Bullous Pemphigoid Complicated by MRSA Cellulitis and Bacteremia
ROY SOUAID, MD; JING WANG, BA, MD’19; SHOSHANA M. LANDOW, MD, MPH; AMANDA NOSKA, MD, MPH

ABSTRACT
Unrecognized skin conditions are highly prevalent among the elderly population. Bullous pemphigoid (BP), an autoimmune dermatologic disease with greater incidence in the elderly, typically features pruritus, tense bullae formation, and negative Nikolsky’s sign.

We describe a case of BP in an elderly Veteran that developed insidiously for months before it presented with a life-threatening secondary infection due to Methicillin Resistant Staphylococcus Aureus (MRSA).

KEYWORDS: bullous pemphigoid, cellulitis, bacteremia, MRSA

CASE REPORT
A 94-year-old male Veteran who lived alone and received monthly home visits from a home-based primary care nurse presented to the emergency department with right arm swelling, warmth, redness and pain that had been growing progressively worse over the past week. He described an itchy pink rash that began on his upper chest and spread to his right neck and arm about four months prior to presentation; the primary care provider had prescribed topical triamcinolone. Unsuccessful attempts by family members were made to have him evaluated more frequently for this persistent rash, because the patient resisted additional medical visits. He did not have any constitutional symptoms and denied any trauma, animal or pest exposures, recent travels, or use of new soaps, detergents, lotions, or clothes. The patient’s past medical history was notable for hypertension, type 2 diabetes, chronic kidney disease stage 4, and mild Alzheimer’s dementia. His home long-term medications were notable for Aspirin 81 mg daily, Atorvastatin 10 mg daily, Amlodipine 2.5 mg daily, Metoprolol tartrate 25 mg twice daily and Insulin long-acting twice daily. No new medications were started in the past two years.

In the emergency department, the patient’s vitals were all within normal range. Physical exam demonstrated an elderly man in no acute distress, but with right arm edema, tenderness, and warmth. No crepitus was noted in the right upper extremity. The patient’s skin exam showed large discrete excoriated and crusted plaques on the upper chest, right arm, and right arm; tense and flaccid bullae with positive Nikolsky’s sign were also noted in the same distribution (Figures 1–3). Isolated tense bullae were present in the right arm, and right arm.

Figure 1. Lower lip has healed crusted lesions, indicating mucosal involvement.

Figure 2. Upper left chest shows multiple healed excoriations and crusted lesions, with a tense bulla (red arrow).

Figure 3. Posterior aspect of right forearm shows similar excoriations and lesions, with flaccid bullae (red arrows) that had positive Nikolsky’s signs.
groin fold and right anterior shin, without inflammation or erythema.

Initial workup was notable for a white blood cell count of 10.3 cells/mm$^3$, erythrocyte sedimentation rate (ESR) of 46 mm/hour, and an X-ray of the arm showing soft tissue swelling suggesting infection without gas. The patient’s MRSA nare swab was positive, and a right upper-extremity doppler ultrasound was negative for thrombosis.

The patient was initially treated for right upper-extremity cellulitis with IV piperacillin-tazobactam 2.25 gram every 8 hours and vancomycin 1500 mg every 48 hours for broad-spectrum coverage and clindamycin 600 mg every 8 hours for anti-toxin effect due to concern for toxin-mediated infection from noted bullae; medications were renally dosed due to a glomerular filtration rate (GFR) of 20-25 mL/min/1.73 m$^2$. The patient’s admission blood cultures returned positive for MRSA in two of two bottles and his anti-Streptolysin-O (ASO) titer returned negative. Clindamycin and piperacillin-tazobactam were thereafter discontinued and his antibiotics narrowed to intravenous vancomycin to treat MRSA right-arm cellulitis and associated bacteremia. Transthoracic echocardiography was performed due to mild leg edema on exam, unknown cardiac function, and the possibility of needing IV fluids should he progress to sepsis; imaging was normal with an ejection fraction of 60–65%.

Given low clinical suspicion for endocarditis with one major criterion (Staphylococcal bacteremia in two blood cultures) and zero minor criteria, a trans esophageal echocardiography was not performed.

