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CLINICAL IMAGE

Rash in an Elderly Bed-Bound Patient

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A 91-year-old afebrile female with a history of bilateral below-the-knee amputations and congestive heart failure presents to the emergency department by ambulance with a vesicular and excoriated rash to her upper and lower extremities *(Figure 1 and Figure 2)*. The patient was being evaluated by a wound care specialist and was advised to report to the emergency department for the possibility of infection. The vesicular lesions have been progressing in size and number for two weeks, although localized to the patient's upper and lower extremities.

The lesions have enlarged to bullae as large as 6 cm in diameter, with worsening pruritus and resultant excoriations. There is no induration, tenderness to palpation or surrounding erythema noted and very minimal pigmentation changes surrounding the lesions. Nikolsky sign is not present and there is no involvement of the oral mucosa, palms, or soles. Initial laboratory tests reveal an elevated C-reactive protein and are otherwise unremarkable. Medications include daily furosemide.

FIGURE 1:

Vesicular and excoriated rash to upper extremities

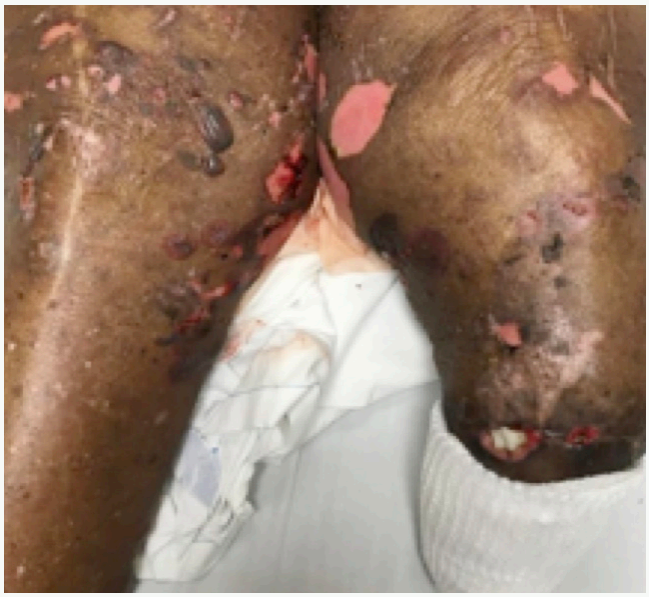

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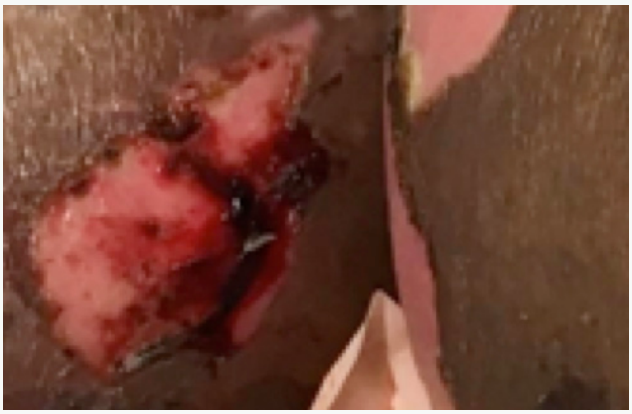
FIGURE 2:

Vesicular and excoriated rash to lower extremities



QUESTIONS

1. What is the most likely diagnosis?

A. Staphylococcal Scalded Skin Syndrome
B. Cellulitis
C. Bullous Pemphigoid
D. Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis
E. Pemphigus Vulgaris

2. What is the most common etiology of this rash in the patient's age group?

A. Autoimmune
B. Photosensitivity
C. Type IV Hypersensitivity reaction
D. Medication Induced
E. Fungal

3. Given that the patient has two below-the-knee amputations and is bedridden, what is the first line of treatment in this patient?

