SKIN

SKINmages

Severe Bullous Hypersensitivity Reaction After Copperhead Snakebite and Antivenom Therapy

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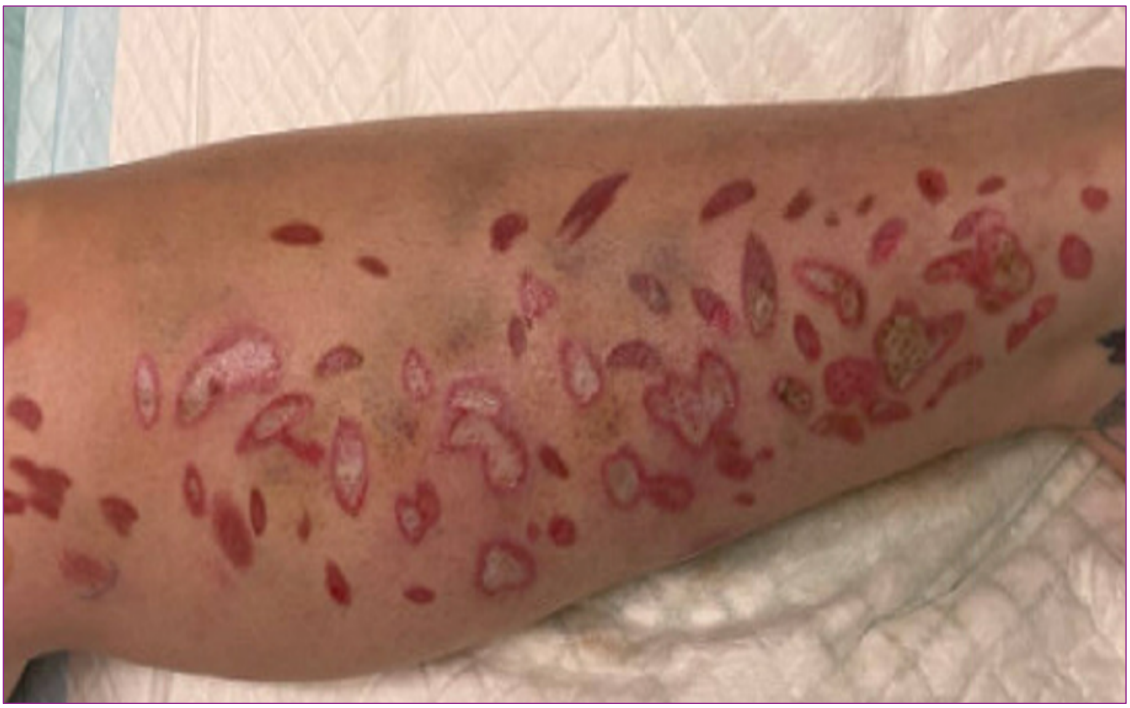

Figure 1: Left lower extremity with multiple flaccid bullae and erosions

CASE PRESENTATION

The patient is a 28-year-old female who sustained a copperhead snakebite near her left medial malleolus. She initially presented to an outside hospital with worsening swelling, pain, and erythema ascending her left calf. She was started on Anavip [crotalidae immune $f(ab')_2$ equine] antivenom. Following the third antivenom infusion, she experienced nausea, vomiting, and increased lower extremity swelling. Five days later, a painful, itchy bullous rash presented on the left lower extremity and trunk. Due to worsening symptoms and suspected serum sickness, the patient was transferred and admitted with subsequent evaluation by dermatology.

On physical exam, multiple erosions and flaccid bullae were scattered on the abdomen

and on the left ankle and shin with two areas of erythematous patches with central clearing as shown in **Figure 1**. Few bullae were also noted on the left thigh, left dorsal hand and chest. Wound cultures revealed *Streptococcus pyogenes.* A punch biopsy of the abdomen revealed acute full-thickness epidermal necrosis with perivascular lymphocytic inflammation as depicted in **Figure 2**. Treatment was initiated with vancomycin, piperacillin-tazobactam, and hydroxyzine. Treatment was escalated with the addition of methylprednisolone. Two days later, the bullae began to improve clinically. Upon discharge, the patient was prescribed amoxicillin-clavulanate, doxycycline, mupirocin ointment, and a two-week prednisone taper.

