were significantly associated with onychomycosis. As expected, verrucous lesions (40.91%) were significantly associated with nail warts.

Longitudinal melanonychia was the most frequent complaint in patients with pigmentary disorders. Most of their biopsied lesions were due to benign melanonychia (26.54 %), while only 6.79% of them had malignant melanoma (Table 2).

DISCUSSION

Nail abnormalities occur due to systemic and local disorders, including infections, medications, vascular disorders, environmental conditions, trauma, and benign and malignant tumors. Nail disorders are sometimes missed during general physical examinations despite being readily detectable. However, they may be the early manifestations of a specific disease. In the present study, most nail biopsies were obtained due to pigmentary lesions, including benign melanonychia, nail trauma, and junctional nevus.

Lichen planus can involve 1 to 20 nails in 10% of cases [4]. The matrix involvement in lichen planus presents with longitudinal ridges, a common manifestation in our cases and the patients of

Table 1. The frequency of nail presentations in each nail disorder

Skin disorders (No. of patients)	Nail changes	No.	Percent (%)	OR (95%CI)	*P*-value
Lichen planus (N=24)	Subungual hyperkeratosis	11	45.83	13.49 (5.37-33.91)	<0.001
	Onycholysis	9	37.5	5.38 (2.19-13.22)	0.001
	Dystrophy	4	16.67	2.13 (0.68-6.67)	0.257
	Longitudinal ridges	8	33.3	23.71 (7.64-73.53)	<0.001
	Longitudinal melanonychia	3	12.5	0.16 (0.04-0.56)	0.001
	Pterygium	4	16. 7	NC	<0.001
Psoriasis (N=32)	Onycholysis	13	40.63	6.86 (3.08-15.26)	<0.001
	Longitudinal ridges	7	21.88	11.30 (3.79-33.72)	<0.001
	Subungual hyperkeratosis	8	25	4.46 (1.80-11.03)	0.003
	Dystrophy	7	21.88	3.28 (1.29-8.31)	0.017
	Beau's lines	1	3.13	NC	0.088
	Discoloration	4	12.5	3.49 (1.06-11.43)	0.052
	Pitting	13	40.63	225.78 (28.04-1817.90)	<0.001
	Paronychia	1	3.13	0.24 (0.03-1.81)	0.231
Onychomycosis (N=13)	Dystrophy	4	30.8	4.92 (1.42-16.95)	0.023
	Paronychia	2	15.4	1.49 (0.31-6.99)	0.643
	Discoloration	1	7.69	1.74 (0.21-14.21)	0.47
	Onycholysis	4	30.77	3.54 (1.04-12.05)	0.055
	Distal subungual hyperkeratosis	4	30.8	5.31 (1.53-18.40)	0.018
	Lateral subungual hyperkeratosis	1	7.7	NC	0.036
Wart (N=22)	Verrucous lesion	9	40.91	58.32 (15.87-214.35)	<0.001
	Dystrophy	3	13.64	1.63 (0.45-5.85)	0.437
	Hyperkeratotic papules	3	13.6	17.78 (3.36-94.09)	0.003
	Subungual hyperkeratosis	3	13.6	1.76 (0.49-6.33)	0.419
	Onycholysis	5	22.73	2.34 (0.81-6.71)	0.161
	Hyperkeratosis	2	9.1	3.31 (0.67-16.13)	0.16
Paronychia (N=24)	Nail fold inflammation	11	45.83	9.04 (3.72-21.99)	<0.001
	Discoloration	4	16.7	5.01 (1.49-16.7)	0.02
	Onycholysis	4	16.7	1.53 (0.50-4.73)	0.508
	Dystrophy	4	16.7	2.13 (0.68-6.67)	0.257
	Scaling	2	8.3	NC	0.004
	Hyperkeratosis	4	16.7	8.27 (2.29-29.83)	0.005
	Melanonychia	1	4.2	0.049 (0.007-0.36)	<0.0001
Glomus tumor (N=6)	Onycholysis	0	0	NC	1
	Nodular lesion	4	66.70	49 (8.26-290.42)	<0.001
	Bluish nodule	2	33.30	178 (13.28-2384.27)	0.001
	Longitudinal erythronychia	2	33.30	NC	<0.001
Onychomatricoma (N=15)	Subungual hyperkeratosis	4	26.7	4.32 (1.28-14.49)	0.031
	Dystrophy	1	6.7	0.70 (0.90-5.54)	1
	Hyperkeratotic papule	3	20	28.75 (5.24-157.47)	0.001
Fibrokeratoma (N=6)	Nodular lesion	2	33.3	10.65 (1.81-62.55)	0.031
	Dystrophy	2	33.3	5.25 (0.92-29.86)	0.095
	Hyperkeratotic polypoid lesion	2	33.3	28.75 (5.24-157.47)	0.001
Superficial acral fibromyxoma (N=4)	Nodular lesion	2	33.3	10.65 (1.81-62.55)	0.031
	Bluish nodule	1	25	59.50 (4.17-847.09)	0.033
	Paronychia	1	25	2.73 (0.27-26.94)	0.37
	Exophytic lesion	1	25	NC	0.011
Squamous cell carcinoma (N=4)	Dystrophy	2	50	10.58 (1.44-77.73)	0.043
	Hyperkeratosis	1	25	10.54 (1.01-109.6)	0.126
	Onycholysis	1	25	2.51 (0.25-24.74)	0.397
	Verrucose lesion	1	25	9.63 (0.93-99.58)	0.136

