

Onychodystrophy and Scarring Alopecia in Epidermolysis Bullosa Acquisita: A Case Based Review of the Literature

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Abstract

Introduction: Epidermolysis bullosa acquisita is a rare, autoimmune subepidermal bullous disease. Besides blisters appearance which heals with scars and milia cysts formation, nails undergo different changes: onychomadesis, onycholysis, onychorrhexis and matrix destruction.

Case report: We present the case of a 59 years old patient, which showed multiple blisters, erosions, crusts located on the elbows, knees, hands, and feet; some lesions healed and formed hypo or hyperpigmented. scars in the evolution. On the scalp were observed areas of scar alopecia. In the oral cavity there were extensive erosions, painful dysphagia to both solid and liquid food, which in time contributed to significant weight loss. To the fingers and toes, the patient underwent nail loss, these being to be replaced with scar tissue. The only remaining nails are at the fourth and fifth fingers of both hands, but also those showing lesions of onycholysis and onychorrhexis leading to a thin epidermal nail.

Conclusions: Our case report is the third case described in the literature. Onychomadesis manifestations and nail absence, although rare, complete the cutaneous manifestations of Epidermolysis bullosa acquisita.

Keywords: Epidermolysis bullosa acquisita; Onychomadesis; Nail loss; Scarring alopecia; Indirect immunofluorescence

Introduction

Epidermolysis Bullosa Acquisita (EBA) is a rare, autoimmune subepidermal bullous disease. The main target of the antibodies is collagen VII, the major component of the anchoring fibrils of the dermo-epidermal junction.

Patients have either blisters after mechanical trauma, whose features are similar to those observed in dystrophic epidermolysis bullosa, or undifferentiated clinical features from bullous pemphigoid or mucous membrane pemphigoid. This disease can occur in both children and adults, being one of the rare subepidermal bullous disease in West Europe [1]. Informal reports mention the association of EBA with inflammatory bowel disease (particularly Crohn's disease), myeloma, systemic lupus erithematosus, rheumatoid arthritis, thyroiditis and diabetes mellitus. The disease is chronic, refractory to treatment, and the diagnosis is supported by immunopathology examination, immunofluorescence microscopy, electron microscopy and immunological studies evidencing antibodies against collagen VII. Total loss of the nail, which is rarely described, is the result of nail bed scarring post bullous lesions. The same post erosions scars are the cause of the scarring alopecia.

Onychomadesis represent the nail exfoliation from the proximal nail fold. It is an effect of the nail matrix arrest and involve both finger nails and toe nails [2].

Case Report

We present the case of a 59 years old patient, which showed multiple blisters, erosions, crusts located on the elbows, knees, hands, and feet; some lesions healed and formed hypo or hyperpigmented. Scars in the evolution. On the scalp was observed areas of scar alopecia. The oral cavity presented extensive erosions, painful dysphagia to both solid and liquid food, which in time contributed to significant weight loss. To the fingers and toes, the patient underwent nail loss, these being to be replaced with scar tissue. The only remaining nails are at the fourth and fifth fingers of both hands, but also those showing lesions of onycholysis and onychorrhexis (Figure 1).

The disease started in 2010, initially with erosions in the vermilion lip and oral mucosa. The patient followed topical treatments but without effect. A biopsy was performed and the diagnosis bullous pemphigoid was established. Followed treatment with dapsone, originally 150 mg/day then 100 mg/day, which was interrupted after one year because the patient complained of breathing problems. Another therapeutically drug, Doxycycline was also tried, without any effect. Corticotherapy was recommended, but the patient refused to follow it. Meanwhile the patient had dysphagia and lost weight.

In July 2014 the patient agreed to be reinvestigated. Thus histopathology examination showed normal epidermis layer, covered with a corneum network. Papillary dermal presented a very discreet oedema and a rare perivascular infiltrate. In the interstitium were observed rare granulocytes and eosinophils. Subcutaneous tissue was not present. The changes described are not diagnostic and histopathological criteria for epidermolysis bullosa were not met. Indirect immunofluorescence showed positive BZM IgG and negative BZM IgA; salt split skin showed IgG deposits on the dermal side of the blister. After performing ELISA technique, antibodies to collagen VII were positive while desmoglein 1 and 3, BP 180, BP 230 were negative. The diagnosis established was epidermolysis bullosa acquisita, and recommended treatment was methylprednisolone 32 mg / day and mycophenolate mofetil 500 mg/ day, aiming to stop the disease progression. Three months after the treatment initiation, the antibodies titer was reduced, but the clinical manifestations persisted.

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Figure 1: Images of nail manifestation in Epidermolysis bullosa acquisita.

- A.** Flaccid bullae and erosions on the finger and dorsum of the hand.
- B.** Right hand: the nail loss is replaced by a thin epithelial nail to the fingers 2nd and 3rd; persistence of the nail with onycholysis and onychorrhexis to the fingers 4th and 5th. At the proximal fold of the 2nd and 3rd finger could be observed a scar formation. The 3rd finger present an erosion after a bullae.
- C.** Left hand: the presence of a thin epithelial nail that replace the normal nail to the fingers 2nd and 3rd. The 4th and 5th fingers have dystrophic nails with onycholysis and onychorrhexis.
- D.** Nail loss at the thumbs which are replaced by a scar. The scar formation starts from the proximal fold of the both nails.
- E.** Left foot: all of the nails are lost, these being replaced by a thin epithelial nail. To the hallux could be observed scars. At the first and second toe can be observed the nail bed, suggesting the former format of the nail. To be noted the milia formation and the flaccid bullae.
- F.** Right foot: nail loss to all the fingers, scar and milia formation.