A. Symptomatic care
B. Topical corticosteroids
C. Oral terbinafine
D. Topical bacitracin
E. Oral corticosteroids

ANSWERS:

1. What is the most likely diagnosis?

Correct Answer: C) Bullous Pemphigoid

The fluid-filled blisters began developing with no known exposure to infectious or hypersensitivity agents. Originating as vesicles less than 1 cm in diameter, the lesions progressed over several days to bulla as large as 6 cm in diameter. This is the typical presentation of bullous pemphigoid.[1] Staphylococcal Scalded Skin Syndrome (SSSS) and cellulitis are both infectious processes, expecting erythema, induration, or warmth on physical exam. Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are serious, immune-mediated responses to medications or infection which result in confluent epidermal necrosis. Pemphigus vulgaris (PV) is an autoimmune blistering disease that can be differentiated from bullous pemphigoid based on unique autoantibodies as well as a physical exam.[2,3]

2. What is the most common etiology of this rash in the patient's age group?

Correct Answer: A) Autoimmune

It is characterized by subepidermal autoantibodies directed against two components of adhesion complexes promoting dermo-epidermal cohesion.[4] These autoantibodies can activate an inflammatory reaction that can cause epidermal-dermal splitting and resultant blistering.[1]

3. Given that the patient has two below-the-knee amputations and is bedridden what is the first line treatment in this patient?

Correct Answer: E) Oral corticosteroids

Topical clobetasol propionate 0.05% (40 grams per day) has been shown to be superior to oral prednisolone (0.5 mg/kg per day) in terms of overall survival, disease control and adverse event profile for patients with extensive BP.[4,5] However, due to poor practicality and compliance in bedridden patients, oral prednisolone or prednisone (0.5–1 mg/kg per day) is recommended as the initial therapy in this patient.[6,7]

DISCUSSION

Bullous pemphigoid (BP) is the most common subtype of autoimmune blistering disease, which although rare, can lead to fatal outcomes. Typically, it manifests with large, tense blisters preceded by urticarial plaques and severe pruritus.[7] BP ranges from mildly itchy welts to severe blisters that can be complicated by infection. It may affect a small area of the body or be widespread, commonly affecting the lower abdomen, inner or anterior thighs, and flexor forearms. The clear majority of those affected are elderly, but it has been seen at all ages.[6,8] Commonly progressing over several days to weeks, small vesicles progress to larger bullae accompanied by this severe pruritus.[8] This can inevitably lead to excoriation and infection if proper treatment is not initiated promptly.

The pathophysiology of this skin disease involves autoantibodies against hemidesmosomal antigens. The binding of autoantibodies leads to complement activation, recruitment of inflammatory cells, and release of proteolytic enzymes.[3] It is this onslaught of immunological and inflammatory mediators involving the hemidesmosome and its components that leads to urticaria and consequent subepidermal blisters.

Medical knowledge regarding bullous pemphigoid has progressed considerably over recent years, allowing for rapid detection and differentiation from other autoimmune blistering diseases such as pemphigus vulgaris. The location of blistering and immunoglobulin deposition distinguishes bullous pemphigoid from pemphigus vulgaris.[9]

In pemphigus vulgaris, blister formation and antibody deposition occur within the epidermis/epithelium, where keratinocytes in the epidermis and mucus membranes lose cell-cell adhesion from direct attack of autoantibodies to the desmosome.[9,10] Bullous pemphigoid differs because these autoantibodies fix complement and mediate inflammation secondary to binding to hemidesmosomal components. This differentiation has enabled diagnostic testing for these diseases by enzyme-linked immunosorbent assays and dissection of various pathophysiological mechanisms that have led to targeted therapeutic strategies.[9]

DIAGNOSIS

In a setting of tense bullae with dermal-epidermal separation on histology and positive direct immunofluorescence for IgG or C3, the diagnosis of bullous pemphigoid can be made if three of the four following criteria are present:

1. Age more than 70 years,
2. absence of atrophic scars,
3. Absence of mucosal involvement,
4. Absence of predominant bullous lesions on the head and neck.[7,11]