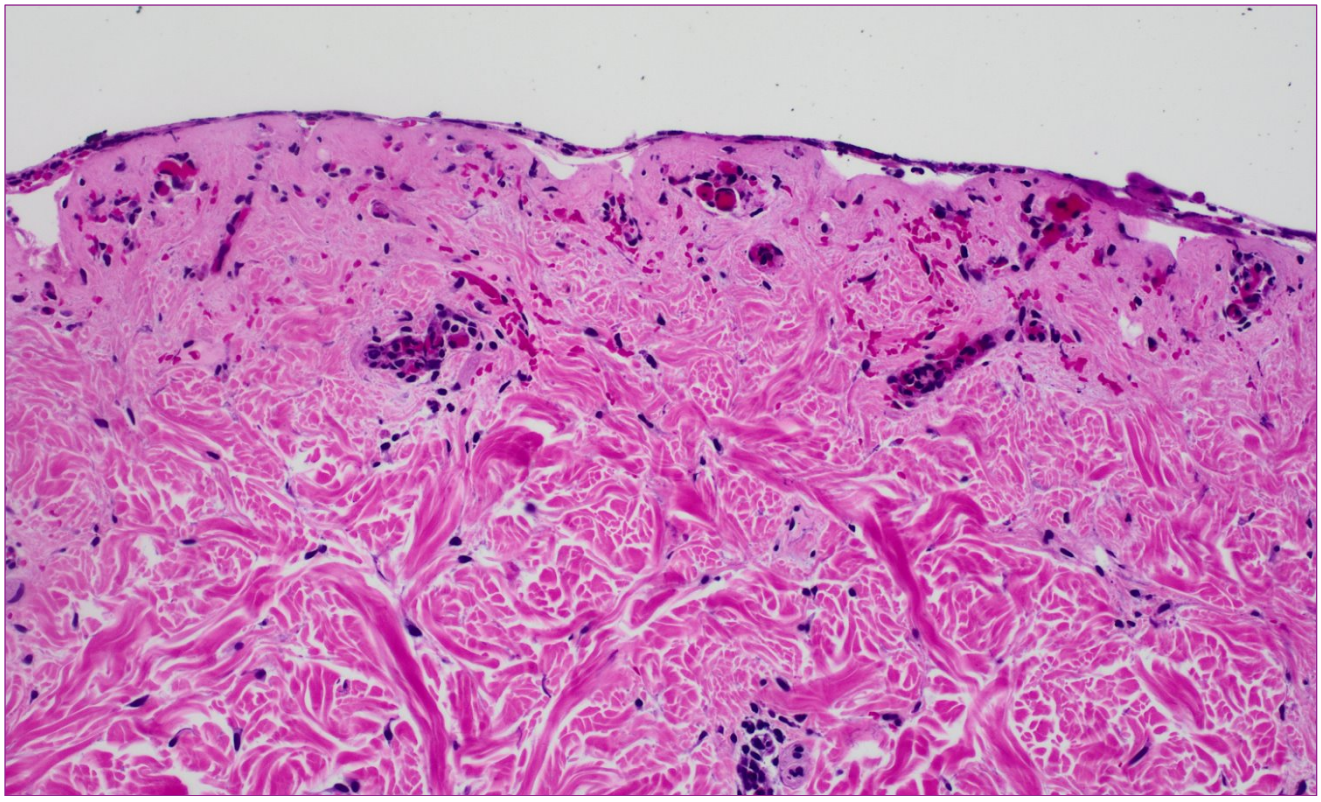

Figure 2: Punch biopsy of abdomen showing full-thickness epidermal necrosis with mild perivascular lymphocytic inflammation and vascular congestion (hematoxylin and eosin stain 100x)

DISCUSSION

Serum sickness is a type III hypersensitivity reaction, where antigen-antibody complexes accumulate in tissues. The reaction follows the administration of antibiotics, nonsteroidal anti-inflammatory drugs, anticonvulsants, biologics, allopurinol, and antivenom.[1] The incidence of serum sickness with antivenom is estimated at 5-23%.[2] Common symptoms include fever, malaise, arthralgias, gastrointestinal disturbances, lymphadenopathy, and urticarial or erythema multiforme-like cutaneous eruptions.[3]

Rarely, serum sickness can lead to severe cutaneous reactions, such as one documented case of cutaneous infarction following streptokinase administration.[4] However, upon literature review, no prior cases of serum sickness from antivenom

have involved a severe bullous reaction. There is a reported bullous reaction following programmed cell death protein 1 immunotherapy, suggesting potential overlap in immune-mediated skin reactions between antivenom and checkpoint inhibitors.[5]

This case highlights a rare hypersensitivity reaction and raises questions regarding the underlying mechanisms driving severe immune responses to antivenom. The severity and localization of the bullous rash – concentrated on the insulted extremity – suggest that localized immune activation from the initial snakebite may have heightened the body's reactivity to antivenom. This case hints at a potential interplay between the site of venom exposure and systemic immune response, which is a factor that may need further exploration to better understand localized versus systemic hypersensitivity reactions to antivenom.

Additionally, this case emphasizes the importance of early recognition and intervention. Serum sickness is a severe dermatologic reaction that can mimic other conditions, potentially delaying targeted treatment. For healthcare providers, this case serves as a reminder to maintain vigilance when treating patients with antivenom. Early identification of unusual symptoms such as bullae or other cutaneous manifestations after antivenom therapy could prompt timely adjustments in therapy and reduce morbidity and mortality.

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