

Single Case

Diffuse Bullous Eruptions in an Elderly Woman: Late-Onset Bullous Systemic Lupus Erythematosus

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Keywords

Bullae · Systemic lupus erythematosus · Lupus · Bullous lupus · Epidermolysis bullosa acquisita · Cutaneous

Abstract

Vesiculobullous eruptions in the elderly represent a diverse range of varying pathophysiologies and can present a significant clinical dilemma to the diagnostician. Diagnosis requires a careful review of clinical history, attention to detail on physical and histomorphological examination, and appropriate immunofluorescence testing. We describe the case of a 73-year-old female who presented to our hospital with a painful blistering skin rash developed over 2 days. Examination of the skin was remarkable for numerous flaccid hemorrhagic bullae on a normal-appearing nonerythematous skin involving both the upper and lower extremities. Histopathology of the biopsy lesion showed interface change at the epidermo-dermal region with subepidermal blister formation, mild dermal fibrosis, and sparse interstitial neutrophilic infiltrate. Immunohistological analysis was significant for positive IgG basement membrane zone antibodies with a dermal pattern of localization on direct immunofluorescence and positive IgG antinuclear antibodies on indirect immunofluorescence. Evidence of antibodies to type VII collagen suggested the diagnosis of epidermolysis bullosa acquisita versus bullous systemic lupus erythematosus (BSLE). A diagnosis of BSLE was made based on positive American College of Rheumatology criteria, acquired vesiculo-bullous eruptions with compatible histopathological and immunofluorescence findings. This case illustrates one of many difficulties a physician encounters while arriving at a diagnosis from a myriad of im-

munobullous dermatoses. Also, it is important for internists and dermatologists alike to be aware of and differentiate this uncommon and nonspecific cutaneous SLE manifestation from a myriad of disorders presenting with vesiculobullous skin eruptions in the elderly.

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Published by S. Karger AG, Basel

Case Presentation

A 73-year-old female presented to our hospital with a painful blistering skin rash since 2 days. Her past medical history was significant for hypertension on thiazides, hyperlipidemia, rheumatoid arthritis (not on disease-modifying antirheumatoid drugs), and thrombocytopenia of unclear etiology. She first noticed the rash 2 days ago and noticed the lesions to be sudden in onset, spontaneously occurring, and progressively involving all areas of the body. The lesions were extremely painful to touch, nonpruritic, and would rupture with a bloody discharge. She denied arthralgias, photosensitivity, fevers or chills, cough, sore throat, hemoptysis, diarrhea or vomiting, epistaxis, hematemesis, or melena. Of note, she had been prescribed a course of Bactrim for a urinary tract infection, which she completed 2 days prior to the onset of the rash. She had a similar presentation 2 months ago, when she was admitted to our hospital for an extensive workup of the underlying etiology. Clinical history, then, did not disclose any identifiable medication triggers. She had not experienced any rashes previously in her life. Examination of the skin, on current admission, was remarkable for numerous various-sized flaccid hemorrhagic bullae on a normal-appearing nonerythematous skin involving both the upper and lower extremities, including the palms, axillae, back, and inguinal regions (fig. 1). Some of the ruptured bullae had left tender, weeping erosions. A careful examination of her oral cavity revealed ulcers on the palate and buccal mucosa with numerous 2- to 3-mm blood-filled blisters on the tongue. The remainder of her exam was unremarkable.

Labs were significant for hemoglobin 8.8 g/dl, platelet count 17,000/mm³, and albumin 3 g/dl. Iron studies were consistent with anemia of chronic disease. Urinalysis was bland with mild proteinuria (30 mg/dl) without red or white blood cell casts. Autoimmune antibody panel was significant for positive antinuclear antibody titers (1:80) with a speckled pattern on immunofluorescence, low C3 complement (72 mg/dl), positive anti-RNP, anti-chromatin, and anti-Smith antibodies. Immunoglobulin levels were high for IgA (1,080 mg/dl). The following blood tests were either normal or within normal limits: white blood cell count, coagulation studies, ADAMTS13, serum protein electrophoresis, urticarial-induced basophil activation, β 2 glycoprotein antibody; anti-SSA, anti-SSB, anti-centromere, Scl-70, myeloperoxidase, serine protease, anti-BP180, anti-BP230, acute and chronic hepatitis panel.

Histopathology of the biopsy lesion showed interface change at the epidermo-dermal region with subepidermal blister formation, mild dermal fibrosis, and sparse interstitial neutrophilic infiltrate. Immunohistological analysis was significant for positive IgG basement membrane zone antibodies with a dermal pattern of localization on direct immunofluorescence and positive IgG antinuclear antibodies on indirect immunofluorescence. Negative IgA, anti-BP180, and anti-BP230 on immunofluorescence testing helped rule out linear IgA bullous disease, anti-BP180 pemphigoid, and anti-BP230 pemphigoid, respectively. Evidence of antibodies to type VII collagen suggested the diagnosis of epidermolysis bullosa acquisita (EBA) versus bullous systemic lupus erythematosus (BSLE) and made a drug-induced bullous reaction an unlikely possibility [1]. Our patient met 4 of the 11 American College of

Rheumatology (ACR) SLE criteria, i.e., abnormal antinuclear antibody titers, positive anti-Smith antibodies, immune thrombocytopenia, and oral ulcers. A diagnosis of BSLE was made based on positive ACR criteria, acquired vesiculo-bullous eruptions with compatible histopathological and immunofluorescence findings.

