Volume 21 Number 3
March 2015

Case presentation

Pemphigus vulgaris presenting with multiple lesion morphologies

Philip I. Song MD, Sherrie J. Divito MD PhD, Daniela Kroshinsky MD MPH

Dermatology Online Journal 21 (3): 17

Department of Dermatology, Massachusetts General Hospital, Boston, Massachusetts

Correspondence:

Daniela Kroshinsky
Dermatology Associates
50 Staniford Street, 2nd Floor
Boston, MA 02114-2517
Phone: 617-726-2914
Fax: 617-726-7768
Email: dkroshinsky@partners.org

Abstract

Pemphigus vulgaris is an uncommon intraepidermal blistering disorder that typically presents with flaccid bullae or erosions. We report a patient with pemphigus vulgaris who presented with several unusual clinical features: tense bullae with dependently layered pus, true target lesions coalescing into annular configurations, and diffuse desquamation that initially raised concern for toxic epidermal necrolysis. We discuss the differential diagnosis and implications of these morphological findings.

Introduction

Pemphigus vulgaris is characterized by intraepidermal acantholysis caused by IgG antibodies against desmoglein 3 and/or 1. Pemphigus vulgaris typically presents with flaccid and fragile bullae and erosions of the skin, in addition to mucosal erosions. More atypical clinical presentations of pemphigus vulgaris include onychodystrophy/onychomadesis, acral dyshidrosis and ulcers, or even pustules [1-3]. We report a patient with biopsy and serology-confirmed pemphigus vulgaris who presented with several unusual features: late onset of disease at 82 years of age, tense bullae with dependently layered pus, true target lesions coalescing into annular configurations, and diffuse desquamation close to 30% of body surface area that initially raised concern for toxic epidermal necrolysis.

Case synopsis

An 82-year-old woman with an unremarkable medical history other than depression treated with citalopram initially presented to an outside dermatologist with numerous red painful lesions on her scalp. She was clinically diagnosed with discoid lupus and was treated with topical mometasone. She used the mometasone for approximately three months, but she developed caudal progression of an erythematous rash onto her neck and body, as well as painful erosions in her mouth. Several days prior to her hospitalization, her abdomen, chest, and extremities became more diffusely involved with the rash and blisters had begun to form.

Physical examination revealed several oral ulcerations and diffuse scalp erosions with serous and hemorrhagic crust. Her back and shoulders had widespread desquamation with sloughed-off skin pushed to the side of the eroded areas, with about 30% body surface area involvement (Figure 1A). The Nikolsky sign (the ability to induce a blister by applying lateral pressure on an area of

nonblistered skin[4]) was negative on non-eroded areas of skin. On her flanks and abdomen, she had diffuse tense vesicles and bullae with a negative Asboe-Hansen sign (the ability to spread a blister to adjacent nonblistered skin by applying pressure to the top of the blister)[5]. Many of these bullae had layering of white fluid in the inferior portion of the bullae (Figure 1B). She had scattered erythematous target lesions with three zones of color, some of which were coalescing into annular configurations, on her anterior thighs (Figure 1C) and upper arms (Figure 1D).

