Bullous Pemphigoid Masked as Severe Tinea Pedis Infection After Recent Covid Booster and Ankle Trauma

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Statement of Purpose

The purpose of this case study is to 1) report an unusual presentation of bullous pemphigoid masked initially as erythemato us tinea pedis with severe maceration and cellulitis 2) to better understand the influence of recent vaccinations and trauma in the development of bullous pemphigoid. Additionally, we present this case 3) to advocate for early lesion biopsy to prevent delay in treatment and 4) to broaden our understanding of rare presentations of bullous pemphigoid to guide appropriate podiatric intervention.

Literature Review

Bullous pemphigoid (BP), an acquired dermatologic autoimmune disease, is commonly considered a chronic disease process characterized as dormant until exacerbated by certain external factors that target the immune system (1,2,3). Incidence in the U.S. of BP is 2.4-23 cases per million in the general population each year, and as high as 190-312 per million per year in patients >70y/o ⁽⁴⁾. Bullous pemphigoid lesions can be described as erythematous serous or sanguinous filled bullae of the extremities or trunk ⁽³⁾. Patients older than 70 years old is the primary population at risk to develop bullous pemphigoid (3,5). The current proposed mechanism for bullous pemphigoid has been linked to IgG autoantibodies directed against self antigens BP 180 and BP 230. These antigens are essential in the development of hemidesmosomes which aid to facilitate epidermal dermal adhesions. When the integrity of the hemidesmosomes are violated, a separation in the epidermis and dermis can result leading to bullae formation. Additional histological findings consistent with BP includes the infiltration of eosinophils which are essential for IgE mediated blister formation which also may play the role in the bullous formation (3,5,6).

External factors that are well known can cause an exacerbation of BP include cocksackie virus (mainly in pediatric patients), trauma, surgery, present autoimmune disorder(s), and patients who are positive for HLA ^(3,5). Recent literature reports increasing incidence of BP reported in patients who have undergone recent COVID-19 and RSV vaccines and boosters.

Literature Review continued

Adverse reactions after COVID-19 vaccines are uncommon and have been previously reported as drug induced hypersensitivity, DRESS syndrome, and Stevens-Johnson syndrome^(1,2,5-9) However, there a has been an increasing incidence of bullous pemphigoid after recent COVID-19 and RSV vaccines and boosters, especially in high-risk populations. These new findings warrant further investigation in-order to understand the risk as well as adequate timing in diagnosis of BP to prevent delay in treatment and wound progression.

Methods/Case Study

- A 75-year-old male presented to the emergency department for lower extremity cellulitis, maceration of interdigital spaces, right medial arch ulceration, and upper trunk erythematous rash. Labs revealed leukocytosis although patient was afebrile and hemodynamically stable.
- PMHx of idiopathic peripheral neuropathy, Hepatitis
 C, previous scabies, prior displaced fibular fracture (now healed), rheumatoid arthritis, recent COVID-19 booster (#2), RSV, and T-dap immunizations
- Patient was admitted for further rash work up and podiatry and dermatology services were consulted

Day X Since Admission	Physical Exam	Treatment/Plan
Day 1-2	Macerated interdigital ulcers with right plantar-medial bullae & ulcer	Betadine paint & DSD
Day 3	Maceration resolved, serous bulla remained at right plantar-medial arch and new hemorrhagic bulla left arch	Triamcinolone with miconazole powder, Lanced plantar medial bulla due to pain with WB, betadine, telfa, & DSD
Day 4	New serous bulla of hip, continued hemorrhagic bullae of plantar-medial arch b/l with worsening upper trunk rash	Dermatology consulted, upper trunk biopsy obtained

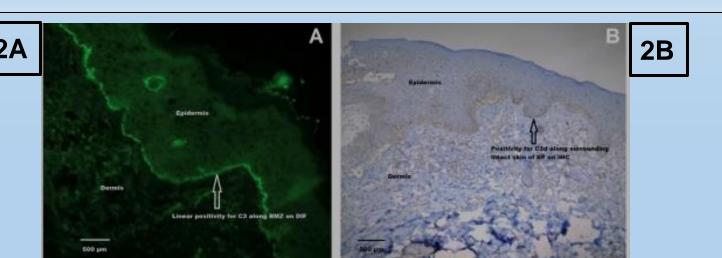
Results







<u>Figure 1.</u> Day 1 ER presentation with notable macerated interdigital and right plantar-medial arch ulcer wit cellulitis (gentian violet from prior outpatient visit). <u>1B.</u> Day 3 of admission with improvement of interdigital maceration with new eruption of left hemorrhagic plantar bullae. <u>1C.</u> Day 4 of admission with continued hemorrhagic bullae. <u>1D.</u> 4-weeks post discharge with no interdigital maceration and resolving hemorrhagic bulla of the left foot, and near resolution of lesion to the right arch (s/p 4 weeks oral prednisone and topical triamcinolone).



<u>Figure 2 A.</u> Direct immune-fluorescence of lesion biopsy with linear deposits of C3 at the basement mebrane. <u>B.</u> C3d immunohistochemistry of lesion biopsy showing immunoreactivity at the basement membrane.⁽¹⁴⁾

- Histological analysis: positive for bullous pemphigoid
- Direct immunofluorescence analysis revealed +2 staining for C3 complement

Conclusion & Discussion

Recent literature reports increasing incidence of bullous pemphigoid after trauma and vaccinations in immunocompromised patients, usually but not limited to geriatric aged patients, likely due to an aging population (10,11).

Current modalities of treatment for BP lesions include 60-80mg daily prednisone combined with topical corticosteroids for 4 weeks duration and can include dapsone, azathioprine, mycophenolate mofetil, rituximab or IVIG infusions for refractory cases. (12)

As podiatric surgeons and clinicians, we understand the importance of protecting the integrity of the skin envelope in events of trauma and wound formation, especially in immunocompromised patients, to help provide an optimal healing environment and prevent infection.

With the increasing accessibility of COVID-19 and RSV boosters, and an aging population, it is important to have a higher index of suspicion for bullous pemphigoid which may warrant earlier viral and HLA screening and/or earlier prednisone treatment post-BP lesion development in trauma patients. Caution is needed with the use of prednisone in diabetics and warrants a multidisciplinary approach with medicine and dermatology colleagues (3-8, 12).

The mechanism of bullous pemphigoid remains poorly described in the current literature. More research is warranted in-order to better understand the etiology and management course of this progressive disease process.

This case report draws awareness to the importance of considering bullous pemphigoid higher on the differential diagnosis in patients presenting with atypical tinea and bullous type lesions.

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