

## Nail Involvement in Pemphigus Vulgaris

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Sir,

Nail involvement is a rare clinical finding in pemphigus. It is usually seen in severe cases and may occur early or late in the course of the disease (1). The most common clinical manifestations are chronic paronychia and onychomadesis (the entire separation of the nail plate from the nail bed). Topical therapy is not sufficient; systemic therapy is required.

Over the last 3 years, we have observed 15 cases of pemphigus: 10 of pemphigus vulgaris (PV) and 5 of pemphigus foliaceus. All patients showed typical clinical, histological and immunofluorescence findings of these diseases.

We report here 3 patients with PV associated with nail involvement.

### CASE REPORTS

#### Case 1

A 59-year-old white woman with a 4-month history of recurrent episodes of pruritic blisters and erosions on the whole body and oral mucosa. At clinical examination, she showed inflammation over the periungual areas of the third finger of both hands for 3 months, accompanied by onychomadesis; no toenail involvement was detected (Fig. 1).

Histological examination of the affected skin revealed suprabasal clefting containing acantholytic cells. Epidermal intercellular deposition of IgG and C<sub>3</sub> was noted on direct immunofluorescence (DIF). Indirect immunofluorescence (IIF) on monkey oesophagus was positive at a titre of 1:1280. The serum levels of auto-antibodies to desmoglein (DSG)1 and DSG3 were tested by enzyme-linked immunosorbent assay (ELISA): DSG1=index: 30.7 (normal values: 0–14) DSG3=index: 192.1 (normal values 0–7 index). The bacterial and fungal cultures from paronychia were negative.

A diagnosis of PV was made and the patient was treated with oral steroids (prednisolone) at an initial dose of 2 mg/kg/day,

progressively reduced, and azathioprine 2 mg/kg/day, resulting in the clinical resolution of mucocutaneous and nail lesions.

#### Case 2

A 35-year-old white man presented with a 3-month history of painful erosions in the oral cavity and genital area, several blistering erosions and thick adherent crust on the arms. Nail involvement appeared a few weeks after the initial lesions, as paronychia, onychorrhexis, onychomadesis of the first and third nail of both hands, Beau's lines of both third fingernails and pterygium of the first fingernail of the left hand (Fig. 2).

Bacterial and fungal cultures of the nail were negative. Biopsies were performed on perilesional skin for routine histology and DIF, giving pathognomonic findings. IIF on monkey oesophagus was positive at a titre of 1:1280; level serum concentration detected by ELISA was 6.3 index for DSG1 and 120.2 index for DSG3, thus a diagnosis of PV was made.

He was treated with prednisolone 1.8 mg/kg/day and azathioprine 2 mg/kg/day with no improvement. Azathioprine was therefore replaced by cyclosporine 4 mg/kg/day. Because of inefficacy, this drug was stopped and methotrexate 25 mg/week, in association to prednisolone 1.5 mg/kg/day, was administered. Because of side-effects, such as thrombocytopenia and a persistent high serum level of pancreatic enzymes, this treatment was also stopped. Thereafter, cyclophosphamide 1.5 mg/kg/day and prednisolone 1.5 mg/kg/day was started, but was stopped immediately because of neutropaenia. Finally, intravenous immunoglobulin (IVIG) 500 mg/kg/day for 4 days a week every 4 weeks, together with prednisolone 1.5 mg/kg/day, were administered with a partial clinical improvement. After 6 months of IVIG and a simultaneous progressive decrease in dose of steroids to 0.15 mg/kg/day, the PV lesions on the body and mucosa resolved, even though the DSG3 serum level remained high (index = 75.1), and mild paronychia and onychorrhexis were still present, while pterygium on the first left finger obviously persisted (Fig. 3).

#### Case 3

A 27-year-old white woman presented with a 5-month history of multiple painful erosive lesions, mainly involving the oral



Fig. 1. Yellowish discoloration, loss of cuticle, paronychia and early onychomadesis involving the first three fingernails. Transverse leukonychia on the third fingernail (case 1).



