Nail Involvement during Pemphigus

Bouchra Baghdad Soumiya Chiheb

Department of Dermatology Venereology, Hospital Ibn Rochd, University Hassan II, Casablanca, Morocco

Keywords

Pemphigus · Nails · Desmoglein 3 · Desmoglein 1 · Paronychia

Abstract

Background: Pemphigus is an autoimmune bullous disease affecting the skin and mucous membranes. Associated nail involvement is underestimated and is characterized by a variety of clinical manifestations. Our aim was to describe the clinical aspects of nail involvement during pemphigus. **Patients and Methods:** A retrospective study was conducted of patients with pemphigus over a period of 12 years. The diagnosis of pemphigus was based on clinical and immunopathological data. Clinical data were collected from patient records prior to initiation of treatment. **Results:** Overall, 141 cases of pemphigus were collected. Of these, 60 patients had nail involvement. After eliminating fungal origin, we selected 37 patients in our study. The main clinical forms were paronychia and dystrophy. Two cases of destruction of the nail apparatus were found in patients with pemphigus vegetans. The disease was bilateral in 11 cases (29.7%). The presence of unguis involvement was correlated with severity of pemphigus, particularly severe oral disease ($p = 0.002$). **Conclusion:** Nail lesions were polymorphic in our patients. These signs show accumulated inflammation of the nail after a long evolution of the disease. Nail involvement may precede, be concomitant, or follow the mucocutaneous lesions of pemphigus and be a sign of severity or relapse of the disease.

© 2019 S. Karger AG, Basel

Introduction

Pemphigus is a chronic, autoimmune, mucocutaneous bullous disease which can be potentially life-threatening [1]. It is characterized by intraepidermal bullae with suprabasal acantholysis and IgG autoantibody against a desmosomal-associated glycoprotein, desmoglein. The clinical diagnosis is confirmed by direct and indirect immunofluorescence. Nail involvement has been reported in a few series mainly in pemphigus vulgaris and is usually underestimated [2, 3]. It appears to be an important clinical sign reflecting the severity and evolution of pemphigus considering the presence of target antigen in the nail [3]. Our aim was to analyze the frequency and the clinical particularities of nail changes in all types of pemphigus through a case series.

Patients and Methods

We conducted a retrospective study between 2006 and 2017 including all patients hospitalized for pemphigus in our department. The diagnosis of pemphigus was based on clinical and immunopathological data. Clinical data were collected through an information sheet before the initiation of treatment.

The following variables were recorded: age, gender, type of pemphigus, duration of evolution, severity of skin involvement (according to the pemphigus disease area index), mucosal involvement, clinical aspects, as well as treatment received and disease evolution.

The clinical signs analyzed were: chronic paronychia, hemorrhagic paronychia, onychomadesis, onycholysis, perungual bullae,

Table 1. Characteristics of pemphigus patients with nail involvement (*n* = 37)

Characteristics	Patients, <i>n</i> (%)
Mean age $\pm$ SD, years	53.25 $\pm$ 15.6
Gender	
Male	15 (40.5)
Female	22 (59.5)
Type of pemphigus	
Vulgaris	20 (54)
Foliaceus	11 (29.8)
Vegetans	2 (5.4)
Paraneoplastic	2 (5.4)
Herpetiform	2 (5.4)
Clinical aspects (<i>n</i> = 56 lesions)	
Onycholysis	12 (21.5)
Pachyonychia	14 (25)
Paronychia	14 (25)
Onychomadesis	6 (10.7)
Beau's lines	4 (7.1)
Periungual blister	4 (7.1)
Subungual hemorrhage	2 (3.6)
Severity	
Moderate	7 (19)
Severe	30 (81)
Location	
Hands	17 (46)
Feet	9 (24.3)
Hand and feet	11 (29.7)
Mucosal involvement	24 (64.8)
Treatment received	
Oral corticotherapy	35 (94.6)
Local steroids	16 (43.2)
Azathioprine	20 (74)
Disulone	5 (13.5)
Rituximab	2 (5.4)
Cyclins	2 (5.4)
Evolution	
Remission	12 (32.4)
Relapse	13 (35.2)
Stable	4 (10.8)
Death	3 (8.1)
Unknown	5 (13.5)

nail dystrophy, trachyonychia, subungual hemorrhage, pyogenic pseudogranuloma, perionyxis, and striations. Bacteriological and fungal cultures as well as direct mycological cultures were performed to exclude infections in every case of nail involvement and chronic paronychia. Statistical analysis was performed with SPSS 16.0 software. Firstly, it consisted of a simple descriptive analysis. Quantitative variables were expressed as mean $\pm$ SD. Qualitative variables were expressed as percentage. Thereafter, a bivariate analysis was carried out to study possible associations between some variables. We used the χ^2 test and Fisher's exact test for qualitative variables, and Student's *t* test for quantitative variables with a threshold of 0.05.