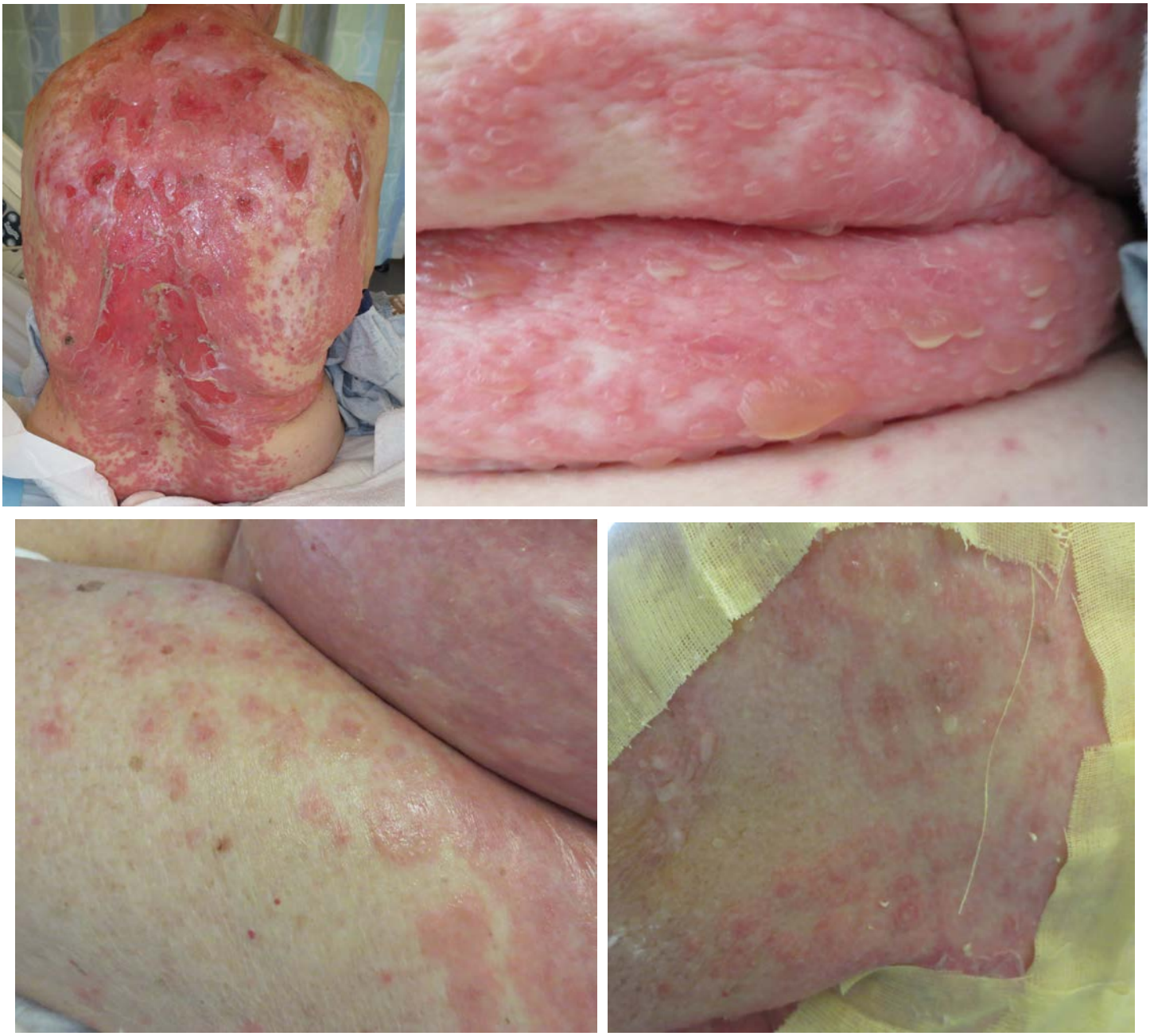

Figure 1. Clinical presentation of pemphigus vulgaris in an 82-year-old woman. A. Widespread desquamation. B. Tense bullae with dependent layering of pus on the right flank. C. Erythematous target and targetoid lesions on the left anterior thigh. D. Target lesions coalescing into annular configurations on the left upper arm.

Frozen section examination of a sample of sloughed skin from the patient's back revealed fragments of epidermis with partial necrosis, whereas a skin biopsy from her abdomen revealed suprabasilar acantholysis (Figure 2A). Direct immunofluorescence of skin from her abdomen showed positive 3+ immunoreactivity for IgG, IgG whole, and C3 in an intercellular pattern in the epidermis (Figure 2B). No specific immunoreactivity was detected for IgA, IgM, fibrinogen, or albumin. Indirect immunofluorescence was positive for intercellular IgG antibodies on monkey esophagus, and was negative on basement membrane zones and on rat bladder epithelium.

The patient was treated with topical steroids, 1 mg/kg of intravenous methylprednisolone daily, and 500mg of mycophenolate mofetil twice a day. After three to four weeks, she had reepithelialized most of her skin and was discharged on 1.5 mg/kg of oral prednisone daily with intent to taper and 1 gram of mycophenolate mofetil twice a day. To date, she continues on 1.5 grams of

mycophenolate mofetil twice a day and a steroid taper currently at 20 mg of prednisone daily without development of new skin or oral lesions.

