

The Association Between Nail Involvement and Disease Severity in Patients with Pemphigus - A Retrospective Study

 Zeynep Altan Ferhatoğlu,  Gürbüz Yıldırım

Department of Dermatology and Venerology, Cerrahpaşa Faculty of Medicine, Istanbul University Cerrahpaşa, Istanbul, Türkiye

Abstract

Introduction: Pemphigus, a group of chronic, potentially fatal mucocutaneous bullous disorders, often presents with limited evidence of nail involvement. This study investigated the relationship between nail manifestations and disease severity in patients with pemphigus.

Methods: We conducted a meticulous retrospective review of medical records of 18 patients (9 males, 9 females) diagnosed with pemphigus, focusing on patients with and without nail manifestations. We documented a comprehensive set of demographic and clinical parameters, including the nature of the nail involvement. Disease severity was evaluated using the Pemphigus Disease Area Index (PDAI).

Results: Of the 18 participants, 8 exhibited nail involvement, with an equal gender distribution. Pemphigus vulgaris was the predominant type, diagnosed in 14 patients, followed by pemphigus foliaceus in 4 patients. Nail manifestations included involvement of both the finger and toenails, most commonly presenting as paronychia, onychomadesis, and nail discoloration.

Discussion and Conclusion: As pemphigus is a life-threatening group of diseases, monitoring its effects and follow-up are crucial. Even though nail involvement is often dismissed as a rare manifestation, it could potentially serve as a significant prognostic indicator for pemphigus. We believe that conducting larger-scale studies could offer invaluable insights into the prognosis and disease duration among pemphigus patients with nail involvement.

Keywords: Disease severity; nail manifestations; pemphigus; pemphigus disease area index; retrospective analysis.

Pemphigus encompasses a cluster of autoimmune conditions manifesting as chronic, potentially fatal mucocutaneous blistering disorders^[1]. These conditions are characterized by the generation of IgG autoantibodies that target desmoglein, an essential component of intercellular junctions within the epidermis. The diagnostic procedures typically incorporate histopathological examination coupled with immunofluorescence techniques. Although some studies have discussed nail involvement in patients

with pemphigus^[1,2], considering the occurrence of target antigens in the nails, nail alterations could be significant prognostic markers for pemphigus disorders.

This study aimed to investigate the association between nail alterations and the severity of pemphigus. A deeper understanding of this association could provide critical insights into disease mechanisms and may inform therapeutic strategies. Previous studies^[3,4] have proposed that specific nail changes may be associated with disease

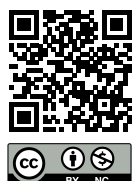
Correspondence: Zeynep Altan Ferhatoğlu, M.D. Department of Dermatology and Venerology, Cerrahpaşa Faculty of Medicine, Istanbul University Cerrahpaşa, Istanbul, Türkiye

Phone: +90 534 878 77 48 **E-mail:** zeynepaltanferhatoglu@gmail.com

Submitted Date: 27.03.2024 **Revised Date:** 30.05.2024 **Accepted Date:** 27.07.2024

Haydarpaşa Numune Medical Journal

OPEN ACCESS This is an open access article under the CC BY-NC license (<http://creativecommons.org/licenses/by-nc/4.0/>).



activity and can thus be employed as a practical clinical marker for disease monitoring.

Therefore, this study aimed to bridge a significant gap in the existing literature by exploring the relationship between nail alterations and disease severity in pemphigus. This endeavor paves the way for future research focusing on this clinically pertinent yet underexplored facet of pemphigus.

Materials and Methods

This investigation was conceptualized as a retrospective review of patients diagnosed with pemphigus at the Bullous Diseases outpatient clinic, under the Department of Dermatology and Venereology at Cerrahpaşa Medical Faculty, spanning 2021–2022. A diagnosis of pemphigus was established based on histopathological evaluation and immunofluorescence techniques. The study sample comprised a total of 8 patients exhibiting nail involvement and 10 patients without any nail-related manifestations.

Patient-centric data were gleaned from an information form completed by the patients before initiating treatment. Following the receipt of informed consent, data related to demographic characteristics (age, sex), type of pemphigus, Pemphigus Disease Area Index (PDAI) scores for hair, mucosa, and scalp; duration of mucosal lesions; and levels of desmoglein 1 (dsg1) and desmoglein 3 (dsg3) were documented.

Furthermore, a comprehensive examination of the patients' nails was undertaken to identify any changes. Various nail

changes, such as paronychia, Beau's lines, onychomadesis, onycholysis, pitting, subungual hyperkeratosis, subungual hematoma, nail discoloration, and nail avulsion, were noted in both the fingernails and toenails.

