

Annular bullous pemphigoid: A case report and review of literature

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Abstract

Bullous pemphigoid is an autoimmune blistering disease that primarily affects the geriatric population. It often presents as urticarial erythematous plaques, which evolve into subepidermal blisters accompanied by pruritus. Although rare, clinical variants of bullous pemphigoid have been documented. We present a rare case of annular bullous pemphigoid in a 50-year-old male and offer a brief review of the literature. Only five other case reports, including three in adults, have described this unusual presentation, which can mimic other autoimmune blistering diseases, including linear IgA bullous dermatosis and pemphigus herpetiformis. Therefore, histopathology and immunologic studies were essential in properly diagnosing this patient. Our case supports that annular blistering lesions can be a clinical variant of bullous pemphigoid.

Keywords

Bullous pemphigoid, annular, autoimmune blistering diseases

Introduction

Bullous pemphigoid (BP) is the most common acquired subepidermal autoimmune blistering disease (AIBD). BP is associated with autoantibodies directed against hemidesmosomal proteins BP180 and BP230, which participate in epithelial–stromal adhesion in the skin.¹ This disease predominantly affects the elderly. The annual cumulative incidence of BP is 8.2 per million people globally, with a general trend of increasing incidence over time.² BP often presents in the prodromal phase as urticarial plaques and/or papular erythematous lesions with mild to severe pruritus, which evolve into vesicles and tense bullae on erythematous or normal-appearing skin affecting primarily the trunk and flexural aspects of the extremities.¹ However, clinical presentation can be very polymorphic, and clinical variants have been documented in the literature.¹ We herein report a rare case of annular BP in a 50-year-old male. Diagnosis was confirmed with histologic and immunologic studies. Treatment consisted of topical and systemic steroids, with no documented relapse over a year after prednisone was tapered.

Case report

A 50-year-old man of Pakistani origin was referred to the dermatology clinic for a new-onset pruritic bullous eruption. Past medical history revealed past hepatitis B as well as a history of pruritic plaques located on his legs for several

years treated with topical corticosteroids. The patient was not taking any medications, and history revealed no recent use of non-prescription medications or supplements. The review of systems was negative, including for signs and symptoms of neoplasia. On physical examination, tense bullae and vesicles were clustered in an annular string-of-pearls arrangement on an erythematous base on both forearms (Figure 1). Lichenified erythematous plaques with overlying vesicles and some bullae were distributed acral on dorsal hands and feet (Figure 2). Mucous membranes were spared. Given the patient's age and configuration of lesions, linear IgA bullous dermatosis (LABD) versus pemphigus herpetiformis was initially suspected. Skin biopsy and direct immunofluorescence (DIF) were performed, and the patient was started on prednisone 20 mg/day. Serum analysis revealed an

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Figure 1. Erythematous annular plaques with vesicles in a string-of-pearls configuration on the right forearm.



Figure 2. Lichenified erythematous plaques with vesicles and crusted lesions on dorsal hands and fingers.

elevated eosinophil count at 1.0×10^9 g/L with the remainder of complete blood count and comprehensive metabolic panel within normal limits.

Histopathology with hematoxylin and eosin staining showed subepithelial bullous dermatitis with numerous eosinophils as well as perivascular chronic inflammation rich in eosinophils (Figure 3). DIF of perilesional skin revealed linear IgG and C3 binding along basement membrane zone (BMZ), while IgA binding was weak and considered negative. Salt-split skin study revealed IgG and C3 deposits along both epidermal and dermal sides of the split (Figure 4). Based on these findings, diagnosis of annular BP was confirmed.

At 1-month follow-up, complete resolution of bullous lesions was observed, with only some persistent pruritus on the lower legs. Topical clobetasol was prescribed as a maintenance treatment, and prednisone was slowly tapered over

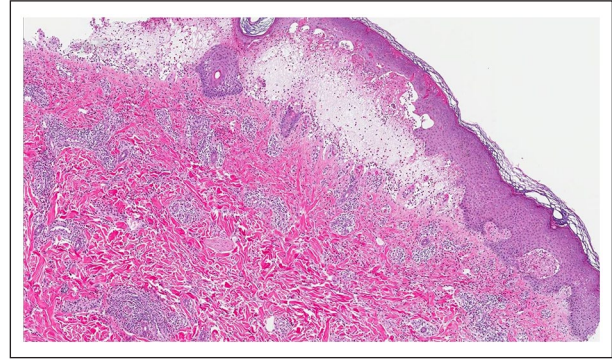


Figure 3. Subepidermal blister rich in eosinophils with perivascular eosinophilic inflammatory infiltrates on hematoxylin-eosin staining (magnification $\times 10$).

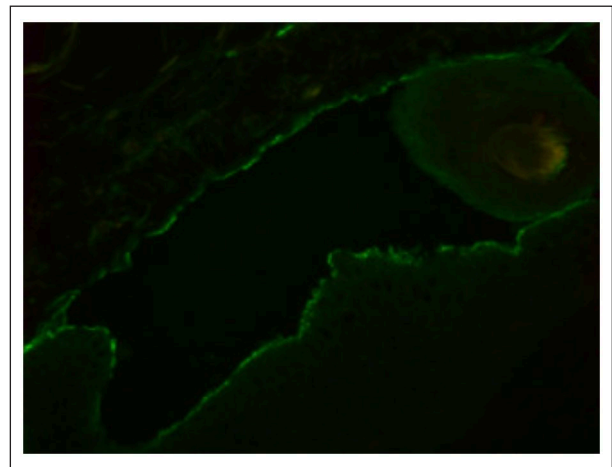


Figure 4. IgG and C3 deposits on both epidermal and dermal sides on the salt-split technique of direct immunofluorescence study (magnification $\times 40$).