Fig. 1. Clinical aspects of nail lesions in pemphigus. **a** Beau's lines and onycholysis. **b-d** Paronychia. **e** Periungual blister. **f** Paronychia and ungual dystrophy.

Results

Over a period of 12 years, 141 cases of pemphigus were collected. Of these, 60 patients had nail involvement (42%). After eliminating onychomycosis, we included 37 patients (27%) in our study (Table 1). There were 15 men and 22 women. The mean age was 53.25 years ($\pm$ 15.6, range 16–80). The mean duration of evolution was 14.7 months ($\pm$ 22, from 20 days to 8 years), and lesions could precede, be concomitant, or follow the mucocutaneous lesions of pemphigus.

Ungual involvement was statistically more common during pemphigus vulgaris (*p* = 0.006) followed by seborrheic pemphigus. Associated mucosal involvement was found in 24 patients (64.8%). Clinical aspects were mainly represented by onycholysis and paronychia (Table 1, Fig. 1). Two cases of destruction of the nail apparatus

Fig. 2. Nail involvement during pemphigus vegetans.

were found in patients with pemphigus vegetans (Fig. 2). Nail involvement of the hands was noted in 17 cases (46%) with predominance of the thumb, index, and middle fingers, and it was noted on toes in 9 cases (24.3%) with predominance of the big toe (Fig. 3). Lesions of nails were bilateral in 11 cases (29.7%). The presence of nail disease was correlated with severity of pemphigus, particularly severe oral involvement ($p = 0.002$).

Patients were mainly treated with oral corticotherapy (94.6%), and complete remission of nail involvement was observed in 12 patients (32.4%) after 6 months of treatment.

Discussion

Pemphigus is a group of chronic blistering disorders of the skin and mucosal membranes. IgG autoantibodies are directed against cell-cell adhesion molecules of keratinocytes (desmoglein 1 and desmoglein 3), thereby causing loss of adhesion or acantholysis [4]. There are five major categories of pemphigus: pemphigus vulgaris, pemphigus foliaceus, paraneoplastic pemphigus, drug-induced pemphigus, and IgA pemphigus. Diagnosis is based on clinical manifestations and confirmed with histological and immunochemical testing [1]. As shown by Sinclair et al. [5], all antigens of normal skin are also normally expressed in the proximal nail fold, nail matrix, and hyponychium including desmoglein 1 and 3

Fig. 3. Distribution of lesions among fingers and toenails.

explaining nail involvement occurring in pemphigus. Incidence estimates of pemphigus substantially vary around the world, and nail involvement was believed to be uncommon [6–13]. Otherwise, some recent studies indicate that the incidence of nail involvement was underestimated [2, 14, 15]. Even if nail involvement has often been reported with pemphigus vulgaris, our study showed that nail involvement could occur with any type of pemphigus.

Ungual lesions during pemphigus are secondary to the appearance of blisters in the nail bed/nail matrix or due to the acantholysis of the lateral fold of the nail as part of the autoimmune process [3]. The most reported signs are paronychia and onychomadesis [2, 8, 16, 17]. Paronychia, which was seen on 14 of our patients, is often a warning symptom of an outbreak of the disease and occurs following epidermal acantholysis of the nail fold [14, 18].

The Beau's lines represent an interesting sign to describe, because their distance from the proximal nail fold is correlated to the time from disease onset, and their number indicates the number of subsequent outbreaks [2].

Onychomadesis indicates complete cessation of nail matrix activity, reflecting an important inflammatory process and may also be secondary to the appearance of subungual blisters [9].

Patients with a longer duration of disease and accumulated inflammation are more likely to present with nail changes. This could be explained by the fact that the normal human nail immune system is very similar to the hair follicle immune system, including a known area of relative "immune privilege" in the proximal nail matrix, which can constitute a safe-guard against autoimmunity

[3]. In our study, the fingernails are the most affected, especially the first three which could be explained by the greater activity of these fingers resulting in more local trauma [3].

Although poorly reported [19], our study found nail lesions in two patients with paraneoplastic pemphigus and in two patients with pemphigus vegetans. The latter has led to more severe injuries resulting in the complete destruction of the nail unit with bad esthetic appearance. Topical therapy of nail involvement in patients with pemphigus is ineffective, and systemic treatment is necessary. Nail recovery is usually complete, leaving no permanent disfigurement [8].

Our study is very broad, otherwise, the retrospective nature could possibly underestimate the actual number of pemphigus patients with nail involvement. Nail biopsies and onychoscopy would have been useful tools to confirm the autoimmune disease.

