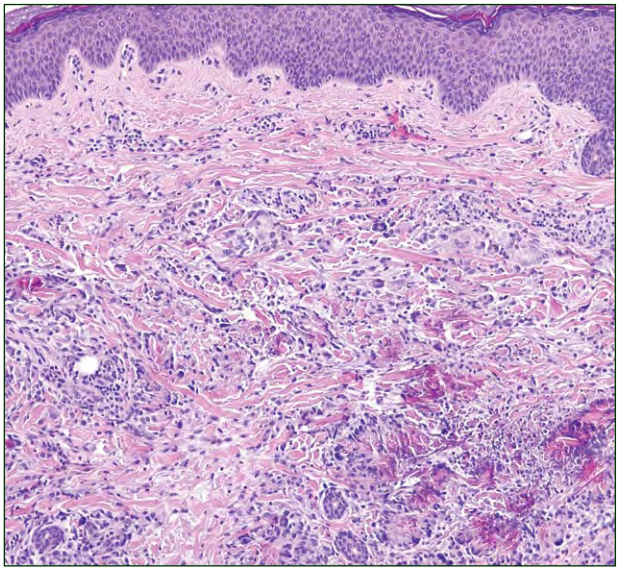
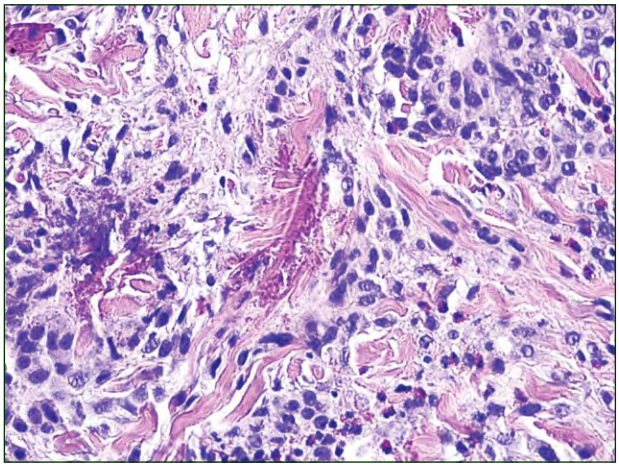


H&E, original magnification ×100.



H&E, original magnification ×200.

The best diagnosis is:

a. granuloma annulare
b. granuloma faciale
c. leukocytoclastic vasculitis
d. urticaria
e. Wells syndrome

PLEASE TURN TO PAGE 38 FOR DERMATOPATHOLOGY DIAGNOSIS DISCUSSION

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The authors report no conflict of interest.
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Wells Syndrome

Wells syndrome, also known as eosinophilic cellulitis, was first described in 1971.[1,2] Patients develop pruritic or painful urticarial and cellulitislike plaques on the skin.[3] Biopsy generally reveals edema, flame figures, and numerous eosinophils in an interstitial location (Figures 1 and 2). Wells syndrome likely represents a hypersensitivity phenomenon, but the precise etiology is not known. Arthropod bite reactions or parasitic infections are major causes of Wells syndrome. Some patients with Wells syndrome may exhibit arthropod sensitivity, and an increased proportion of CD4 helper T cells may be encountered.[4,5]

Based on the infiltrate pattern, the differential diagnoses for Wells syndrome can include a variety of dermatoses, such as granuloma annulare, granuloma faciale, leukocytoclastic vasculitis, and urticaria. Granuloma annulare typically is associated with areas of necrobiosis that may have an eosinophilic appearance (Figure 3). Increased mucin is noted in the areas of necrobiosis. Flame figures consisting of collagen surrounded by eosinophilic granules are not encountered. Granuloma faciale typically presents as red-brown papules and plaques in the head and neck area. Eosinophils are associated with a polymorphous infiltrate separated from the overlying epidermis by a grenz zone. Degranulated eosinophils and altered collagen are not identified in granuloma faciale; instead, an infiltrate of neutrophils, plasma cells, lymphocytes, and siderophages is noted in the dermis (Figure 4). Leukocytoclastic vasculitis may be associated with eosinophilic areas, but careful review of biopsy material reveals that the eosinophilic areas represent fibrin surrounding inflamed blood vessels. The angiocentric nature of the infiltrate and the presence of neutrophilic debris (leukocytoclasis) allow for differentiation (Figure 5). Urticaria presents with excess fluid splaying apart collagen fibers and fibrils with venules showing margination of