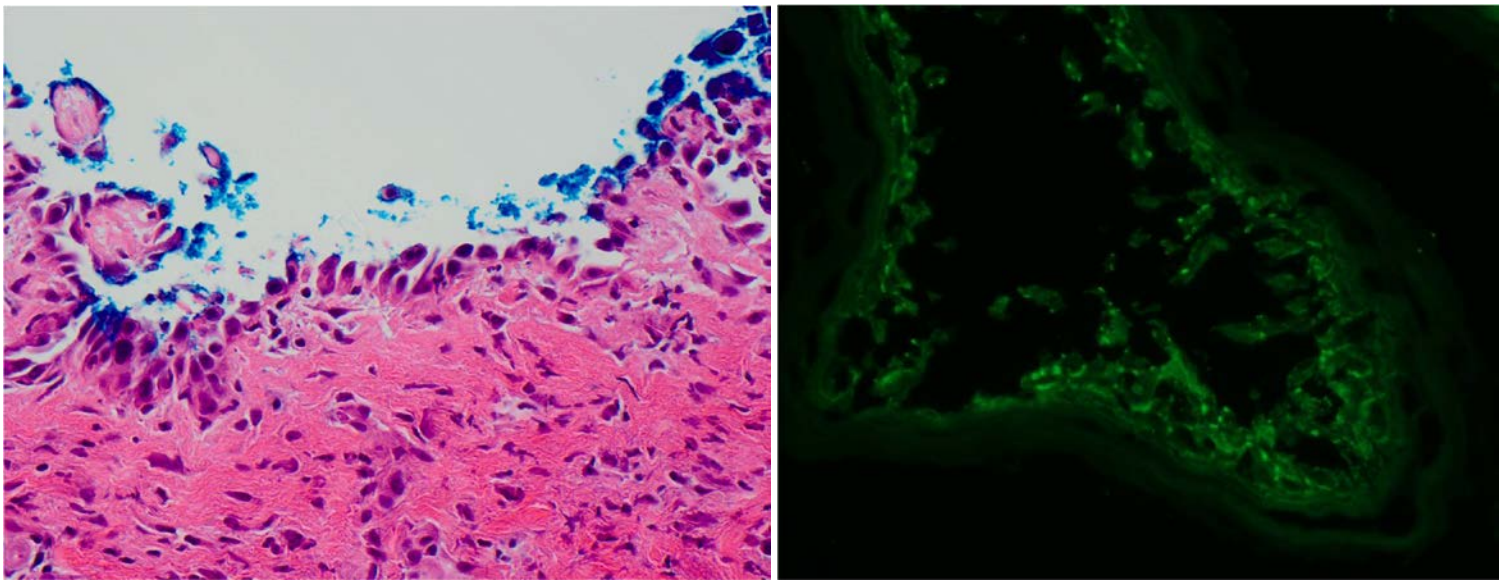

Figure 2. Histology A. Histology demonstrating intraepidermal suprabasilar acantholysis with classic “tombstoning” along the basal layer (hematoxylin-eosin, original magnification x 40). B. Direct immunofluorescence showing intracellular pattern of staining of IgG and C3 in the epidermis (original magnification x 10).

Discussion

Pemphigus vulgaris is an intraepidermal blistering disorder in which autoantibodies target desmogleins 3 and/or 1. This classically leads to the production of flaccid, fragile bullae and erosions because the antibody-targeted antigens are intraepidermal. The majority of patients with pemphigus vulgaris also have oral or other mucosal erosions due to the predominance of desmoglein 3 in mucosal surfaces [6, 7]. For the patient reported above, there was initial diagnostic uncertainty due to the variety of her skin findings. Her differential diagnosis upon presentation included Stevens-Johnson syndrome/toxic epidermal necrolysis owing to the raw appearance and extent of desquamation on her trunk. Other possibilities included bullous pemphigoid because of her tense and intact bullae, as well as IgA pemphigus, linear IgA bullous dermatosis, or paraneoplastic pemphigus because of the layered pus in her bullae, her target and annular lesions, and her extensive oral disease. Further workup including histology, direct immunofluorescence, and indirect immunofluorescence studies were all consistent with pemphigus vulgaris, thereby ruling out other autoimmune bullous disorders.

The differential diagnosis for “half-half” blisters with layered pus typically includes the subcorneal pustulosis-type of IgA pemphigus, Sneddon-Wilkinson disease, pustular psoriasis, or acute generalized exanthematous pustulosis [8]. The mechanism by which our patient developed large, tense bullae that had dependent layering of pus rather than flaccid bullae is unclear, but her findings suggested the presence of massive systemic inflammation.

True target lesions with at least 3 zones of color (as well as targetoid lesions with two zones of color) have a broad differential diagnosis, but are classically seen in erythema multiforme or early Stevens Johnson syndrom/toxic epidermal necrolysis. Targets or targetoid lesions can also be associated with fixed drug eruption, erythema chronicum migrans, polymorphic eruption of pregnancy, and rarely linear IgA bullous dermatosis and bullous pemphigoid [9, 10]. The varying color zones of concentric target lesions are thought to represent different stages of inflammation or pathogenesis in these conditions [9-11]. Some of our patient’s target lesions did have central early vesicle formation with concentric surrounding normal skin and then an outer ring of erythema.