Conclusion

Nail involvement in patients with pemphigus should be systematically reported and recognized by physicians. It occurs most often after a long course of the disease and could represent a sign of evolution and gravity of the disease.

Statement of Ethics

This study was conducted according to the principles specified in the Declaration of Helsinki and under local ethical guidelines (Ethics Committee for Biomedical Research, Faculty of Medicine and Pharmacy, Casablanca, Morocco). All patients have given written informed consent.

Disclosure Statement

The authors report no conflicts of interest.

References

- 1 Kasperkiewicz M, Ellebrecht CT, Takahashi H, Yamagami J, Zillikens D, Payne AS, et al. Pemphigus. *Nat Rev Dis Primers*. 2017 May; 3(1):17026.
- 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 May-Jun;84(3):373–373.
- 3 Tosti A, André M, Murrell DF. Nail involvement in autoimmune bullous disorders [xi]. *Dermatol Clin*. 2011 Jul;29(3):511–3.
- 4 Pietkiewicz P, Bowszyc-Dmochowska M, Gornowicz-Porowska J, Dmochowski M. Involvement of nail apparatus in pemphigus vulgaris in ethnic Poles is infrequent. *Front Med (Lausanne)*. 2018 Aug;5:227.
- 5 Sinclair RD, Wojnarowska F, Leigh IM, Dawber RP. The basement membrane zone of the nail. *Br J Dermatol*. 1994 Oct;131(4):499–505.
- 6 Alpsoy E, Akman-Karakas A, Uzun S. Geographic variations in epidemiology of two autoimmune bullous diseases: pemphigus and bullous pemphigoid [PubMed]. *Arch Dermatol Res*. 2015 May;307(4):291–8.
- 7 Carducci M, Calcaterra R, Franco G, Mussi A, Bonifati C, Morrone A. Nail involvement in pemphigus vulgaris. *Acta Derm Venereol*. 2008;88(1):58–60.
- 8 Engineer L, Norton LA, Ahmed AR. Nail involvement in pemphigus vulgaris. *J Am Acad Dermatol*. 2000 Sep;43(3):529–35.
- 9 Patsatsi A, Sotiriou E, Devliotou-Panagiotidou D, Sotiriadis D. Pemphigus vulgaris affecting 19 nails. *Clin Exp Dermatol*. 2009 Mar;34(2):202–5.
- 10 Kim BS, Song KY, Youn JI, Chung JH. Paronychia—a manifestation of pemphigus vulgaris. *Clin Exp Dermatol*. 1996 Jul;21(4):315–7.
- 11 Baupal A, Robinson MJ. Nail bed involvement in pemphigus vulgaris. *Arch Dermatol*. 1973 May;107(5):751.
- 12 Kolivras A, Gheeraert P, André J. Nail destruction in pemphigus vulgaris. *Dermatology*. 2003;206(4):351–2.
- 13 Apalla Z, Chaidemenos G, Karakatsanis G. Nail unit involvement during severe initial pemphigus vulgaris development. *Eur J Dermatol*. 2009 May-Jun;19(3):290–1.
- 14 Serratos BD, Rashid RM. Nail disease in pemphigus vulgaris. *Dermatol Online J*. 2009 Jul; 15(7):2.
- 15 Reich A, Wiśnicka B, Szepietowski JC. Haemorrhagic nails in pemphigus vulgaris. *Acta Derm Venereol*. 2008;88(5):542.
- 16 Habibi M, Mortazavi H, Shadianloo S, Balighi K, Ghodsi SZ, Daneshpazhooh M, et al. Nail changes in pemphigus vulgaris. *Int J Dermatol*. 2008 Nov;47(11):1141–4.
- 17 Cahali JB, Kakuda EY, Santi CG, Maruta CW. Nail manifestations in pemphigus vulgaris. *Rev Hosp Clin Fac Med Sao Paulo*. 2002 Sep-Oct;57(5):229–34.
- 18 Akiyama C, Sou K, Furuya T, Saitoh A, Yasaka N, Ohtake N, et al. Paronychia: a sign heralding an exacerbation of pemphigus vulgaris. *J Am Acad Dermatol*. 1993 Sep;29(3):494–6.
- 19 Patsatsi A, Sotiriou E, Devliotou-Panagiotidou D, Sotiriadis D. Pemphigus vulgaris affecting 19 nails. *Clin Exp Dermatol*. 2009 Mar;34(2):202–5.
- 20 Wieczorek M, Czernik A. Paraneoplastic pemphigus: a short review. *Clin Cosmet Investig Dermatol*. 2016 Sep;9:291–5.