Discussion

This case illustrates one of many difficulties a physician encounters while arriving at a diagnosis from a myriad of immunobullous dermatoses. Histopathological and immunofluorescence testing play a key diagnostic role in narrowing an extensive differential diagnosis of vesiculobullous disorders. BSLE needs to be differentiated from pemphigoid, a much more common immunobullous disorder in elderly patients over 70 years old [2]. The negative pemphigoid serologies and incompatible immunofluorescence findings helped rule out pemphigoid. BSLE must also be differentiated from EBA, a disorder which shares many clinical and histopathological features of BSLE [3]. Immunopathological criteria of BSLE are similar to EBA and can present a significant diagnostic dilemma, especially in a patient with no known prior history of SLE. Differentiating these two disorders is important to inform the physician on optimum management and prognosis. A careful history taking focusing on characteristics of the lesions, relevant serologies, and response to dapsone help differentiate these two disorders [4]. Lesions of EBA are predominantly mechanobullous in nature and characteristically occur on trauma-exposed areas like the elbows, knees, ankles, and dorsum of the hands [5]. Also, EBA skin lesions are more resistant to treatment with steroids and other immunomodulatory agents, an important differentiating characteristic. Positive antinuclear antibody titers with fulfillment of ACR SLE criteria and response to steroids favored the diagnosis of BSLE in our patient [3, 6]. It was her first clinical manifestation of elderly-onset SLE, a specific SLE subset with significantly poor morbidity and mortality outcomes [7, 8]. BSLE is a very uncommon and nonspecific cutaneous manifestation of SLE occurring in less than 1% of patients [9]. It generally occurs in middle-aged adults but has also been rarely reported in the elderly [3]. BSLE may coexist with other immunobullous and nonimmunobullous diseases [5]. BSLE may occur as the initial manifestation of SLE and requires the diagnostician to maintain a high degree of clinical suspicion [10]. Secondly, SLE features are common in rheumatoid arthritis, and the two diseases can coexist in the same individual, as in our patient [11]. Our patient was initiated on empiric pulsed steroids, while diagnostic workup was in progress, and showed a good clinical response to treatment (fig. 2). BSLE lesions have a dramatic response to dapsone, making it the therapeutic agent of choice with a significant diagnostic value [12]. Responses to corticosteroids are less definite, but case reports have documented effectiveness to steroid administration [13]. It is important for internists and dermatologists alike to be aware of and differentiate this uncommon and nonspecific cutaneous SLE manifestation from a myriad of disorders presenting with vesiculobullous skin eruptions in the elderly. At the time of this writing, the patient was asked to follow up with the dermatologist to discuss her diagnosis and institute definitive management.

Statement of Ethics

The patient's written informed consent was obtained.

Disclosure Statement

The authors have no affiliations with or involvement in any organization or entity with any financial or nonfinancial interest in the subject matter or materials discussed in this work.

References

- 1 Hallel-Halevy D, Nadelman C, Chen M, et al: Epidermolysis bullosa acquisita: update and review. *Clin Dermatol* 2001;19:712–718.
- 2 Raap U, Werfel T: Bullous pemphigoid. *N Engl J Med* 2015;373:1659.
- 3 Vassileva S: Bullous systemic lupus erythematosus. *Clin Dermatol* 2004;22:129–138.
- 4 Hall RP, Lawley TJ, Smith HR, Katz SI: Bullous eruption of systemic lupus erythematosus. Dramatic response to dapsone therapy. *Ann Intern Med* 1982;97:165–170.
- 5 Ludwig RJ: Clinical presentation, pathogenesis, diagnosis, and treatment of epidermolysis bullosa acquisita. *ISRN Dermatol* 2013;2013:812029.
- 6 Camisa C, Sharma HM: Vesiculobullous systemic lupus erythematosus. *J Am Acad Dermatol* 1983;9:924–933.
- 7 Lazaro D: Elderly-onset systemic lupus erythematosus: prevalence, clinical course and treatment. *Drugs Aging* 2007;24:701–715.
- 8 Mak SK, Lam EK, Wong AK: Clinical profile of patients with late-onset SLE: not a benign subgroup. *Lupus* 1998;7:23–28.
- 9 Hall RP III, Lawley TJ, Katz SI: Bullous eruption of systemic lupus erythematosus. *J Am Acad Dermatol* 1982;7:797–799.
- 10 Huang C-Y, Chen T-C: Bullous pemphigoid associated with systemic lupus erythematosus: the discrimination of antibasement membrane zone antibody. *Int J Dermatol* 1997;36:40–42.
- 11 Fujimoto W, Hamada T: Bullous systemic lupus erythematosus as an initial manifestation of SLE. *J Dermatol* 2005;32:1021–1027.
- 12 Icen M, Nicola PJ, Maradit-Kremers H, Crowson CS, Thorneau TM, et al: Systemic lupus erythematosus features in rheumatoid arthritis and their impact on overall mortality. *J Rheumatol* 2009;36:50–57.
- 13 Tincopa M, Puttgen KB, Sule S, Cohen BA, Gerstenblith MR: Bullous lupus: an unusual initial presentation of systemic lupus erythematosus in an adolescent girl. *Pediatr Dermatol* 2010;27:373–376.



Fig. 1. Hemorrhagic flaccid bullae involving the right arm with surrounding normal skin.



Fig. 2. Bullae replaced by patches of postinflammatory hypopigmentation.