The amassed data underwent analysis using the SPSS Statistics software (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp). Descriptive statistics, including mean, standard deviation, and frequency, were used to depict the data. Differences in continuous variables among groups were analyzed using the independent-samples t-test, while the Chi-square tests were leveraged to discern associations between categorical variables. A p -value < 0.05 was deemed statistically significant. Additionally, correlation analyses were carried out to investigate relationships between nail involvement and Pemphigus Disease Area Index (PDAI) scores.

The Ethics Committee of İstanbul University-Cerrahpaşa Rectorate approved the study (date: 09.02.2024, approval number: 909814), and it was conducted per the Declaration of Helsinki. The procedures involving human participants complied with the ethical guidelines of the institutional and/or national research committee. Written informed consent was obtained from all participants. Patient data privacy was upheld throughout the research, with all personal identifiers excised and securely stored data. No financial incentives were offered, and participation was voluntary. Patients were provided with a comprehensive explanation of the study's purpose and procedures before obtaining their consent.

Table 1. Demographic and Clinical Features of Patients by Nail Involvement

Clinical Features	Nail Involvement			
	Yes		No	
	N*	%**	N*	%**
Gender				
Male	4	50.0%	5	50.0%
Female	4	50.0%	5	50.0%
Age*	54±17*	35 – 77**	48±13*	35 – 79**
Pemphigus Types				
P.vulgaris	7	87.5%	7	70.0%
P.foliaceus	1	12.5%	3	30.0%
PDAI – Skin	19±12*	0 – 31**	4±12*	0 – 32**
PDAI – Mucosa	8±13*	0 – 39**	4±8*	0 – 26**
PDAI – Scalp	0±2*	0 – 4**	0±2*	0 – 4**
DSG-1 level	94±83*	12 – 201**	102±87.5*	0 – 201**
DSG-3 level	200±71*	17 – 201**	62±88.4*	0 – 201**

*median±standard deviation; **min-max.

Results

The study included a total of 18 patients, with an evenly balanced gender ratio: 9 females and 9 males. Of these, nail involvement was discerned in 8 patients, while it was not observed in 10 patients. In terms of disease type, 14 patients were diagnosed with pemphigus vulgaris, and the remaining 4 had pemphigus foliaceus. A comprehensive breakdown of the patients' demographic and clinical characteristics stratified by nail involvement is shown in Table 1.

In the context of nail involvement, it was confined to only the fingernails in 2 patients, solely the toenails in 1 patient, and both the fingernails and toenails in 5 patients. The most commonly observed nail changes included

Features	n	%
Localization of involved nails		
Finger nails	2	25.0
Toe nails	1	12.5
Both	5	62.5
Number of involved nails	5±5*	2-16**
Paronychia	5	62.5
Beau Line	1	12.5
Onychomadesis	3	37.5
Onycholysis	2	25.0
Pitting	0	0.0
Subungual hyperkeratosis	2	25.0
Subungual hematoma	1	12.5
Nail Discoloration	3	37.5
Nail Avulsion	1	12.5

*median±standard deviation; **min-max.



Figure 1. Periungual active pemphigus vulgaris lesions (erythema, bulla and hemorrhagic crusts) on the left 2nd and 3rd fingers and a bulla on the erythematous base compatible with pemphigus vulgaris on the proximal phalanx of the 4th finger of the right hand.



Figure 2. Onychomadesis in the right thumb and onychatrophy in the second finger associated with pemphigus vulgaris.

paronychia in 5 patients, nail discoloration in 3, and onychomadesis in 3. The other manifestations are rare. The diverse array of nail changes discerned in patients is shown in Table 2.

Discussion

Pemphigus is a cluster of potentially fatal, chronic, mucocutaneous bullous disorders. IgG4-type antibodies against desmoglein 1 and desmoglein 3 significantly contribute to the pathogenesis of the disease. Previous studies have identified these proteins in the nail bed, shedding light on the possibility of nail involvement in patients with pemphigus [3]. Although the incidence of pemphigus varies widely in studies, nail involvement is generally believed to be rare [4-6]. Our study aimed to investigate the association between nail involvement and the severity of pemphigus disease.

Our data revealed that out of the 18 patients included in the study, 8 exhibited nail involvement. Among these, 7 were diagnosed with pemphigus vulgaris and 1 with pemphigus foliaceus. Most literature suggests a correlation between nail involvement and pemphigus vulgaris, rarely

with other types of pemphigus [1,4-6]. Given the global prevalence of pemphigus vulgaris, it seems plausible that nail involvement may be more frequent in these patients. Nonetheless, we hypothesize that nail involvement could potentially occur in other forms with antibodies against desmoglein 1 and desmoglein 3.