Conclusions

This patient demonstrates several unusual morphologies of pemphigus vulgaris presenting concurrently. To our knowledge, both tense bullae with layering of pus and target lesions have not previously been reported in pemphigus vulgaris. Clinicians should include the possibility of pemphigus vulgaris in their differential diagnoses when encountering these lesions. In a patient presenting with manifold atypical morphologies such as this patient, it is prudent to maintain a broad differential diagnosis including erythema multiforme, Stevens Johnson syndrom/toxic epidermal necrolysis, and the autoimmune bullous disorders. It is also notable that our patient presented at age 82 although the typical age of onset of pemphigus vulgaris is in the 50s to 70s [12, 13]. We hypothesize that even though the pathophysiology of pemphigus vulgaris is intraepidermal, underlying features of aged skin such as decreased collagen synthesis, thinning of collagen bundles, and haphazard elastic fibers may have contributed to the

varied morphologies of skin findings in this patient [14, 15]. A thorough workup such as this includes a careful drug chart to evaluate for possible drug-induced eruptions, skin biopsies including a sample of peri-lesional skin for direct immunofluorescence, and indirect immunofluorescence serological studies performed on both monkey esophagus and rat bladder substrates to rule out paraneoplastic pemphigus.

References

1. Engineer L, Norton LA, Ahmed AR. Nail involvement in pemphigus vulgaris. J Am Acad Dermatol. 2000;43(3):529-535. [PMID 10954669]
2. Tan HH, Tay YK. An unusual case of pemphigus vulgaris presenting as bilateral foot ulcers. Clin Exp Dermatol. 2000;25(3):224-226. [PMID 10844502]
3. Yang Y, Lin M, Huang SJ, Min C, Liao WQ. A rare presentation of pemphigus vulgaris as multiple pustules. Indian J Dermatol. 2010;55(3):293-295. [PMID 21063530]
4. Arndt KA, Feingold DS. The sign of Pyotr Vasilyewich Nikolsky. N Engl J Med. 1970;282(20):1154-1155. [PMID 5439414]
5. Asboe-Hansen G. Blister-spread induced by finger-pressure, a diagnostic sign in pemphigus. J Invest Dermatol. 1960;34:5-9. [PMID 13794642]
6. Amagai M, Tsunoda K, Zillikens D, Nagai T, Nishikawa T. The clinical phenotype of pemphigus is defined by the anti-desmoglein autoantibody profile. J Am Acad Dermatol. 1999;40(2 Pt 1):167-170. [PMID 10025740]
7. Sirois DA, Fatahzadeh M, Roth R, Ettlin D. Diagnostic patterns and delays in pemphigus vulgaris: experience with 99 patients. Arch Dermatol. 2000;136(12):1569-1570. [PMID 11115183]
8. Nishikawa T, Hashimoto T. Dermatoses with intraepidermal IgA deposits. Clin Dermatol. 2000;18(3):315-318. [PMID 10856663]
9. Hughey LC. Approach to the hospitalized patient with targetoid lesions. Dermatol Ther. 2011;24(2):196-206. [PMID 21410609]
10. Wolf R, Lipozencic J. Shape and configuration of skin lesions: targetoid lesions. Clin Dermatol. 2011;29(5):504-508. [PMID 21855725]
11. Huff JC, Weston WL, Tonnesen MG. Erythema multiforme: a critical review of characteristics, diagnostic criteria, and causes. J Am Acad Dermatol. 1983;8(6):763-775. [PMID 6345608]
12. Huang YH, Kuo CF, Chen YH, Yang YW. Incidence, mortality, and causes of death of patients with pemphigus in Taiwan: a nationwide population-based study. J Invest Dermatol. 2012;132(1):92-97. [PMID 21850023]
13. Langan SM, Smeeth L, Hubbard R, Fleming KM, Smith CJ, West J. Bullous pemphigoid and pemphigus vulgaris--incidence and mortality in the UK: population based cohort study. BMJ. 2008;337:a180. [PMID 18614511]
14. Sherratt MJ. Tissue elasticity and the ageing elastic fibre. Age (Dordr). 2009;31(4):305-325. [PMID 19588272]
15. Varani J, Warner RL, Gharaee-Kermani M, et al. Vitamin A antagonizes decreased cell growth and elevated collagen-degrading matrix metalloproteinases and stimulates collagen accumulation in naturally aged human skin. J Invest Dermatol. 2000;114(3):480-486. [PMID 10692106]