SKIN

BRIEF ARTICLE

Unilateral and Localized Bullous Eruption in a 71-year-old Woman

Karishma Daftary, BA[1], Raj Chovatiya, MD, PhD[1]

[1]Department of Dermatology, Feinberg School of Medicine at Northwestern University, Chicago, IL

CASE REPORT

A 71-year-old South Asian woman presented with a 2-month, pruritic, bullous eruption localized only to the right leg, refractory to topical triamcinolone. Her history was notable for a stage IVB small-cell neuroendocrine tumor in the mediastinum diagnosed two years prior. Following initial carboplatin and etoposide, she was transitioned to combined ipilimumab / nivolumab for the past year. Her tumor treatment course was notable for autoimmune hypothyroidism secondary to immunotherapy. She had otherwise stable disease without progression. Skin examination revealed tense bullae filled with clear fluid, denuded vesicles, and post-inflammatory hyperpigmentation at sites of healed bullae localized only to the right mid-lateral leg **(Figure 1).**

Punch biopsy of an active bulla revealed a subepidermal acantholysis with spongiosis and numerous eosinophils**,** and direct immunofluorescence showed linear IgG and C3 deposits at the dermal-epidermal junction (**Figure 2**). These findings were consistent with unilateral, localized bullous pemphigoid (LBP). The eruption resolved completely without recurrence following twice-daily betamethasone dipropionate 0.05% ointment.

DISCUSSION

Bullous pemphigoid (BP) is the most commonly occurring autoimmune blistering dermatosis, affecting predominantly elderly patients in the 7th decade of life. It classically presents with diffuse pruritus and bullae. Pathogenesis involves autoantibodies directed at hemidesmosomal proteins located at the dermal-epidermal junction – most commonly BP230 and BP180 (BP antigens 1 and 2, respectively). Because these proteins are expressed throughout the skin, BP typically presents in a diffuse, symmetric pattern. In addition to thorough physical examination, diagnosis of BP is made with histology demonstrating subepidermal blisters with eosinophils, immunofluorescence depicting linear deposits of IgG and C3 along the basement membrane, and quantification of autoantibodies using enzyme-linked immunoassay.

LBP is a variant of BP in which lesions are restricted to certain sites. This variant is uncommon, with a recent cohort study suggesting a prevalence of 2.5% among BP patients.[1] LBP often arises in areas of previous trauma or radiation and has been more frequently reported in the pretibial, vulvar, peristomal, and umbilical regions.[2]

(c) 2022 THE AUTHORS. Published by the National Society for Cutaneous Medicine.

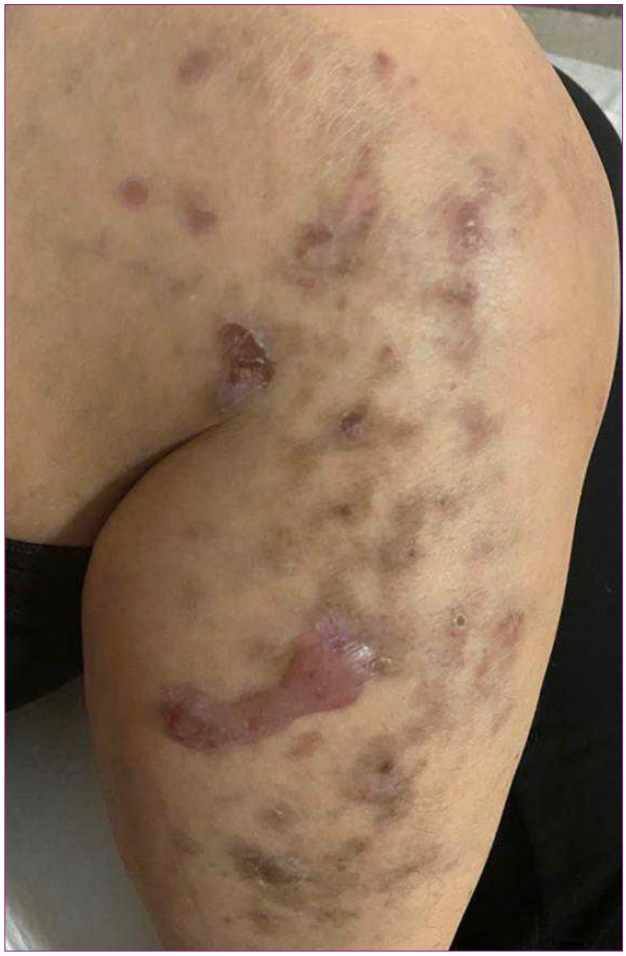

Figure 1. Bullae localized to the right mid-lateral leg.