Dermatology was consulted within 24 hours of admission due to suspicion for pemphigus vulgaris (PV), which can be fatal without aggressive immunosuppressive treatment, because providers noted mucous membrane involvement and a positive Nikolsky sign on admission. Dermatology obtained confirmatory lesional skin biopsy for hematoxylin & eosin (H&E) stain and perilesional biopsy for direct immunofluorescence (DIF) assay to distinguish among bullous disorders including PV and BP. The primary team began treatment with prednisone 1 mg/kg daily per dermatology’s recommendation.

Histopathology subsequently showed “Subepidermal bullae with scattered lymphocytes, neutrophils, and rare eosinophils,” which is consistent with diagnosis of BP. DIF confirmed the BP diagnosis due to linear IgG and C3 at the basement membrane zone.

After seven days of high-dose prednisone, the patient clinically improved, with no new bulla formation and healing pink plaques [Figures 4-5]. He was discharged with a peripherally inserted central catheter (PICC) to complete a two-week course of intravenous vancomycin, as well as oral prednisone beginning at 40 mg daily and tapering by 10 mg every week with close dermatology follow-up. His home medications were continued without change.

**DISCUSSION**

Bullous pemphigoid (BP) can present in an insidious, polymorphous way, and one of the “great imitators” that can present as eczematous dermatitis or urticaria in its prodromal state. In this case, our patient presented with clinical manifestations that were initially eczematous, and then to the primary providers concerning for PV. His delayed presentation for dermatologic evaluation led to a life-threatening bacteremia and cellulitis.

BP is classically less lethal and non-scarring than other diseases that present with bullae and erosions, such as PV, mucous membrane pemphigoid, or Stevens-Johnson syndrome/toxic epidermal necrolysis, all of which are associated with higher rates of morbidity and mortality.

On initial presentation, our patient had flaccid bullae, one notably affecting his lower lip, and a positive Nikolsky’s sign, [positive when exfoliation of the outermost layer of skin occurs with slight rubbing of the lesion], a sign that...
is more commonly associated with PV. However, given our patient’s late presentation, the flaccid bullae and erosions noted on exam may have represented secondary changes to the skin. In addition, oral mucosal lesions are found in only 10-30% of BP cases, and Nikolsky’s sign has been reported in BP, although less commonly than in PV.

Given the clinically overlapping appearance of bullous dermatologic conditions, definitive diagnosis of BP requires histopathology of lesions or blistered tissue, as well as direct immunofluorescence of perilesional tissue. Correct diagnosis rests upon a skin biopsy for histopathologic evaluation, and is critical for determining the appropriate treatment. Rapid diagnosis serves to minimize risk of secondary infections and medical complications from overly aggressive immunosuppression, and also expedites wound healing.

CONCLUSION
This case demonstrates a severe consequence of delayed diagnosis of BP in an elderly, home-bound patient. MRSA cellulitis and bacteremia developed secondary to skin barrier breakdown that went undetected due to a combination of lack of provider suspicion as well as patient and structural obstacles to care. We recommend that evaluation of cellulitis in the absence of obvious prior trauma invoke a total body skin exam for potential primary dermatologic conditions that compromise the skin barrier. Skin barrier integrity remains the first-line of defense against life-threatening secondary infections in the elderly. This case illustrates the importance of prompt evaluation of skin rashes and properly training medical personnel to consider unusual conditions that could have life-threatening consequences if diagnosis is delayed.

References

Authors
Roy Souaid, MD, Department of Internal Medicine, Kent Hospital; The Warren Alpert Medical School of Brown University, Providence, RI.
Jing Wang, BA, MD’19, The Warren Alpert Medical School of Brown University, Providence, RI.
Shoshana M. Landow, MD, MPH, The Warren Alpert Medical School of Brown University, Providence VA Medical Center, Dermatology Section, Providence, RI.
Amanda Noska, MD, MPH, The Warren Alpert Medical School of Brown University, Providence VA Medical Center, Infectious Disease Section, Providence, RI.

Disclosures
The statements in this article are those of the authors and not of the Veterans’ Health Administration.

Correspondence
Roy Souaid, MD
roy_souaid@brown.edu