

## SKINimages

**Acquired Hemophilia A Associated With Bullous Pemphigoid**

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**Figure 1.** Extensive burst bullae across the upper limbs.

An 81-year-old female presented to the dermatology outpatient office with worsening tense bullae on the lower limbs and body (**Figure 1**). She was started on oral prednisolone, doxycycline and clobetasol ointment for presumed bullous pemphigoid (BP), with slow clinical response. Blood work taken at presentation showed an eosinophilia of 2.2 (local reference range: 0.1-0.4  $\times 10^9$  /L) and indirect immunofluorescence was positive for anti-BP 180 and 230.

Four weeks later the patient re-presented with a three-day history of a painful left shoulder and extensive atraumatic ecchymosis (**Figure 2**). She also reported mild ongoing epistaxis since her BP diagnosis.

Urgent blood tests showed an acute hemoglobin drop from 11.2 to 7.9g/dL and an activated partial thromboplastin time (APTT) of 97 seconds (local reference



**Figure 2.** Extensive spontaneous ecchymosis across the lower limbs.

range: 22-36s). She was admitted under Haematology where further testing showed that the APTT failed to correct with either an 80:20 or 50:50 mix with control plasma, demonstrating that a clotting factor inhibitor was present as opposed to a factor deficiency. There was an unrecordable factor VIII level, and a factor VIII inhibitor was found to be 28.6 Bethesda units. The patient was diagnosed with acquired hemophilia A (AHA) and prednisolone was up-titrated to 1mg/kg. There was no response in the factor VIII or inhibitor levels, so rituximab 375mg/m<sup>2</sup> weekly was initiated for four weeks to reduce the circulating inhibitor.<sup>1</sup> Following 3 doses of rituximab, the patient was admitted to hospital with persistent oozing from a small skin graze and required treatment with FEIBA (anti-inhibitor coagulant complex) twice daily for 5 days before hemostasis was achieved. The factor VIII and inhibitor levels showed minimal response to rituximab so mycophenolate mofetil (MMF) was titrated to

1g twice daily with factor VIII levels normalizing following this, signifying remission from AHA.<sup>2</sup> MMF was ultimately stopped due to recurrent neutropenia, but the patient remained in remission. The BP had been in remission since the initial course of oral steroids.

AHA is a rare condition that develops from autoantibodies against factor VIII, preventing it from binding to other clotting factors, resulting in an abnormal clotting cascade.<sup>1</sup> 50% of cases are idiopathic but there are known associations with autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus and multiple sclerosis, malignancy (solid organ or hematological), medications and pregnancy.<sup>3</sup> There have been case reports of AHA associated with autoimmune bullous disorders such as BP and pemphigus vulgaris.<sup>5</sup> AHA is more common in the elderly with a variable mortality rate of 16% attributable to bleeding, but an overall

mortality of 38% when deaths due to underlying causes of AHA and secondary to immunosuppressive therapy are included.<sup>3,4</sup> As seen in this case, treatment is with immunosuppression, with first line prednisolone and second line rituximab, and acute bleeding can be treated with recombinant active factor VII or activated prothrombin complex concentrate to bypass factor VIII.<sup>1</sup> Bullous pemphigoid-associated AHA is a potentially life-threatening complication and should be suspected in any BP who presents with mucocutaneous bleeding.<sup>5</sup>

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