

## Case report

## Photodynamic therapy induced pemphigus: Atypical clinical, pathological and immunological features

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The term pemphigus comprises a group of autoimmune diseases of the skin and mucous membranes characterized by blistering and acantholysis due to antibodies against epidermal antigens [1]. Herein, we report a case of pemphigus developing after treatment with methyl aminolevulinate natural daylight photodynamic therapy.

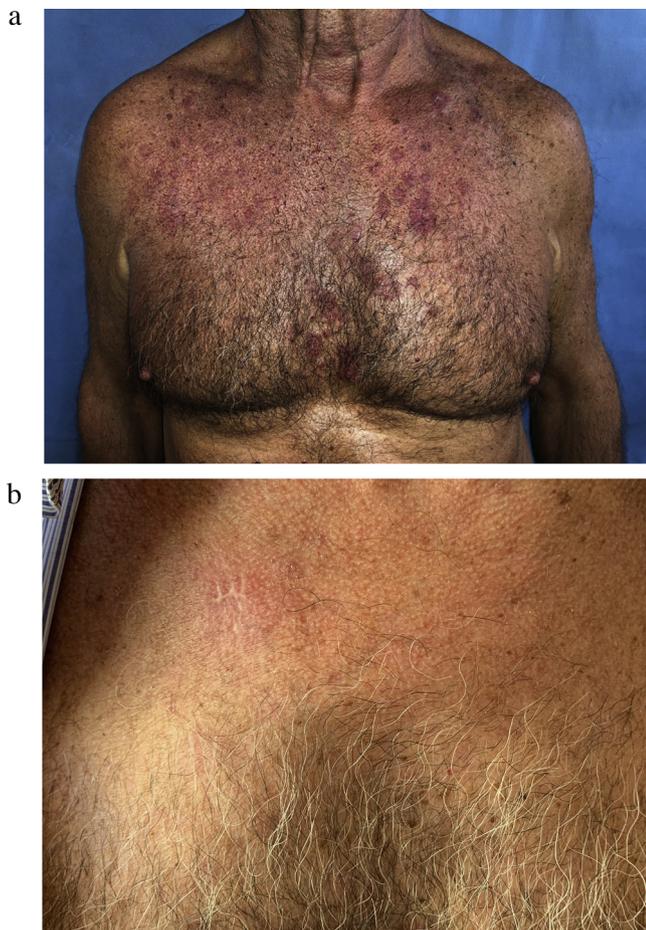
A 73-year-old man who had received treatment with methyl aminolevulinate natural daylight photodynamic therapy 1 month before current presentation, was evaluated for facial and chest lesions. Approximately 2 weeks before current presentation, he noted several itchy red macules that subsequently developed flaccid bullae which burst easily. There was no other history of trauma or injections to the affected area, nor of preceding illness. He was otherwise asymptomatic. On clinical examination he had multiple round, superficially eroded and crusted erythematous macules and patches (Fig. 1a) affecting the chest and face. There was no oral, conjunctival or genital mucosal involvement.

Medical history was unremarkable, except for hypertension and actinic keratosis. Family history was negative for autoimmune diseases. Urinalysis, renal function tests, liver enzymes, and a complete blood count were within normal values. Antinuclear antibodies and extractable nuclear antibodies were negative. A chest radiography and an abdominal ultrasound study were performed, without any pathological finding. A punch biopsy of the chest found superficial focal acantho-

lysis, basal cell layer vacuolization and a mild perivascular lymphocytic infiltrate accompanied by sparse plasmatic cells, neutrophils and eosinophils (Fig. 2a). Lupus band test and Alcian blue stain for stromal mucin were both negative. Direct immunofluorescence displayed IgG and C3 deposition in a characteristic honeycomb pattern surrounding upper epidermal keratinocytes (Fig. 2b). Indirect immunofluorescence was positive for anti-desmoglein 3 antibodies and negative for anti-desmoglein 1 and anti-BP180/230 antibodies. A diagnosis of pemphigus was made. The patient was initiated on topical clobetasol propionate cream every 12 h before histopathology results. One month after presentation, erosions had healed without systemic therapy (Fig. 1b). At 6 months he was stable without new lesions.

There is a wide range of triggers for pemphigus initiation in susceptible individuals, including drugs, emotional stress, radiotherapy, pregnancy, etc [2]. Photodynamic therapy has been described as having a significant effect on the immune system which may be either immunostimulatory or, in some circumstances, immunosuppressive [3]. In addition to stimulating local inflammation, it has been speculated that photodynamic therapy may cause a direct injury to the basement membrane, with the possibility of subsequent antibody formation [4]. Three patients with blistering diseases induced by photodynamic therapy have been reported, two of them belonging to the bullous pemphigoid group [4–6]. The remaining patient developed pemphigus

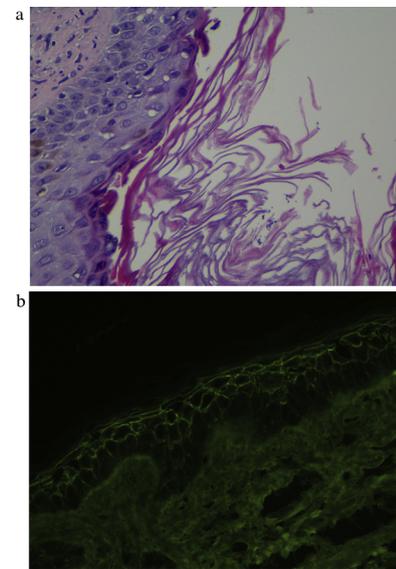
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**Fig. 1.** Clinical presentation and follow-up. (a) Multiple round superficially eroded and crusted erythematous macules and patches affecting the chest and face. (b) One month after presentation, erosions had healed without systemic therapy.

vulgaris after 5-aminolaevulinic acid-based photodynamic therapy, and it was clinically characterized by cutaneous involvement with mucosal sparing. Unfortunately, indirect immunofluorescence was negative [6]. Our case represents the first methyl aminolevulinate natural daylight photodynamic therapy induced pemphigus, confirmed by histopathology, direct immunofluorescence and indirect immunofluorescence. Skin manifestations resembled those of pemphigus foliaceus in terms of their distribution, histopathology and clinical appearance. However, desmoglein antibody profiles pointed to a pemphigus vulgaris without mucosal manifestations. The lack of clinicopathological and immunological correlation may be due to the atypical trigger factor.

In conclusion, we have reported the fourth patient developing a bullous autoimmune disease after being treated by photodynamic therapy and the first developing pemphigus after receiving methyl aminolevulinate natural daylight photodynamic therapy with a complete pathological and immunological profile. Although there is no conclusive evidence that it was caused by the PDT treatment, strong clinical clues reinforcing that hypothesis include the close time



**Fig. 2.** Skin biopsy. (a) Superficial focal acantholysis, basal cell layer vacuolization and a mild perivascular lymphocytic infiltrate accompanied by sparse plasmatic cells, neutrophils and eosinophils. (b) Direct immunofluorescence IgG deposition in a characteristic honeycomb pattern surrounding upper epidermal keratinocytes.

relationship and the rapid resolution with topical treatment and without flares at follow-up. In our opinion, pemphigus should be considered in any subject developing bullae after methyl aminolevulinate photodynamic therapy. Photodynamic therapy should be added to the list of possible external triggers of pemphigus vulgaris. A large case-control study is needed to further validate this relation.

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#### Declaration of Competing Interest

None declared.

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