The gender distribution among the 8 patients with nail involvement was equal, with 4 males and 4 females. However, owing to the limited sample size, drawing any inferences regarding the incidence across genders would be imprudent. Past studies suggest a comparable impact of pemphigus vulgaris and pemphigus foliaceus on both genders. Moreover, the age range of our patients aligns with the standard demographic reported in the literature [7,8].

In terms of nail involvement distribution, 5 patients exhibited involvement in both finger and toenails, 2 only in fingernails, and 1 exclusively in toenails. Paronychia was the most frequently observed condition among our patients, with no instances of pitting (Fig. 1). Additionally, subungual hyperkeratosis, nail discoloration, onychomadesis, and onycholysis were reported in a few patients, while Beau's lines, subungual hematoma, and avulsion (Fig. 2) were each observed in a single patient. These findings align with Baghdad et al.'s [1] study, where paronychia was the most commonly reported nail alteration. However, the rate of nail involvement differs significantly across other studies with diverse sample sizes [9].

The Pemphigus Disease Area Index (PDAI) is essential to ascertain the severity of involvement in pemphigus patients. We observed comparable PDAI scores in patients with and without nail involvement, advocating for a separate evaluation of nail involvement. In our study, the PDAI median score was higher in patients with nail involvement. Some studies also report a correlation between nail involvement and PDAI [10]. Therefore, we think evaluating nail involvement when monitoring pemphigus patients is important.

Conclusion

Since pemphigus is a life-threatening group of diseases, monitoring its effects and ensuring proper follow-up are crucial. Even though nail involvement is often dismissed as a rare manifestation, it could potentially serve as a significant prognostic indicator for pemphigus. We believe

that conducting larger-scale studies could offer invaluable insights into the prognosis and disease duration among pemphigus patients with nail involvement.

Ethics Committee Approval: The study was approved by Istanbul University-Cerrahpaşa Rectorate Ethics Committee (No: 909814, Date: 09/02/2024).

Peer-review: Externally peer-reviewed.

Use of AI for Writing Assistance: Not declared.

Authorship Contributions: Concept – Z.A.F.; Design – Z.A.F.; Supervision – Z.A.F.; Fundings – Z.A.F.; Materials – Z.A.F.; Data collection &/or processing – Z.A.F.; Analysis and/or interpretation – G.Y.; Literature search – G.Y.; Writing – G.Y.; Critical review – G.Y.

Conflict of Interest: The authors declare that there is no conflict of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Baghdad B, Chiheb S. Nail involvement during Pemphigus. *Skin Appendage Disord* 2019;5:362–5.
2. Gopal V, Shenoy MM, Bejai V, Nargis T. Nail changes in autoimmune blistering disorders: A case-control study. *Indian J Dermatol Venereol Leprol* 2018;84:373.
3. Eachus E, DeLamielleure LE, Mitha S, Rasul TF, Faiz A. Scalp, oral, and nail pemphigus vulgaris: Clinical characteristics and a review of the literature. *Cureus* 2023;15:e38334.
4. Alpsoy E, Akman-Karakas A, Uzun S. Geographic variations in epidemiology of two autoimmune bullous diseases: Pemphigus and bullous pemphigoid. *Arch Dermatol Res* 2015;307:291–8.
5. Carducci M, Calcaterra R, Franco G, Mussi A, Bonifati C, Morrone A. Nail involvement in pemphigus vulgaris. *Acta Derm Venereol* 2008;88:58–60.
6. Engineer L, Norton LA, Ahmed AR. Nail involvement in pemphigus vulgaris. *J Am Acad Dermatol* 2000;43:529–35.
7. Joly P, Litrowski N. Pemphigus group (vulgaris, vegetans, foliaceus, herpetiformis, brasiliensis). *Clin Dermatol* 2011;29:432–6.
8. James KA, Culton DA, Diaz LA. Diagnosis and clinical features of pemphigus foliaceus. *Dermatol Clin* 2011;29:405–12.
9. De D, Kumar S, Handa S, Mahajan R. Fingernail involvement in pemphigus and its correlation with disease severity and other clinicodemographic parameters. *Br J Dermatol* 2019;180:662–3.
10. Habibi M, Mortazavi H, Shadianloo S, Balighi K, Ghodsi SZ, Daneshpazhooh M, et al. Nail changes in pemphigus vulgaris. *Int J Dermatol* 2008;47:1141–4.