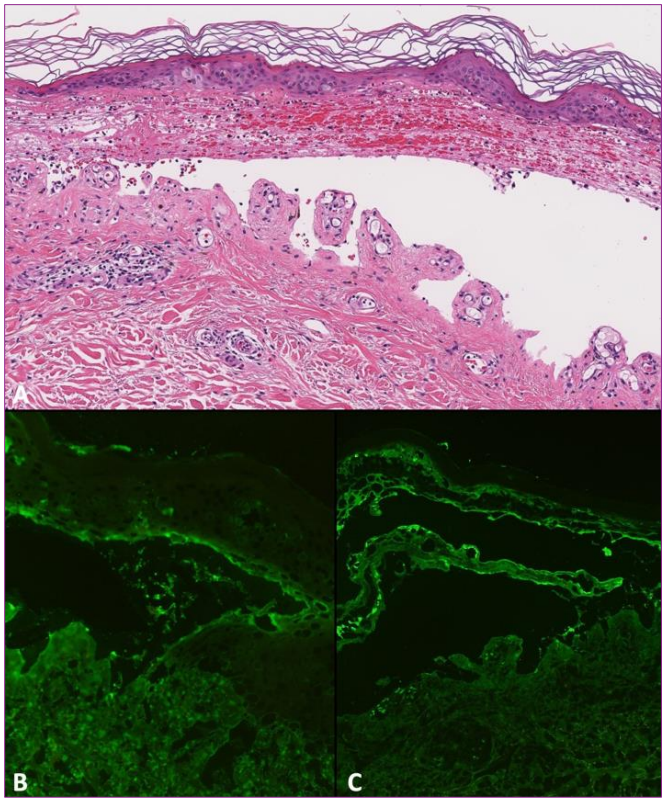

Figure 2. (A) Lesional punch biopsy of active bulla demonstrating subepidermal acantholysis with spongiosis and numerous eosinophils (hematoxylin & eosin, 10X); Peri-lesional punch biopsy showing IgG (B) and C3 (C) deposits at the dermal-epidermal junction (direct immunofluorescence, 10X).

The disease course is more benign than generalized BP due to its responsiveness to topical steroids, though LBP may also progress to generalized disease.[3,4]

Triggering factors implicated in the development of LBP include radiation, burns, surgical procedures, phototherapy, venous stasis, and bacterial infections.[1] Several medications (e.g., angiotensin-converting-enzyme inhibitors, loop diuretics, gabapentin, iodine, dithranol, and tar) have also been reported to cause this variant.[5] In our case, immunotherapy was the likely causative factor leading to the development of LBP. While widespread immunobullous eruptions like BP are well-described cutaneous adverse reactions associated with anti-CTLA-4 and -programmed cell death protein-1 (PD-1) immunotherapy, reports of LBP following the use of these medications are extraordinarily rare.[6]

Diagnosis of LBP is often delayed compared to generalized BP, as the differential diagnosis of a localized bullous eruption on the leg is broad and includes trauma (e.g., burn, friction, pressure), edema, arthropod assault, contact dermatitis, leukocytoclastic vasculitis, bullous diabeticorum, acute eczema, photodermatitis, and infection (namely herpesvirus and bacterial). For new-onset bullous eruptions in patients receiving immunotherapy, it is important to consider clinical correlation alongside skin biopsy and

(c) 2022 THE AUTHORS. Published by the National Society for Cutaneous Medicine.

immunofluorescence to differentiate between etiologies.

Conflict of Interest Disclosures: RC has served as an advisory board member, consultant, and/or investigator for AbbVie, Arcutis, Arena, Argenx, Beiersdorf, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, EPI Health, Incyte, LEO Pharma, L'Oréal, National Eczema Association, Pfizer Inc., Regeneron, Sanofi, and UCB, and speaker for AbbVie, Arcutis, Dermavant, Eli Lilly and Company, EPI Health, Incyte, LEO Pharma, Pfizer Inc., Regeneron, Sanofi, and UCB. KD has no conflicts to disclose.

Funding: None

Corresponding Author:
Raj Chovatiya, MD, PhD
Department of Dermatology
Northwestern University Feinberg School of Medicine
676 N St Clair St, Suite 1600
Chicago, IL 60611
Email: raj.chovatiya@gmail.com

References:

1. Ständer S, Kasperkiewicz M, Thaçi D, et al. Prevalence and presumptive triggers of localized bullous pemphigoid. J Dermatol 2021;48(8):1257-1261. (In eng). DOI: 10.1111/1346-8138.15912.
2. Bernard P, Antonicelli F. Bullous Pemphigoid: A Review of its Diagnosis, Associations and Treatment. Am J Clin Dermatol 2017;18(4):513-528. (In eng). DOI: 10.1007/s40257-017-0264-2.
3. Salomon RJ, Briggaman RA, Wernikoff SY, Kayne AL. Localized bullous pemphigoid. A mimic of acute contact dermatitis. Arch Dermatol 1987;123(3):389-92. (In eng). DOI: 10.1001/archderm.123.3.389.
4. Wang Y, Mao X, Liu Y, Li L. Localized bullous pemphigoid: a case report. Ann Transl Med 2020;8(5):249. (In eng). DOI: 10.21037/atm.2020.01.104.
5. Wenzel D, Droms R, St John J, Luffman C, Levin NA. Localized bullous pemphigoid after knee replacement surgery. Dermatol Online J 2021;27(3) (In eng).
6. Amber KT, Valdebran M, Lu Y, De Feraudy S, Linden KG. Localized pretibial bullous pemphigoid arising in a patient on pembrolizumab for metastatic melanoma. J Dtsch Dermatol Ges 2018;16(2):196-198. (In eng). DOI: 10.1111/ddg.13411.

(c) 2022 THE AUTHORS. Published by the National Society for Cutaneous Medicine.