Burning urticarial plaques in a middle-aged woman

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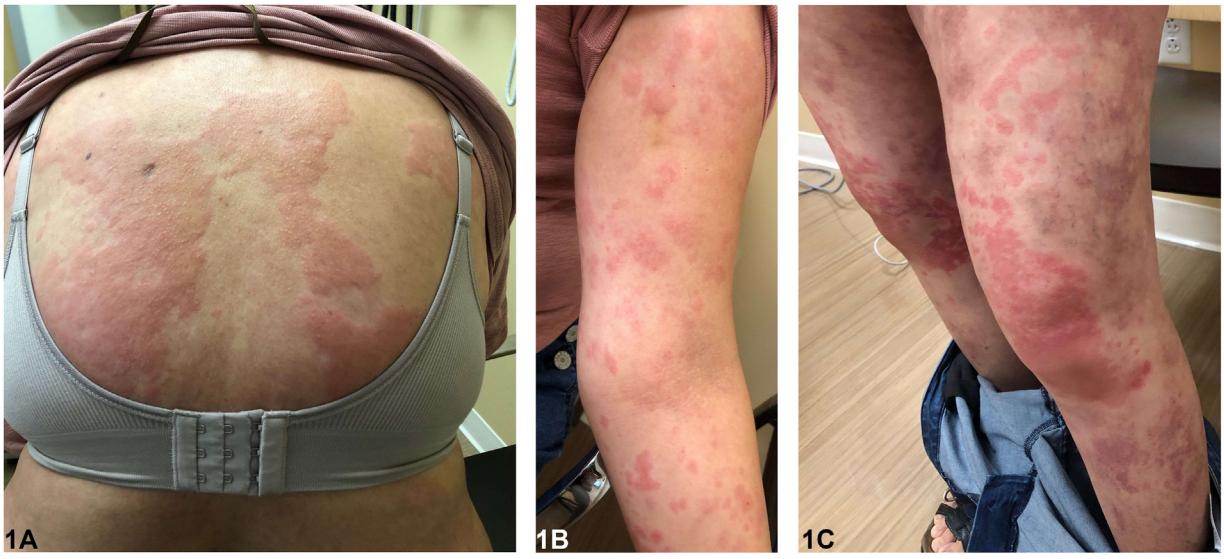