Table 2. The frequency of nail presentations in each pigmentary disorder

Nail changes	Pigmentary disorder	No. of cases	Percent (%)	*P*-value
Longitudinal melanonychia	Benign melanonychia	43	26.54	<0.001
	Malignant melanoma	11	6.79	0.006
	Lentigo	5	3.08	0.016
	Melanotic macule	24	14.81	<0.001
	Nevus	39	24.07	<0.001
	Traumatic nail	40	24.69	0.197
Onycholysis	Benign melanonychia	1	25	0.027
	Traumatic nail	3	75	0.234
Subungual hyperkeratosis	Benign melanonychia	1	20	0.021
	Traumatic nail	4	80	1.00
Splinter hemorrhage	Traumatic nail	1	100	0.086
Pigmented nodule	Malignant melanoma	1	100	0.081

Goettmann *et al.* (89.5%) and Karim *et al.* (25%) [3,5]. According to Goettmann *et al.*'s study, onycholysis, which results from nail bed involvement, is another frequent finding (43.3%) among lichen planus patients [5]. Likewise, 37.5% of lichen planus patients presented with onycholysis in our study. Besides, hyperkeratosis significantly correlated with lichen planus, as seen in previous studies [3,5].

Nail involvement is common in psoriasis patients, accounting for 40 to 45 % of all psoriasis cases. Similar to lichen planus, it could be the only presentation of disease in a small group of patients [4]. Our study results showed that signs such as onycholysis, longitudinal ridges, subungual hyperkeratosis, dystrophy, and pitting increased the odds of a diagnosis of psoriasis. Likewise, in a study by Salomon *et al.*, subungual hyperkeratosis (79.5%), pitting (56.6%), longitudinal ridges (32.5%), and dystrophy (20.5%) were the most prevalent presentations of psoriasis in the fingernails [6].

Onychomycosis is another important differential diagnosis that can have various manifestations. In contrast to psoriasis and lichen planus, it often involves one nail [4]. The clinical findings of onychomycosis in our patients were similar to the cases of Karim *et al.*, where subungual hyperkeratosis accounted for the majority of cases (74.4%), followed by dystrophy (20%) [3]. Similarly, distal and lateral subungual hyperkeratosis, as well as dystrophy, were significantly associated with onychomycosis. Infection with the human papillomavirus causes warts that mostly involve the nail folds [4]. Läuchli *et al.* reported that nail warts present with a verrucous, painful lesion, or onycholysis, similar to our findings [7]. Hyperkeratotic papules with subungual hyperkeratosis are also common manifestations of viral warts [4].

