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## Hemorrhagic Bullous Dermatitis

Bhuvanesh Govind, MD

*Thomas Jefferson University, bhuvanesh.govind@jefferson.edu*

Luis Eraso, MD

*Thomas Jefferson University, luis.eraso@jefferson.edu*

Esteban Gnass, MD

*Thomas Jefferson University, esteban.gnass@jefferson.edu*

Geno Merli, MD

*Thomas Jefferson University, Geno.Merli@jefferson.edu*

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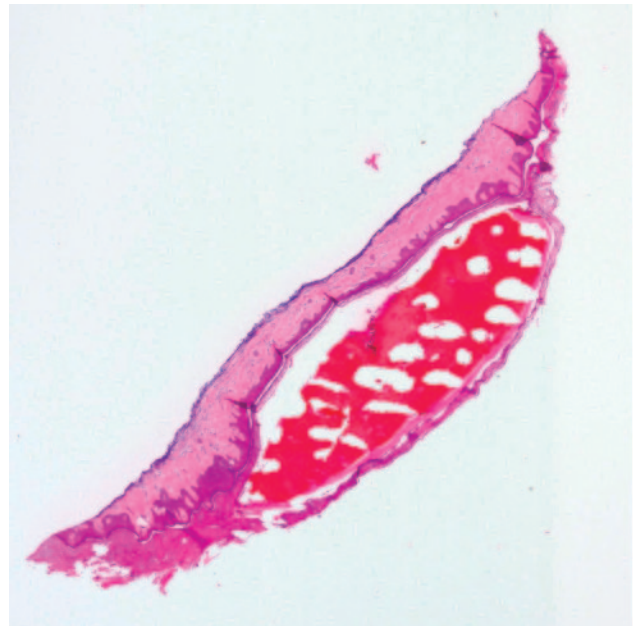
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# Hemorrhagic Bullous Dermatitis

Bhuvanesh Govind, MD, Luis Eraso, MD, Esteban Gnass, MD, Geno Merli, MD

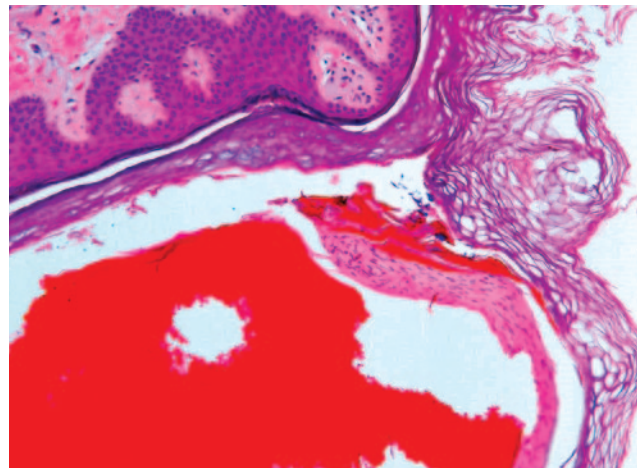


**Figure 1. Hemorrhagic Bullous Dermatitis.** Well-circumscribed, tense, nontender bullae with no significant surrounding erythema.



**Figure 2.** Intraepidermal collection of red blood cells, beneath the keratin layer. (4x power)

The patient is a 64 year old man with active primary central nervous system B-cell lymphoma who was hospitalized for management of a right lower extremity traumatic injury complicated by a calf hematoma. During the hospital stay, the patient was diagnosed with a provoked left lower extremity deep vein thrombosis (DVT) and treated initially with therapeutic dosing of enoxaparin. Five days after low molecular weight heparin (LMWH) initiation, gradual development of tense, well-circumscribed bullae were noted to appear on his arms and hands bilaterally, ranging from 0.5 cm to 1.5 cm in diameter. These lesions were both nonpruritic and nontender with no significant surrounding erythema (Figure 1). Bullae were located distal to the site of enoxaparin injections. Aside from a normocytic normochromic anemia related to chronic medical conditions, results of platelet counts, creatinine levels, and coagulation profiles remained unremarkable. A shave biopsy of one of the lesions revealed an intraepidermal collection of red blood cells without evidence of thrombotic or vasculitic changes (Figures 2 & 3). enoxaparin dose was reduced several days after lesion onset due to increasing calf hematoma size, in an effort to balance anticoagulation benefit for the DVT with risk



**Figure 3.** No evidence of thrombotic or vasculitic changes. Hemorrhagic collection with occasional neutrophils. (210x power)

of continued bleeding into the hematoma. The bullae started to regress approximately two weeks after onset, eventually crusting over. The patient was eventually discharged home.

We present a case of hemorrhagic bullous dermatosis, which is a rare type of cutaneous reaction to heparins with only a handful of cases reported in the literature. Delayed-type (type IV) hypersensitivity and immune-mediated (heparin-induced thrombocytopenia) mechanisms are the most common causes of cutaneous complications attributed to heparin products.<sup>1</sup> Type IV cutaneous hypersensitivity reactions are non-antibody mediated and typically occur several days to weeks following drug exposure. They may manifest as isolated or multiple erythematous plaques with papulovesicles or scaling. Heparin-induced thrombocytopenia, on the other hand, can induce skin erythema that progresses to hemorrhage and subsequent tissue necrosis.<sup>1</sup> Several unusual and rare dermatologic manifestations have been reported in the literature with a broad differential diagnosis including pustulosis, toxic epidermal necrolysis, arthus reaction, baboon syndrome, hypereosinophilia, and calcinosis cutis.<sup>1,3</sup>

There have only been ten cases reported in the literature regarding the clinical setting and course of hemorrhagic bullosis. Mechanisms underlying the pathogenesis of these lesions have not been clearly elucidated, although a hypersensitivity reaction has been suspected.<sup>1,4,5</sup> The histopathology of the bullae reveal intraepidermal collections of red blood cells without any thrombotic or vasculitic changes. Direct immunofluorescence and heparin platelet factor 4 have all been negative in prior case reports.<sup>4-7</sup> Only one of the ten cases has reported unfractionated heparin as an inciting agent for hemorrhagic bullosis,<sup>8</sup> while the remaining have been from LMWH. The age range of affected patients in case reports were 50-90 years old with several having a history of malignancy.<sup>4-8</sup>

Hemorrhagic bullosis seems to take a clinically benign course with no patient report of pain or pruritis. The onset of bullae in our case is consistent with the reported 5 to 21 day window of lesion development reported in the literature. The association between lesion regression and discontinuation of heparin treatment seems to be unclear given that about half of the patients' bullae reported thus far regress despite continuation of

heparin therapy with no changes in dosing. Although the resolution of bullae in our patient occurred several days after enoxaparin dose reduction, it is hard to differentiate whether lesion regression occurred directly due to medication management or the natural history of these seemingly benign, self-limiting, bullae.

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