Pemphigus vulgaris	Pemphigoid group	Epidermolysis bullosa acquisita
Severe nail dystrophy	Affects both nail folds, nail bed and matrix	Dystrophic nails and nail plate
Onychomadesis	Onychomadesis	Periungual/subungual blistering
Paronychia	Paronychia	Periungual granulation tissue
Onycholysis	Nail scarring with atrophy and nail loss	Onycholysis
Discoloration of the nail plate	Pterygium of the fingernails (in cicatricial pemphigoid)	Nail thickening and shortening
		Pterygium and nail atrophy
		Complete nail loss
		Syndactyly

Table 1: Nail involvement in autoimmune bullous dermatoses. Adapted from dermatology.

For this reason, the intravenous immunoglobulin treatment is currently applied and patient's antibody titer is monitored via Enzyme-Linked Immunoabsorbent Assay (ELISA).

The nail lesions started two years after the onset of the disease. In this context we wish to also state that the patient, who worked as a pharmacist, had no trauma on fingers or nails. The first affected nail was the toe nail: the nail fold was erythematous, edematous and pruriginous. The nail presented further onycholysis and a bullae formation. On average it lasted two months until complete nail loss. The nail bed was exposed and followed the apparition of new bullae and scars. The patient mentioned that the worse her general state got, the more affected the nails were. Finally, the nails were replaced by scars or a thin, epithelial nail.

Discussion

Classical manifestations of acquired epidermolysis bullosa are the mechanical non-inflammatory blisters which heal with hypo or hyperpigmented scars and milia formation [3] to the trauma-prone areas such as the dorsal hands, knuckles, elbows, knees, sacral area and toes. Oral mucosa may be affected, with blisters formation and painful erosions. The scalp bullae heal with scars resulting in scarring alopecia. Nail changes are rare, occurring only in severe forms of the disease [4]; nail changes associated with acral involvement may be leading to mutilating deformity of the digits, syndactily, nail dystrophy like onychomadesis or complete nail loss [5,6].

Onychomadesis is spontaneous separation of the nail from the nail bed or from the proximal nail fold and is associated with cessation of the nail growth. At the beginning appears a cleavages in the proximal area, followed by the disappearance of nail surface that is in direct contact with the matrix; this change does not involve the thickness of the stratum corneum. In the latent form of onychomadesis, the nail shows a transverse splitting due to complete transitory inhibition of the nail growth for at least 1-2 weeks. This could be characterized by a Beau line which reached maximum size. Nail growth continues for a while without a detachment to the underlying tissue. Growth stops when it loses this connection [7]. The characteristics of the nail's lesions in immunological bullous dermatosis are presented in Table 1.

To our knowledge, by the moment, only two case reports of EBA with dystrophic finger nails and toe nails are presented in the literature [8]. These two patients had severe disease form and also nail loss. In one communiqué was described the case of a patient with severe impairment, nail loss, syndactily and largely scalp alopecia [9]. The association of the scalp lesions occurs in up to 20% [5,6] of patients, some of these having extensively erosions healed with scarring alopecia. Indeed, our patient presented scarring alopecia, which together with the nail changes are the most rare manifestations of this disease.

Hair loss is also a manifestation in other autoimmune diseases. In bullous diseases that affect the scalp, like Brusting-Perry variant of bullous pemphigoid, scarring alopecia is reported. This is common in discoid Lupus Erythematosus (LE), too, while in acute systemic LE the non-scarring form is present [10]. Hair loss followed by scarring alopecia in EBA patients may also be explained by the traumatic action of hair comb or by pressure and friction of the head on the pillow while sleeping.

Differential diagnosis with bullous pemphigoid was investigated. In the literature only four cases with indisputable aspect of bullous pemphigoid and nail dystrophies were reported [11]. After the immunological analysis, bullous pemphigoid was excluded.

Another possible differential diagnosis to be discussed for the milder form of EBA is the Porphyria Cutanea Tarda (PCT) [12]. Unlike PCT, our patient did not present malar hirsutism, photosensitivity, scleroderma-like changes or urinary porphyrins.

The severe forms of EBA could be similar to hereditary recessive dystrophic epidermolysis bullosa (RDEB) [13] but this may rather be excluded due to the medical history of the patient and the outset of the disease.

According to Tosti et al. [14] nail loss has been rarely described in epidermolysis bullosa acquisita. Nail scars and pterygium unguium are rare complications of bullous pemphigoid and nail changes in pemphigus vulgaris may even precede cutaneous manifestations [14]. The authors have observed that the first three fingers are commonly affected; this aspect was also present in our patient. In addition, the patient had a complete loss of toe nails.

In order to better understand the disease, an additional interesting aspect may be the analysis of the Human Leucocyte Antigen (HLA) haplotype. It is known that the EBA is associated with the HLA-DR2 in African American patients. Zumelzu et al. additionally showed that black patients of African descent have a significantly higher HLA-DRB1*15:03 allelic frequency. Thus, black-skinned patients have a genetic predisposition to develop EBA and EBA should be suspected for each autoimmune blistering disease (AIBD) identified in this community [15,16].

Conclusions

Our case report is the third case described in the literature. Onychomadesis manifestations and nail absence, although rare, complete the cutaneous manifestations of EBA. These nail manifestations, although present in other autoimmune bullous dermatoses, infectious diseases, critical illness and medication induced, could become debilitating both physically and mentally. When associate, nail dystrophies could mean a severe impairment. The presence of nail changes in patients with EBA is not a diagnostic criterion but a consequence of the severity of the chronic inflammatory process characteristic of the disease.

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