6 weeks. No recurrence or relapse of blisters was noted during follow-up period over a year after discontinuation of treatment.

Discussion

Annular BP is a rare variant of BP with only five other cases described in the literature. Clinical diagnosis can be challenging, especially when occurring in a younger age group, as other AIBDs are usually considered when faced with annular blistering lesions. Pemphigus herpetiformis, LABD, epidermolysis bullosa acquisita (EBA), bullous systemic lupus erythematosus (BSLE), and pemphigoid gestationis can mimic annular BP.³

Empiric topical or systemic corticosteroid treatment is typically initiated while awaiting results from histopathology, although for neutrophil-mediated AIBDs, dapsone may be a more appropriate treatment.^{3,4} Histologic and, when available, immunologic findings are essential to confirm

Table 1. Characteristics of patients with annular BP described in the literature.

Case report	Patient characteristics	Immunologic findings	Treatment outcome
Fonseca and Contreras ¹⁰	Male, 4years old	DIF: Linear IgG and C3 along BMZ IIF: NA	Treatment: Methylprednisone, dapsone Outcome: Complete response
Giacaman et al. ¹¹	Male, 40years old Rectal adenocarcinoma	DIF: Linear IgG and C3 along BMZ Salt split: IgG binding on the epidermal side of the split IIF: Negative ELISA: Positive for BP180 and negative for BP230 antibodies	Treatment: Topical corticosteroids, prednisone, mesorectal excision Outcome: Complete response after resection of cancer
Lesniewska et al. ¹²	Male, 35years old Mild oral involvement Psoriasis	DIF: Linear IgG and C3 along BMZ Salt split: IgG binding on the epidermal side of the split IIF: IgG 1:80	Treatment: Topical corticosteroids, methotrexate Outcome: Complete response
Raposo et al. ¹³	Female, 5 months old	DIF: Linear IgG and C3 along BMZ ELISA: Positive for BP180 antibodies	Treatment: Topical corticosteroids, prednisolone, dapsone Outcome: Complete response
Yu-Yang et al. ¹⁴	Female, 64years old	DIF: Linear IgG and C3 along BMZ IIF: NA	Treatment: Prednisolone, azathioprine Outcome: Complete response

BP: bullous pemphigoid; DIF: direct immunofluorescence; BMZ: basement membrane zone; IIF: indirect immunofluorescence; NA: not applicable; ELISA: enzyme-linked immunosorbent assay.

diagnosis.¹ In our case, a diagnosis of BP was made considering peripheral eosinophilia, histologic findings, and linear IgG and C3 binding along BMZ present on epidermal and dermal sides on the salt-split technique. In fact, while pemphigus herpetiformis and LABD were initially suspected, DIF in the former reveals intraepidermal IgG and C3 deposits, while the latter reveals IgA deposition along BMZ.^{3,5} The presence of an eosinophil-rich infiltrate also favors a histologic diagnosis of BP, whereas LABD and BSLE typically exhibit more neutrophils.⁴ Although BP is mainly characterized by linear IgG and C3 binding along the BMZ, IgA can be present in BP and an immunological overlap between BP and LABD has been reported.⁶⁻⁸

Furthermore, salt-split studies can aid in distinguishing BP from other AIBDs with IgG deposition on the dermal side of the BMZ, such as EBA, BSLE, or certain subtypes of mucous membrane pemphigoid.⁹ Although BP classically presents with epidermal staining on salt-split skin, dermal and epidermal staining frequently co-occur, as was the case in our patient.⁹ Although not available at our center, demonstration of IgG anti-BP180/BP230 autoantibodies on enzyme-linked immunosorbent assay (ELISA) can also help confirm the diagnosis.¹

A review of the literature was performed in PubMed using the key terms “bullous pemphigoid,” “annular,” “figurate,” “polycyclic,” “erythema gyratum repens” (EGR), “erythema annulare centrifugum” (EAC), “erythema multiforme,” and “vesicular.” Non-bullous cases, paraneoplastic pemphigus, and anti-p200 pemphigoid were excluded. Among the 15 identified case reports, we retained 5 that demonstrated clinical, histologic, and immunologic compatibility with annular BP (Table 1).¹⁰⁻¹⁴

Clinical presentation in all cases consisted of erythematous plaques with bullae in an annular configuration on the trunk and extremities, with sparing of the head and neck except in one pediatric case.¹³ Mucous membranes were spared in all but one case.¹² Histologic examination revealed subepidermal blistering with eosinophilic infiltrates in all but one case, which did not mention histology, but had compatible DIF as in all five cases.¹²

Out of the five cases found, three cases involved adult patients between the ages of 35 and 64 years, therefore occurring at a much younger age than classic BP.^{11,12,14} Furthermore, one patient was found to have an underlying neoplasia with resolution of BP after resection.¹¹ Although rare, EAC- or EGR-like BP seems to have a more common association with underlying neoplasia.¹⁵⁻¹⁸ As our review revealed an overlap with the terminology used to describe BP variants, including EAC-like and EGR-like BP, we recommended age-appropriate cancer screening in our patient, which was unremarkable. Complete clearance of lesions was obtained in all patients, and no relapse was reported during the follow-up period of 2 months to 10 years.¹⁰⁻¹⁴

In conclusion, our case and previous reports support that BP can rarely present in an annular configuration, and annular BP should be considered in the differential diagnosis of annular bullous eruptions, even in younger populations.

Author's note

A.M. and D.L. contributed as first co-authors.

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Informed consent

The patient provided written consent for publication of the case report.

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