Fig. 2. Paronychia, Beau's lines, onychomadesis and onychorrhexis involving both thumbs, and pterygium involving the left thumb (case 2).

cavity (palate, oral mucosa, tongue and lips) and bullous-erosive lesions and crusts involving the skin of trunk. On physical examination, suppurative inflammation was found on the distal end of the third fingernail of both hands, accompanied by early onychomadesis.

The cutaneous biopsy showed a prominent suprabasal acantholysis. DIF showed intercellular deposition of IgG and C<sub>3</sub> in the epidermis. IIF on monkey oesophagus was positive at a titre of 1:640. The serum levels of DSG1 and DSG3 were 8.5 and 114.2, respectively. Bacterial and fungal cultures from the paronychium were negative.

With a diagnosis of PV, she was treated with prednisolone 2 mg/kg/day and azathioprine 1.5 mg/kg/day, leading to only partial improvement. The disease progressed to involve the arms, thighs, nasal mucosa and scalp; therefore treatment with prednisolone 2 mg/kg/day, gradually reduced to 0.10 mg/kg/day, and cyclophosphamide 1.5 mg/kg/day was required. A partial response was obtained, with the nail damage resolved.

## DISCUSSION

Nail involvement in PV is relatively uncommon, although a recent study shows that it may be present in up to 22% of patients with PV (1). Our data confirm this finding; nail involvement occurred in 30% of our patients.

The most common nail changes in PV are onychomadesis, paronychia, trachyonychia, onychorrhexis, onycholysis, Beau's lines, pterygium, cross ridging, pitting, subungual haemorrhage, and nail plate discoloration (2–8). There is only one paper describing nail involvement during pemphigus foliaceus (PF) (6). None of our 5 patients affected by PF showed nail involvement.

Our 3 patients with PV had common clinical figures of nail involvement, such as onychomadesis, paronychia, onychorrhexis, Beau's lines and pterygium, except for the transverse leukonychia in case 1: this nail change has not been described previously in the course of PV.

Usually, fingernails were more often involved than toenails and the temporal relationship of the nail involvement in PV is variable: it may be noted as part of the initial presentation, concomitant with disease relapse, or as a sign heralding exacerbation (2–6). In our series, nail involvement appeared after the first cutaneous or mucosal manifestation of pemphigus.

Biopsy of the nail bed, matrix or fold for routine histological examination and DIF should be performed to assess the primary involvement of the nail. In our cases,

nail biopsy was not performed because this procedure would have resulted in unnecessary discomfort to the patient, since in our opinion no information would have been gained.

Systemic therapies, traditionally used in the treatment of PV, are necessary to control nail manifestations, because topical drugs have been reported to be ineffective. Nail recovery is usually complete, leaving no permanent disfigurement (2, 4). On the other hand, in case 2, the paronychia and onychorrhexis were still present after 6 months' therapy, probably because the patient was affected by a very aggressive and non-responsive form of PV with a persistent high serum levels of antibody anti-DSG3; the pterygium persisted, as it is a cicatricial stage.

The reason for the rarity of primary nail manifestations in PV is unclear. Although the nail bed, matrix and fold are epithelial structures with an epidermal layer similar to that of the skin and mucosa surfaces, there are likely to be anatomical, structural and molecular differences. It has been hypothesized that a possible reduced expression or relatively lower density of PV auto-antigen in the nail unit, compared with the cutaneous or mucosal epidermidis, or a relative sequestration of the auto-antigen from the immune system in the nail may occur in what is an immunologically "privileged" site (2, 9).

The nail matrix has a pluristratified epithelium similar to the normal epidermis, but without a granular layer, and the nail bed epidermis is usually no more than two or three cells thick (10, 11). Therefore, we postulate that local expression of DSG1 and DSG3 is low and that nail involvement may occur only when a high concentration of auto-antibodies to the two desmosomal glycoproteins is present in the serum, as in our patients.

A better understanding of the nail unit and further investigations are required to elucidate these hypotheses.

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Fig. 3. Paronychia and pterygium present after 6 months' intravenous immunoglobulin and steroid therapy (case 2).

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