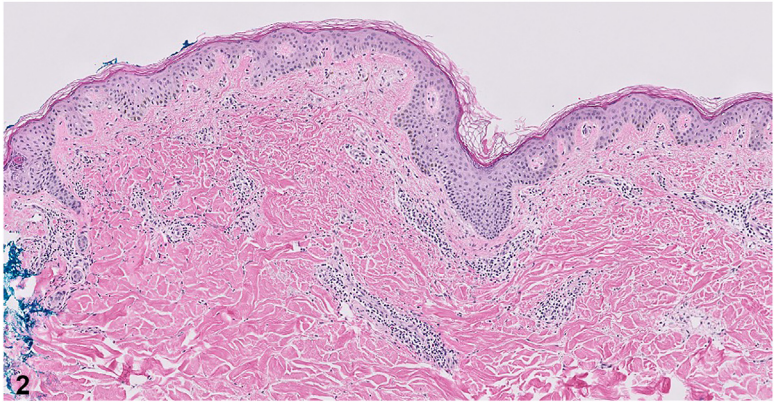

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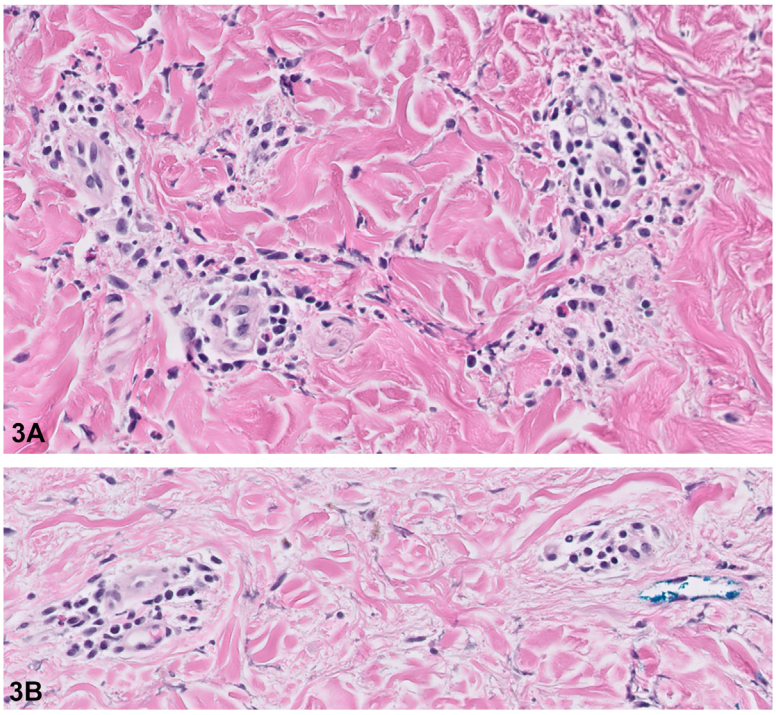

A 52-year-old woman presented to the dermatology department with a 4-day history of hives and a burning sensation, which initially appeared on her abdomen and then spread within several hours to her back, neck, head, and extremities. She showed no improvement with oral antihistamines and prednisone at 40 mg daily. She denied systemic or respiratory symptoms, new medications, and known exposures. Individual lesions persisted longer than 24 hours. Numerous erythematous edematous plaques were seen on the back and extremities, intermixed with bruise-like patches (Figs 1 to 3). A punch biopsy was performed, and direct immunofluorescence was negative for immune complex deposition.

Question 1: What is the most appropriate next step?

A. Check for glucose-6 phosphate dehydrogenase deficiency

B. Start doxycycline and niacinamide

C. Order urinalysis and serum chemistries

D. Start high-dose aspirin and refer to the rheumatology department

E. Start oral danazol and famotidine

Answers:

A. Check for glucose-6 phosphate dehydrogenase deficiency — Incorrect. This would be necessary prior to starting systemic dapsone, which has shown partial or complete remission of cutaneous symptoms in a subset of patients with urticarial vasculitis (UV). However, dapsone is not the recommended first-line therapy.[1] Additionally, further workup is needed at this point to rule out end-organ damage and other acute processes.[2]

B. Start doxycycline and niacinamide — Incorrect. The clinical differential diagnosis includes early bullous pemphigoid, which can be treated with this regimen. However, the patient's burning sensation is inconsistent with this diagnosis. Further, the biopsy findings are not characteristic of pemphigoid, which is ruled out by the negative direct immunofluorescence result.

C. Order urinalysis and serum chemistries — Correct. The differential diagnosis includes chronic urticaria, UV, mast cell disorders, hypereosinophilic syndrome, lupus, neutrophilic urticarial dermatosis (NUD), and autoinflammatory disease. Some of these conditions confer the potential for end-organ damage, which should be checked using urinalysis and serum chemistries.[2]

D. Start high-dose aspirin and refer to the rheumatology department — Incorrect. Aspirin can be

used to treat physical urticaria and urticarial vasculitis, which are included in the differential diagnosis; however, further workup should be done before considering this therapy.

E. Start oral danazol and famotidine — Incorrect. A systematic review has shown both these medications to be ineffective for UV.[1] Additionally, further workup is needed to rule out end-organ damage and other acute processes.[2]

Question 2: Laboratory tests revealed an elevated neutrophil count (9.29/mm^3; normal range [nr], 1.5-8.0/mm^3), erythrocyte sedimentation rate (49 mm/hour; nr 1-20 mm/h), total serum protein level (8.6 g/dL; nr 6.0-8.3 g/dL), and C-reactive protein level (1.3 mg/L; nr 8-10 mg/L) as well as mild leukocytosis (11.2 $\times$ 10^9/L; nr 4.5 $\times$ 10^9/L-11.0 $\times$10^9/L). A comprehensive metabolic panel, complete blood count, and urinalysis were otherwise unremarkable. The level of serum C3 was normal and that of C4 was mildly elevated (53 mg/dL; nr 12-42 mg/dL). What is the most likely diagnosis?

