Large Bullae on the Legs in a Hospitalized Patient Following a Gunshot Wound

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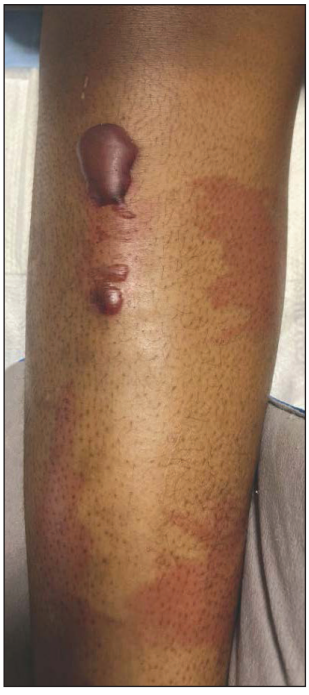

A 19-year-old man developed fluid-filled blisters on both legs within 1 month of a prolonged hospitalization following a gunshot wound that resulted in complete paralysis of the legs. His medical history was otherwise unremarkable. Medications started during hospitalization included moxifloxacin, levetiracetam, and prophylactic subcutaneous enoxaparin. Physical examination by dermatology revealed tense blood-filled bullae measuring several centimeters with well-demarcated, pink to red, irregularly shaped patches on both legs. A biopsy of a blister was taken.

WHAT'S YOUR **DIAGNOSIS?**

a. bullous hemorrhagic dermatosis
b. bullous pemphigoid
c. coma blisters
d. heparin-induced skin necrosis
e. *Vibrio vulnificus* infection

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THE **DIAGNOSIS:** Bullous Hemorrhagic Dermatosis

Biopsy results showed an intraepidermal blister with a floor composed of maturing epidermis. The roof of the blister was composed of necrotic keratinocytes with overlying orthokeratosis, and the cavity was filled with a moderate amount of fibrin and dead cells with neutrophils. Direct immunofluorescence (DIF) using specific antihuman IgG, IgM, IgA, C3, and fibrin was negative. Aerobic, anaerobic, and fungal cultures also were negative. With these histopathologic findings, medication exposure, and timing of bullae onset, our patient was diagnosed with bullous hemorrhagic dermatosis (BHD) secondary to enoxaparin administration. Enoxaparin was continued due to increased risk for coagulopathy, and there was complete resolution of the bullae after 5 weeks with no residual symptoms.

Bullous hemorrhagic dermatosis is a rare eruption that can occur after administration of heparin and low-molecular-weight heparin, with enoxaparin being the most commonly implicated drug.[1] The lesions typically are seen in elderly men in the seventh decade of life and appear within a median of 7 days after drug exposure. The time course for the postexposure eruption can vary from 2 to 21 days, with reports of skin lesions appearing up to 4 months after exposure.[1,2] Bullous hemorrhagic dermatosis manifests as tense hemorrhagic bullae (Figure) typically on the arms and legs, though lesions also can develop on the trunk. The lesions can occur in distant areas from the injection site, suggesting BHD may be a systemic reaction, although the etiology is poorly understood.[1]

Another heparin reaction that can manifest similarly to BHD is heparin-induced skin necrosis.[3] Patients with this condition also may have associated heparin-induced thrombocytopenia upon laboratory investigation and have a more aggressive clinical course than BHD. Biopsy can help differentiate BHD and early heparin-induced skin necrosis if the clinical manifestation is unclear. Histopathologically, BHD typically has intraepidermal bullae filled with blood, whereas heparin-induced skin necrosis has dermal thrombi.[1,4] Treatment of both conditions differs in whether to discontinue anticoagulants: heparin-induced skin necrosis requires discontinuation of the medication, while BHD does not.[2,3]

In patients with BHD, the lesions are self-resolving, and treatment is supportive, although whether enoxaparin is discontinued varies among physicians.[2] Lesions typically resolve within 2 weeks of onset, although it is unclear whether continuing anticoagulants delays resolution.[1] Discontinuing anticoagulants in certain patients can be life-threatening due to complex comorbidities (eg, risk for venous thromboembolism or pulmonary embolism from prolonged hospitalization or severe trauma) and is not necessary for the resolution of BHD.

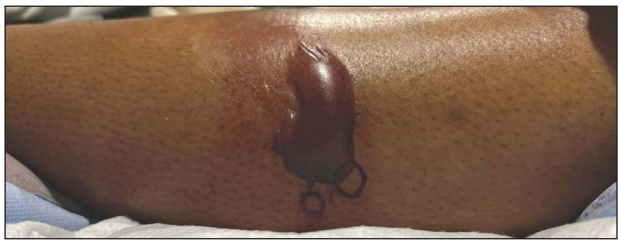

FIGURE. Large tense hemorrhagic bulla overlying a well-demarcated pink patch on the medial aspect of the left lower leg.

In addition to BHD and heparin-induced skin necrosis, our differential diagnosis included bullous pemphigoid, coma blisters, and *Vibrio vulnificus* infection. Although bullous pemphigoid can manifest with tense bullae that are pauci-inflammatory on histology, DIF would show linear IgG and C3 deposition at the dermal-epidermal junction. In our patient, DIF was negative and favored another etiology for the lesions. Coma blisters can occur in areas of sustained pressure and typically develop in patients with a prolonged hospitalization or those who are sedentary for long periods of time. The distribution of bullae on our patient's bilateral pretibial shins made this diagnosis unlikely. *Vibrio vulnificus* infection can manifest as hemorrhagic bullae, though typically after a break in the skin exposed to brackish water. *Vibrio vulnificus* infection can be life-threatening, resulting in septicemia and increased mortality, and a thorough patient history is important for diagnosis.[5]

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