Urticaria

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Aileen Y. Chang

Overview

- Urticaria refers to pink, edematous, pruritic wheals which may be acute (less than 6 weeks of lesions) or chronic (more than 6 weeks); inpatient urticaria is almost always acute
- Acute urticaria is typically due to infections or medications (in the inpatient setting, usually due to recently administered medications)
- IgE-mediated immediate Type I hypersensitivity reaction

Clinical Presentation

- Eruptions tend to arise within minutes to hours of exposure to inciting agent
  - Medications (antibiotics, NSAIDS, opiates) and radiocontrast dye are common triggers; less common causes include viral illnesses, food, and physical triggers (pressure, heat, cold induced urticaria)
- While an urticarial eruption can persist for days, weeks, or sometimes months, the individual lesions should resolve within 24 h (usually within 1–2 h), but patients may have ongoing eruptions with new lesions replacing fading ones at the same anatomic location
- Typical urticarial lesions are generally not painful, and resolve without residua (Fig. 3.1)
  - Urticarial vasculitis presents with wheals that are painful (not pruritic) and persist for hours (often more than 24 h), and resolve with bruising due to the vascular injury; these findings warrant further evaluation as many will have an underlying disease, particularly lupus
  - Urticaria multiforme may occur, particularly in children, as part of a viral exanthema; urticarial wheals can develop central pallor and clear areas
- Angioedema is a form of deep hives with subcutaneous/submucosal swelling, which may be tender, threaten the airway, and last up to 2–3 days
  - Patients with extensive facial urticaria, lip or tongue swelling, or stridor, wheezing, or drooling, should be monitored closely, ideally in an ICU

A. Y. Chang, MD
Department of Dermatology, University of California, San Francisco, CA, USA
e-mail: aileen.chang@ucsf.edu

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Histopathology

- Interstitial dermal edema, dilated venules with endothelial swelling, with a paucity of mixed inflammatory cells although occasional neutrophils and eosinophils may be seen (Fig. 3.2)

Differential Diagnosis

- Urticarial vasculitis: wheals last >24 h, burn rather than itch, fade with bruising
- Erythema multiforme: urticaria may develop central clearing and appear "multiform"—erythema multiforme lesions exhibit central duskiness
- Serum sickness: urticaria tend to be distal and over joints, and patients are systemically ill with joint pain and fever
- Bullous pemphigoid (BP), urticarial phase: the presence of bullae suggests BP, but very early disease may lack blisters; biopsy and immunofluorescence may be necessary
- Auto-inflammatory or autoimmune syndromes (Familial Mediterranean Fever, Muckle-Wells, Stills, Schnitzler, EGPA): family history and disease-specific manifestations from each entity may be necessary
- Parasitic infections, arthropod assault: puncta or bite sites, grouped lesions ("breakfast, lunch, dinner"), or clusters at exposed sites/clothing folds can be helpful clues

Work-Up

- A thorough history and review of systems should screen for concerning "red flag" systemic symptoms such as fever, joint pain, lesions lasting longer than 24 h which burn and fade with bruising
- New medications, recent infection, and other potential triggers should be noted
- Consider physical urticarias: pressure, heat, cold, sun, stress
- Biopsy should be performed in those with red flags or refractory disease in order to rule out other entities and guide treatment
- Extensive laboratory evaluation is not warranted in the absence of specific features prompting further investigation; a trigger is rarely identified in chronic urticaria
- A work-up for specific urticaria mimics should proceed if concerning features are present

Management

- Patients with perioral or airway involvement should be monitored closely; if airway involvement is present patients may warrant ICU level care
- First-line: combination long-acting non-sedating antihistamine therapy for at least 4–8 weeks (H1 and H2 blockers twice daily or more), with breakthrough short acting antihistamines as needed
- Second-line:
  - Consider dapsone or colchicine, particularly if neutrophilic infiltrate on biopsy
  - Consider prednisone for severe cases
  - Consider omalizumab (monoclonal anti-IgE antibody) or immunosuppressive therapies (e.g. mycophenolate) in rare cases

Suggested Readings

1. Tarbox JA, Gutta RC, Radojicic C, et al. Utility of routine laboratory testing in management of chronic urticaria/angioedema. Ann Allergy Asthma Immunol. 2011;107(3):239–43.
2. Kozel MM, Mekkes JR, Bossuyt PM, et al. The effectiveness of a history-based diagnostic approach in chronic urticaria and angioedema. Arch Dermatol. 1998;134(12):1575–80.
3. Kaplan AP. Clinical practice. Chronic urticaria and angioedema. N Engl J Med. 2002;346(3):175–9.