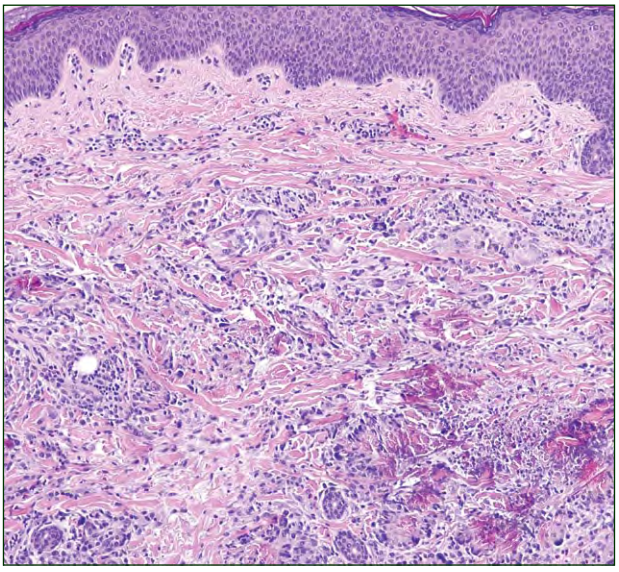

Figure 1. Interstitial inflammatory infiltrate with eosinophils (H&E, original magnification ×100).

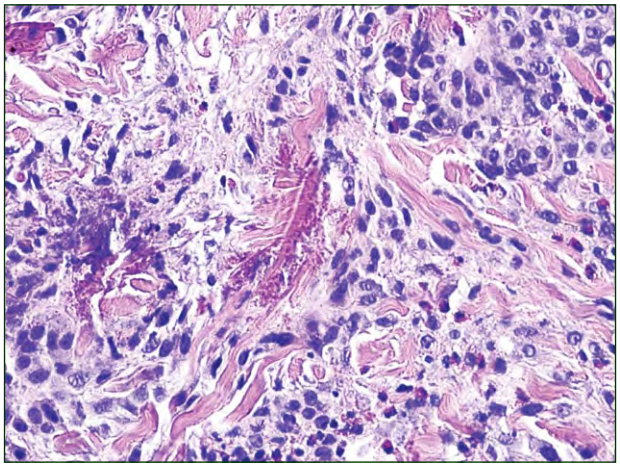

Figure 2. Flame figures consisting of collagen fibers surrounded by eosinophilic granules (H&E, original magnification ×200).

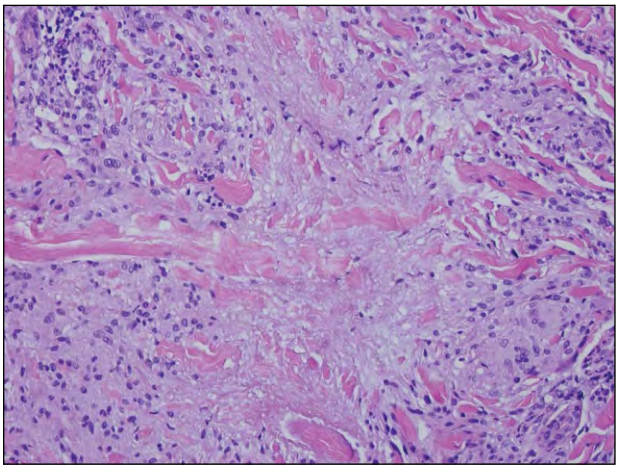

Figure 3. Granuloma annulare may be associated with eosinophilic necrobiotic collagen, but flame figures are not encountered (H&E, original magnification ×200).

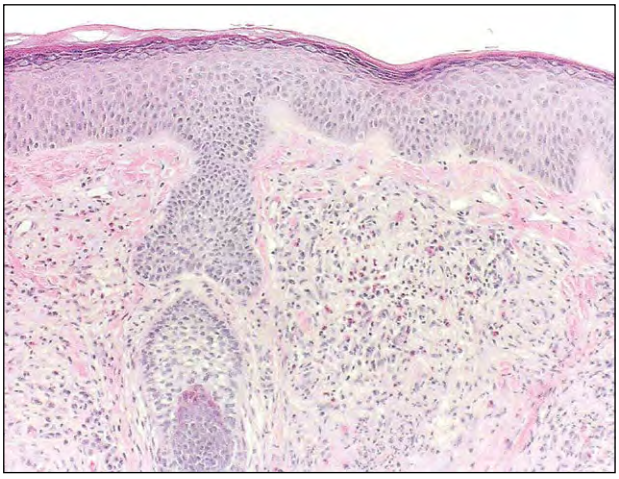

Figure 4. Granuloma faciale is associated with an infiltrate of neutrophils, plasma cells, lymphocytes, and siderophages separated from the overlying epidermis (H&E, original magnification ×100).