A. Normocomplementemic UV

B. NUD

C. Adult-onset Still disease

D. Schnitzler syndrome

E. Hypocomplementemic UV syndrome

Answers:

A. Normocomplementemic UV — Correct. UV is a rare subtype of leukocytoclastic vasculitis that predominantly affects the skin. Individual hive-like lesions of UV characteristically persist longer than 24 hours, a trait distinguishing it from ordinary urticaria. A burning sensation often accompanies edematous plaques, which leave bruise-like patches upon resolution. Based on complement consumption, UV is categorized as normocomplementemic (80% of cases), hypocomplementemic, and rare hypocomplementemic UV syndrome. The serum levels of C3 and C4 should be checked to differentiate normocomplementemic UV from these.[1]

B. NUD — Incorrect. There can be diagnostic and histologic overlap between NUD and UV, and workup for underlying systemic, autoimmune conditions is necessary in unclear cases. Most patients with NUD have fever, polyarthritis, leukocytosis, and associated systemic disease (Still disease, lupus, or Schnitzler syndrome).[3] This patient's lack of systemic symptoms argues against NUD.

C. Adult-onset Still disease — Incorrect. Our patient's lack of fever and arthritis argues against adult-onset Still disease, which classically presents as evanescent salmon-colored papules.[3]

D. Schnitzler syndrome — Incorrect. Although skin biopsy for Schnitzler syndrome most commonly exhibits neutrophilic urticaria (with leukocytoclastic vasculitis seen in 25% of patients), these patients also present with fever, arthralgias, hepatosplenomegaly, and lymphadenopathy, which were absent in this patient.[2]

E. Hypocomplementemic UV syndrome — Incorrect. This is a severe syndrome defined by specific diagnostic criteria — urticaria for 6 months as well as hypocomplementemia and 2 of the following criteria: (1) vasculitis on biopsy, (2) arthralgia or arthritis, (3) uveitis or episcleritis, (4) glomerulonephritis, (5) recurrent abdominal pain, or (6) positive C1q precipitin test result with a low C1q level.[4]

Question 3: Which of the following is most likely to be associated with this diagnosis?

A. Cutaneous melanoma

B. Sporotrichosis

C. Sjögren syndrome (SjS)

D. Elevated serum immunoglobulin E

E. There are no known specific triggers of UV

Answers:

A. Cutaneous melanoma — Incorrect. However, UV may be associated with multiple malignancies, including lymphoma, leukemia, myelodysplasia, solid organ tumors, and myeloproliferative diseases.[2]

B. Sporotrichosis — Incorrect. However, there are infections that can trigger UV, including neurocysticercosis, mononucleosis, Lyme disease, Epstein-Barr virus, and hepatitis B or C.[2]

C. SjS — Correct. Cutaneous findings in patients with SjS may precede sicca symptoms by months or years and, if present, vasculitis is the most important cutaneous finding in patients with SjS because it portends increased morbidity and mortality.[4] Long-term follow-up with the rheumatology

department may be warranted to monitor for gradual emergence of SjS or other underlying autoimmune conditions.

D. Elevated serum immunoglobulin E — Incorrect. UV has been described in association with immunologic immunoglobulin G 4 disease.[2]

E. There are no known specific triggers of UV — Incorrect. UV may be associated with the same triggers as leukocytoclastic vasculitis in general: infections, medications, autoimmunity, or malignancy; however, it is often idiopathic.[2]

Abbreviations used:

NUD: neutrophilic urticarial dermatosis
SjS: Sjögren syndrome
UV: urticarial vasculitis

Conflicts of interest

None disclosed.

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