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Bullous Pemphigoid Mimicking Cellulitis

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Abstract

Bullous pemphigoid (BP) is the most prevalent autoimmune blistering skin disease in the Western world affecting mainly the elderly population. The diagnosis is based on clinical assessment along with specific immunopathologic findings on skin biopsy. Risk factors include genetic factors, environmental exposures, and several infections including hepatitis B, hepatitis C, *Helicobacter pylori*, *Toxoplasma gondi*, and cytomegalovirus. A variety of drugs have been associated with BP including but not limited to dipeptidyl peptidase-4 inhibitors, loop diuretics, spironolactone, and neuroleptics. Associated neurologic disorders (dementia, Parkinson's disease, bipolar disorder, previous stroke history, and multiple sclerosis) have also been described. Common clinical presentation consists of extremely pruritic inflammatory plaques that resemble eczematous dermatitis or urticaria, followed by formation of tense bullae with subsequent erosions. Typical distribution involves the trunk and extremities. Mucosa is typically spared affecting only 10% to 30% of patients. Several unusual clinical presentations of BP have been described such as nonbullous forms with erythematous excoriated papules, plaques, and nodules. Other reported findings include urticarial lesions, prurigo-like nodules, multiple small vesicles resembling dermatitis herpetiformis or pompholyx, vegetating and purulent lesions localized in intertriginous areas, and even exfoliative erythroderma. Recognition and management of such cases can present a diagnostic challenge to clinicians. In this article, we describe another variant which to our knowledge is the first case to present with a cellulitis-like presentation in a patient with a known history of BP.

Keywords

bullous pemphigoid, atypical presentation, autoimmune blistering disease, clinical variants

Introduction

Bullous pemphigoid (BP) is the most common autoimmune blistering disease in the elderly that is associated with multiple environmental and genetic factors. It has various cutaneous manifestations and may imitate other conditions. To our knowledge, cellulitis-like picture has never been previously reported.

Case Report

An 85-year-old man with a history of BP presented with right forearm swelling and erythema for 3 days. The patient had a history of atrial fibrillation, chronic obstructive pulmonary disease, and diabetes mellitus. He was diagnosed with BP about 7 years ago when he presented with a similar rash. The diagnosis of BP was made based on a punch biopsy showing subepidermal bullae containing a dense inflammatory infiltrate with prominent eosinophils. Direct immunofluorescence revealed a strong linear staining pattern of the basement membrane zone with immunoglobulin G and C3. Since then, he has been having similar although less severe recurrent episodes about once every 1 to 2 years involving lower and upper extremities with complete remission in between, every time treated successfully with short courses of intramuscular, oral, and topical steroids. He also required methotrexate maintenance therapy for the initial episode. Medications included insulin, metoprolol, gabapentin, simvastatin, warfarin, lisinopril, tamsulosin, and furosemide. Examination revealed swelling, erythema, and warmth of the right upper extremity from the mid upper arm all the way to the hand (Figures 1 and 2) along with a few deep tense bullae formation of 2 to 3 cm (Figure 3). Laboratory investigations revealed the following: leukocytes 9.3 $\times$ 10 9/L, hemoglobin 13.7 g/dL, creatinine 1.83 mg/dL, platelets 248 $\times$ 10 9/L, procalcitonin $<$0.05 ng/mL, lactic acid 2.3 mmol/L, and negative blood cultures. The patient was initially started on broad-spectrum antibiotics due to suspicion of infectious etiology. However, due to the absence of fever and elevated inflammatory markers, the antibiotics were discontinued, and oral

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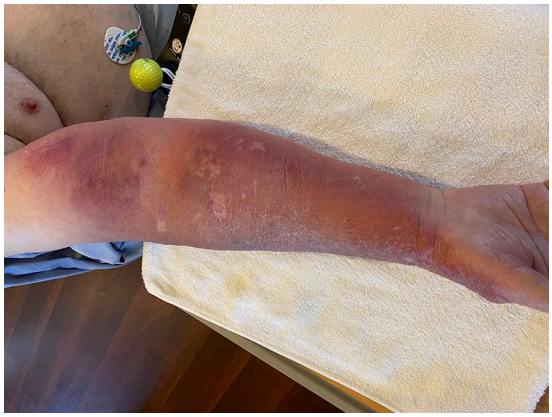

Figure 1. An extensive erythematous and edematous plaque on the right arm and post inflammatory hypo- and hyperpigmentation.

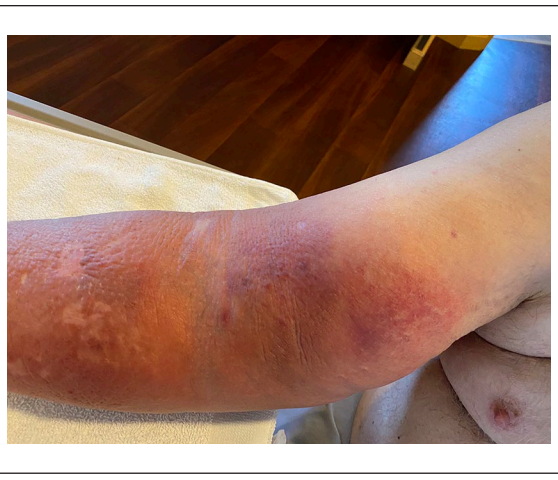

Figure 2. An extensive erythematous and edematous plaque on the right arm and post inflammatory hypo- and hyperpigmentation.

prednisone 40 mg daily was initiated with tremendous and rapid response. His eruption had cleared with no new bullae at the 1-week outpatient follow-up with his dermatologist. The prednisone was tapered accordingly.