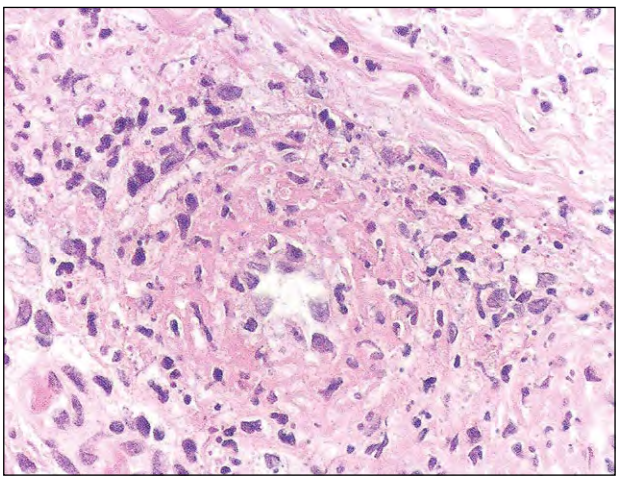

Figure 5. Leukocytoclastic vasculitis is associated with an angiocentric infiltrate, extravasated erythrocytes, and neutrophilic debris (leukocytoclasis)(H&E, original magnification ×400).

neutrophils and eosinophils (Figure 6). Flame figures are not observed, which distinguishes urticaria from Wells syndrome.

Dermatologists should be aware that flame figures can be seen in any extensive eosinophilic infiltrate, and the presence of flame figures should not lead to a reflexive diagnosis of Wells syndrome.[6] In our practice, we have encountered flame figures in scabies infestation, bullous pemphigoid, dermatitis herpetiformis, arthropod bite reactions, and other settings. In the proper clinical setting, flame figures can be a useful clue to the diagnosis of Wells syndrome.

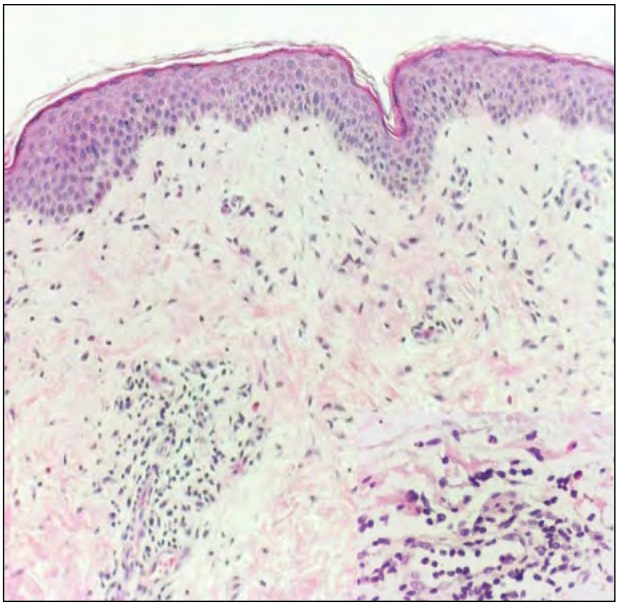

Figure 6. Urticaria is associated with dilated lymphatic vessels and a perivascular infiltrate of lymphocytes, neutrophils, and eosinophils. No flame figures are encountered (H&E, original magnification ×400). Adhesion of leukocytes to a vessel wall shows margination (H&E, original magnification ×100 [inset in bottom right corner]).

REFERENCES

1. Wells GC. Recurrent granulomatous dermatitis with eosinophilia. *Trans St. Johns Hosp Dermatol Soc*. 1971;57:46-56.
2. Wells GC, Smith NP. Eosinophilic cellulitis. *Br J Dermatol*. 1979;100:101-109.
3. Spigel GT, Winkelmann RK. Wells' syndrome: recurrent granulomatous dermatitis with eosinophilia. *Arch Dermatol*. 1979;115:611-613.
4. Koga C, Sugita K, Kabashima K, et al. High responses of peripheral lymphocytes to mosquito salivary gland extracts in patients with Wells syndrome. *J Am Acad Dermatol*. 2010;63:160-161.
5. Lin HL, Lin JN, Chen CW, et al. Eosinophilic cellulitis after honeybee sting. *J Formos Med Assoc*. 2009;108:964-966.
6. Leiferman KM, Peters MS. Reflections on eosinophils and flame figures: where there's smoke there's not necessarily Wells syndrome. *Arch Dermatol*. 2006;142:1215-1218.