Pigmented lesions were the most common clinical presentation in our study. Tosti *et al.* reported a similar finding in their study on 100 patients. Longitudinal melanonychia was the most prevalent manifestation in 65% of melanocytic activation, 8% of melanocytic hyperplasia, 22% of nevus, and 5% of melanoma cases [8].

Onychomatricoma is a nail matrix fibroepithelial tumor [9]. Clinically, this condition features a thickened, over-curved yellow plate with multiple small honeycomb-like holes [10]. In our study, onychomatricoma was associated with subungual hyperkeratosis and hyperkeratotic papules.

Glomus tumors are benign vascular tumors that can also involve the nails [4]. These tumors presented with painful bluish nodules and longitudinal erythronychia in our cases. Comparatively, Dominguez-Charit *et al.* reported erythronychia and distal onycholysis as the most common presentations of glomus tumors [11].

Squamous cell carcinoma (SCC) of the nail has various nonspecific clinical presentations. These include onycholysis, dystrophy, subungual hyperkeratosis, and verrucous lesions. In our study, onycholysis had a significant clinical association with SCC. Furthermore, Dalle *et al.* also reported subungual hemorrhage, trachyonychia, longitudinal melanonychia, erythronychia, and leukonychia as nail SCC presentations [12].

Most nail disorders manifest similar features; however, the patients' clinical history is useful for narrowing down this diagnosis. In our study, patients with pigmentary nail lesions had the most frequent nail biopsy referrals. However, most had benign disorders in the final pathologic diagnosis.

Therefore it is suggested that physicians consider not only the nail appearance but also the clinical history and risk factors of each patient to prevent unnecessary biopsies. However, close monitoring of the nail features and the response to treatment is highly recommended. Yet, in high-risk cases, the biopsy is the only way to confirm the diagnosis.

Acknowledgments: None.

Conflict of interests: None declared.

REFERENCES

1. Reinecke JK, Hinshaw MA. Nail health in women. Int J Womens Dermatol. 2020;6:73-9.
2. Kovich OI, Soldano AC. Clinical pathologic correlations for diagnosis and treatment of nail disorders. Dermatol Ther. 2007;20:11-6.
3. Karim A, Sadeque S, Khan MA, et al. A Study of Nail Changes in Various Dermatosis. Journal of Armed Forces Medical College, Bangladesh, 2015;11:38-44.
4. Fernandez-Flores A, Saeb-Lima M, Martinez-Nova A. Histopathology of the nail unit. Rom J Morphol Embryol. 2014;55:235-56.
5. Goettmann S, Zaraa I, Moulonguet I. Nail lichen planus: epidemiological, clinical, pathological, therapeutic and prognosis study of 67 cases. J Eur Acad Dermatol Venereol. 2012;26:1304-9.
6. Salomon J, Szepietowski JC, Proniewicz A. Psoriatic nails: a prospective clinical study. J Cutan Med Surg. 2003;7:317-21.
7. Läuchli S, Eichmann A, Baran R. Swelling of the proximal nail fold caused by underlying warts. Dermatology. 2001;202:328-9.
8. Tosti A, Baran R, Piraccini BM, et al. Nail matrix nevi: a clinical and histopathologic study of twenty-two patients. J Am Acad Dermatol. 1996;34:765-71.
9. Perrin C, Baran R, Balaguer T, et al. Onychomatricoma: new clinical and histological features. a review of 19 tumors. Am J Dermatopathol. 2010;32:1-8.
10. Miteva M, de Farias DC, Zaiac M, Romanelli P, Tosti A. Nail clipping diagnosis of onychomatricoma. Arch Dermatol. 2011;147:1117-8.
11. Domínguez-Cherit J, Chanussot-Deprez C, Maria-Sarti H, et al. Nail unit tumors: a study of 234 patients in the dermatology department of the “Dr Manuel Gea González” General Hospital in Mexico City. Dermatol Surg. 2008;34:1363-71.
12. Dalle S, Depape L, Phan A, et al. Squamous cell carcinoma of the nail apparatus: clinicopathological study of 35 cases.Br J Dermatol. 2007;156:871-4.