Discussion

Bullous pemphigoid is the most frequent autoimmune blistering disorder in Western Hemisphere with increased incidence in the last decades. It particularly affects the elderly population. The incidence has been reported to be 24 cases per million per year in the United States, with the highest incidence of 42.8 cases per million per year in the United Kingdom.[1] The disease is characterized by autoantibody formation against the hemidesmosome. Several antigens have been identified as potential targets of autoantibodies, mainly

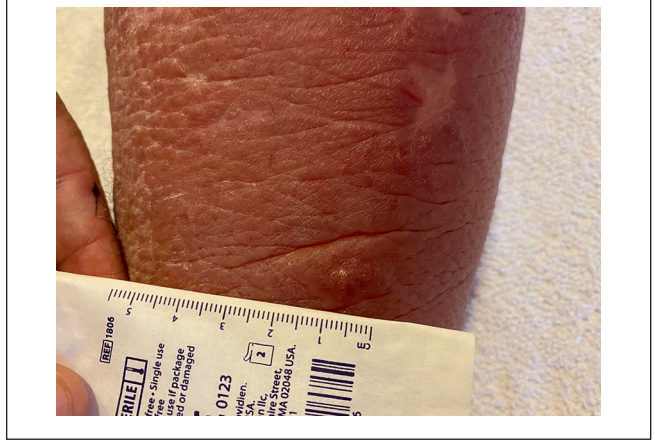

Figure 3. A close-up of large deep-seated tense bullae on the right forearm.

BP antigen 180 (BP180) and BP antigen 230 (BP230).[2] Antibody-mediated activation of the complement apparently contributes to bullae formation. Inflammatory cell recruitment and release of proinflammatory mediators and proteases are also involved in the process. Other potential contributory factors have been described including environmental, genetic, and the so-called phenomenon of epitope spreading. Association with hepatitis B, hepatitis C, *Helicobacter pylori*, *Toxoplasma gondi*, and cytomegalovirus were more prevalent in one small case-control study.[3] A variety of drugs have been associated with BP including a few antihypertensive medications (amlodipine, losartan, lisinopril, and clonidine), glucose-lowering (dipeptidyl peptidase-4 inhibitors), nonsteroidal anti-inflammatory drugs (ibuprofen celecoxib), selective serotonin reuptake inhibitors (fluoxetine), several diuretics (furosemide, spironolactone), proton-pump inhibitors (omeprazole), neuroleptics (risperidone), antibiotics (penicillins, fluoroquinolones, rifampin, and cephalexin), and many others.[4] The epitope spreading phenomenon is an autoimmune response against normal host antigens as a result of the immune-mediated damage secondary to tissue inflammation in the setting of other diseases. This phenomenon has also been implicated in certain neurological disorders such as multiple sclerosis and Alzheimer's disease.[5]

The typical hallmark is an intensely pruritic eruption consisting of excoriated urticarial or eczematous plaques with subsequent formation of tense bullae 1 to 3 cm diameter with negative Nikolsky's sign and subsequent erosions.[6] Resolution appears to be without scarring. The course is usually chronic with spontaneous flare-ups and remissions. On the other hand, BP may be extremely polymorphic with nonbullous lesions, prurigo-like nodules, vegetating and purulent lesions, and many other subtypes mimicking other common cutaneous diseases.[7] Therefore, BP should be considered in every pruritic inflammatory skin eruption in the

elderly. The diagnosis is usually confirmed by the immunopathologic findings that are both highly sensitive and specific. Serologic studies for anti-basement zone antibodies are also useful supporting the diagnosis. Nevertheless, detection of those antibodies is not necessarily indicative of the disease and could be found in patients without clinical or laboratory evidence of BP.

To our knowledge, there have been no reported cases with a presentation resembling cellulitis. In our patient, the history of BP was the main clue in helping to sort out the diagnosis. Contacting his dermatologist who is a staff physician at our facility and reviewing his previous history played a crucial role in the correct approach and management. It is important to note that the patient was a very poor historian making the correct diagnosis difficult. He sought medical attention at times in emergency departments where he was treated with antibiotics for a presumptive diagnosis of cellulitis with minimal improvement in symptoms and several recurrences. He showed a definite and drastic response to steroids, which helped confirm the suspicion that the cellulitis-like lesions were indeed a manifestation of his underlying BP. Another feature worth mentioning was completely nonpruritic rash as opposed to typical BP being extremely itchy.

Bullous pemphigoid remains the disease without clear guidelines regarding treatment. Even assessment of the severity of the disease seems to differ in different countries. However, most guidelines agree that the mainstay of treatment are corticosteroids with various adjuvant options. In mild disease, topical glucocorticoids could be used as a monotherapy. Moderate disease usually warrants an addition of systemic glucocorticoids. Anti-inflammatory antibiotics such as tetracyclines are preferred by some dermatologists. In cases where maintenance therapy is required, immunosuppressive agents may be implemented. Among them are mycophenolate mofetil, azathioprine, dapsone, and methotrexate.[8] New therapies including biologics have been studied showing some promising results.

Despite the unusual presentation of a nonpruritic exacerbation of BP, it should always be among the differential diagnosis in each elderly patient presenting with inflammatory skin disease.

Conclusion

Despite the unusual presentation of a nonpruritic exacerbation of BP, it should always be among the differential diagnosis in elderly presenting with inflammatory skin eruption. By reporting this case, we would like to make the readers aware of this unique presentation that was initially misdiagnosed as cellulitis.

Authors' Note

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Verbal informed consent was obtained from the patient for their anonymized information to be published in this article.

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