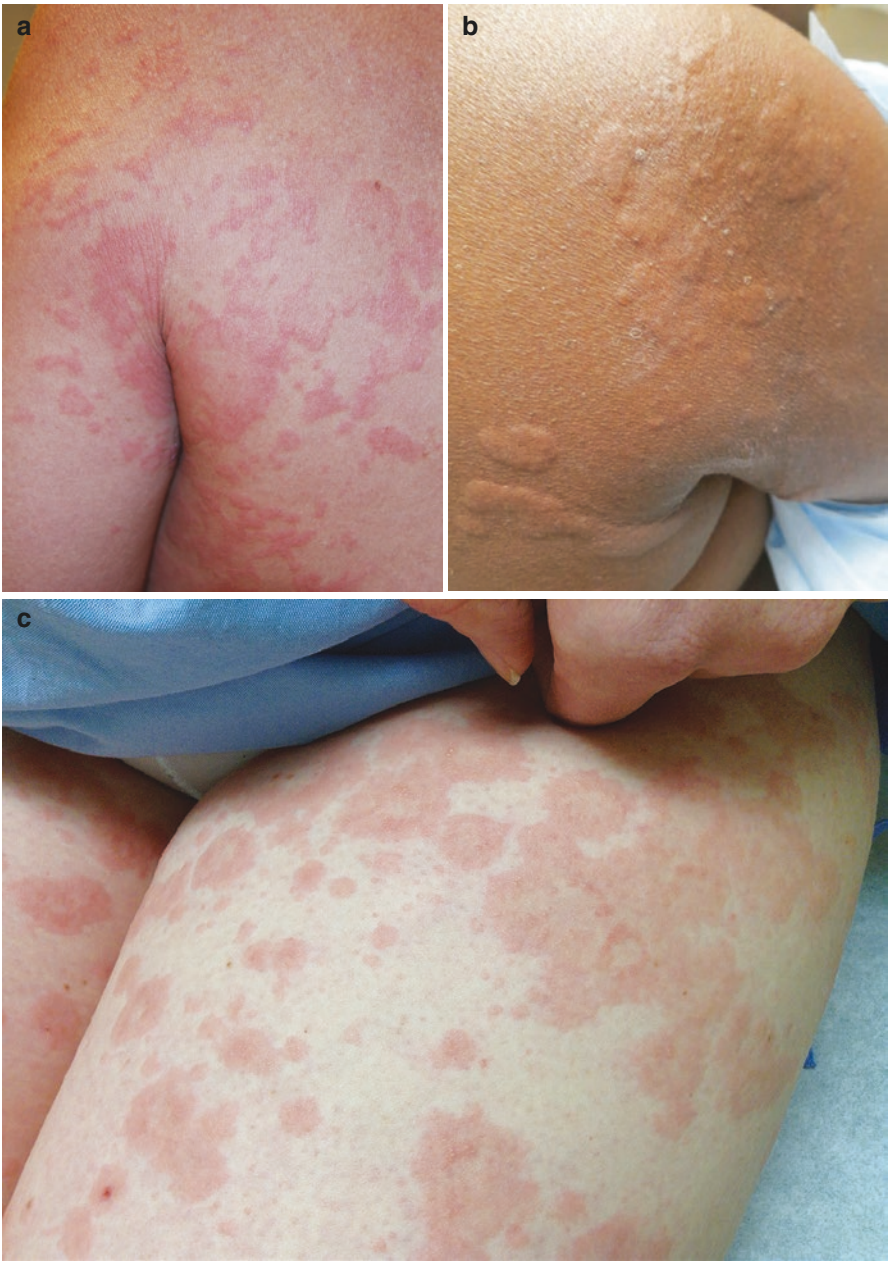

Fig. 3.1 Urticaria: (**a**) Pink, edematous wheals of typical urticaria. (**b**) In dark-skinned patients, urticaria may appear flesh-colored. (**c**) Localized edema may cause the lesions to blanch, resulting in an annular or polycyclic appearance as in this case of urticaria multiforme. The centers are often clear, helping to distinguish these lesions from those of erythema multiforme.

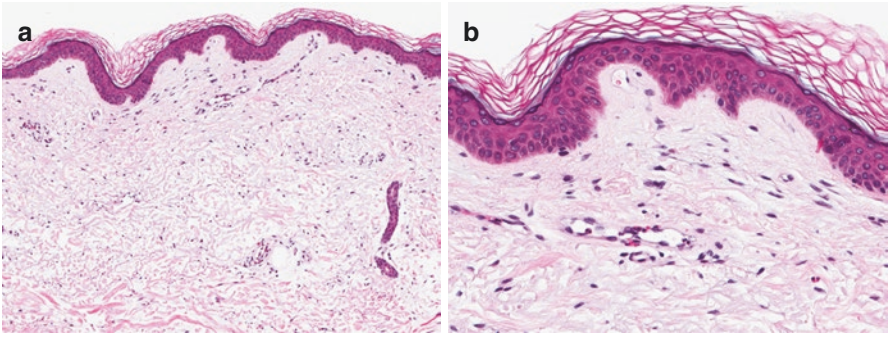

Fig. 3.2 Urticaria (*5×, 10×; H&E*): (**a**) There is interstitial dermal edema with dilated vessels and mixed inflammatory infiltrate. (**b**) Higher power demonstrates eosinophils, neutrophils, and lymphocytes in variable amounts depending on the age of the lesion, with increased spaces between collagen fibers secondary to dermal edema.