This has a sensitivity of 86%, specificity of 90%, and positive predictive value of over 95% when validated using immunoblotting as the gold standard.[7] Therefore, it is recommended to perform a direct immunofluorescent and serological analysis to exclude bullous pemphigoid in all patients with pruritic skin lesions who are at least 65-years-old.[12] ELISA can then be used to further confirm the diagnosis.[7]

There still exists clinical dermatological signs that can aid in the differentiation of blistering diseases. Nikolsky sign is present when slight rubbing of the skin results in exfoliation of the outermost layer, forming a blister within minutes.[4] This technique is useful in differentiating pemphigus vulgaris (positive Nikolsky sign) from bullous pemphigoid (negative Nikolsky sign). Asboe-Hansen sign is also useful clinically, characterized as the extension of a blister to adjacent unblistered skin when pressure is put on top of the bulla. While a regular rounded border is observed in bullous pemphigoid

and other subepidermal blistering disorders including dermatitis herpetiformis, an irregular angulated border is seen in pemphigus vulgaris.[4]

TREATMENT

The treatment of BP should be aimed at decreasing blistering formation and pruritus, promoting the healing of blisters, and improving QOL while having a minimally adverse profile.[13] As discussed before, topical clobetasol propionate 0.05% (40 grams per day) has been shown to be superior to oral prednisolone (0.5 mg/kg per day) and has thus taken over the previous benchmark of bullous pemphigoid therapy, oral corticosteroids, as first line therapy. Due to its impracticality and poor compliance in bed-ridden patients, oral prednisolone or prednisone (0.5-1 mg/kg per day) is recommended as the initial therapy in such cases.[5,6] It is important to note the importance of tapering oral corticosteroids, as a taper of 6-9 months can be initiated once there have been no new lesions or pruritis for at least two weeks.[1,6] Hydroxyzine 10-50 mg has been shown to symptomatically control pruritis when given every four hours as needed.[14,15]

Given the possible adverse side effects seen with oral corticosteroid therapy, alternative therapies have also been studied. A randomized controlled trial found that doxycycline(200 mg daily) was inferior to prednisolone, but such a reduction in effectiveness was acceptable given its favorable safety profile.[2,14] Nicotinamide has been shown to exhibit synergistic effects with antibiotics, as it should be started at 500 mg daily and gradually increased to 1500-2500 mg daily to minimize gastric side effects.[1,6,8,14] Antibiotics and nicotinamide can be continued for as long as one or two months until control is achieved and can be used as monotherapy, concomitantly with oral steroids, or after the disease has been initially controlled with oral steroids to maintain remission during steroid taper.[1,14]

Patients with a neutrophil predominate infiltrate or mucosal involvement have been shown to respond well to dapsone 50-200 mg daily.[6,14] In patients with inadequate response to the aforementioned treatments, further adjuvant therapy has been studied including methotrexate (5-25 mg/week), azathioprine (1-3 mg/kg/day), mycophenolate mofetil(1.5-3 g/day), and IVIG.[1, 6,8,14] Compared with placebo, IVIG at 400 mg/kg/day for five consecutive days is an effective therapeutic approach in such patients and can be repeated every four weeks until remission.[14,16] Cyclosporine and plasmapheresis have been used in patients with severe progressive disease but is seldom required.[1,14]

CONCLUSION

Bullous pemphigoid is an autoimmune blistering disorder, characterized by fluid-filled blisters(bullae) and pruritus. Common in elderly patients, the pruritus and eventual excoriation can be a concern for infection. For this reason, prompt diagnosis and treatment are important to prevent further complications and ensure a better quality of life for the patient. Frequent examinations of the trunk and upper and lower extremities are important to check for developing blisters, especially in elderly patients who live in a nursing home, as these patients may overlook the lesions or fail to mention them to the provider.

AUTHOR DISCLOSURE:
No relevant financial affiliations

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