TERRY DEAN JR. | LOUIS M. BELL

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PEDIATRICS BOARD REVIEW

CERTIFICATION AND RECERTIFICATION

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ELSEVIER

Elsevier
1600 John F. Kennedy Blvd.
Ste 1800
Philadelphia, PA 19103-2899

NELSON PEDIATRICS BOARD REVIEW: CERTIFICATION AND RECERTIFICATION, SECOND EDITION

ISBN: 978-0-323-93419-0

Publisher: Sarah Barth
Senior Content Development Specialist: Ambika Kapoor
Publishing Services Manager: Deepthi Unni
Project Manager: Nayagi Anandan
Design Direction: Renee Duenow

Printed in India

Last digit is the print number: 9 8 7 6 5 4 3 2 1

Contents

SECTION 1

Allergy

2 Atopic Diseases

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Basic Information

- The atopic diseases include atopic dermatitis (eczema), food allergies, allergic rhinitis, and asthma
- "Atopic march" or "allergic march" refers to the sequential presentation of atopic diseases, typically in the order listed above, from infancy through childhood
- Causes
  - Complex interaction between genetic risk factors and environmental influence
  - Early exposure to endotoxins, pets, farm animals, and daycare may be protective against the development of atopic dermatitis ("hygiene hypothesis")
  - Maternal diet and breastfeeding do not play a role in the development of atopy
  - Delaying introduction of solid foods past 4 to 6 months does *not* prevent development of food allergies; however, early introduction of peanuts in infants with moderate to severe eczema lowers the risk of development of peanut allergy

Atopic Dermatitis

Basic Information

- Chronic, inflammatory, and pruritic skin disease
- Prevalence: up to 20% prevalence in children and rising, especially in developed nations
- Etiology is multifactorial (epidermal barrier dysfunction, altered skin flora, immune dysregulation)
- Known risk factors include parental history of atopic disease, genetic variants in filaggrin (FLG), environmental exposures
- Distinct from idiopathic nummular eczema, allergic contact dermatitis, chronic hand eczema
- See Chapter 12 for additional information

Clinical Presentation

- Can present as early as 2 to 6 months of age; 85% to 90% present by age 5 years
- Chronic or relapsing course of red macules and papules with intense pruritus and lichenification
  - <2 years: distribution is face and extensor aspects of extremities
  - >2 years: distribution is flexural areas of extremities
- Exacerbated by infections (e.g., *Staphylococcus aureus*), heat, low humidity, chemical irritants, and environmental allergens in some
- Only one-third of patients with severe eczema have foods that consistently exacerbate atopic dermatitis; thus empiric food elimination is not recommended in the treatment of eczema
  - Food elimination for eczema is not recommended due to negative impact on nutrition and increased overall risk of food allergy development

Diagnosis and Evaluation

- Most cases of eczema are diagnosed by history and examination of skin
  - Distribution of eczema usually differs by age (see above)
  - Appearance of eczema can vary depending on skin color
- Biopsy of skin is generally not needed unless eczema is refractory to conservative therapies or other systemic disorder is suspected
- Differential diagnosis:
  - Allergic or irritant contact dermatitis from plants (i.e., poison ivy), metals (nickel-plated jewelry), and chemical products (e.g., perfumes, cleaning products)
  - Immunodeficiency (HIV, Wiskott-Aldrich syndrome, severe combined immunodeficiency, hyper-IgE syndrome)
  - Metabolic disorders (zinc, vitamin B6, or niacin deficiency)

Treatment

- Mainstays of therapy are emollients/moisturizers and topical corticosteroids; choose strength of steroid based on location and severity of eczema
- Daily baths or showers with unscented or mild soap, followed by application of emollient; wet wrap therapy for severe eczema
- Control of itching with oral antihistamines (cetirizine, hydroxyzine)
- Other topical therapies: topical phosphodiesterase-4 inhibitors (crisaborole), calcineurin inhibitors (tacrolimus, pimecrolimus). Refer to Dermatology for cyclosporin, methotrexate, anti–IL-4/anti–IL-13 therapy for severe eczema
- Management of superinfection:
  - *S. aureus* infections of eczema are common
  - Eczema herpeticum: herpes simplex virus infection; treatment with acyclovir

Food Allergies

- See Chapter 3 for more information

Table 4.1 Disorders Associated With Elevated Serum Immunoglobulin E

Allergic disease
Atopic dermatitis (eczema)
Tissue-invasive helminthic infections
Hyperimmunoglobulin E syndromes
Allergic bronchopulmonary aspergillosis
Wiskott-Aldrich syndrome
Bone marrow transplantation
Hodgkin disease
Bullous pemphigoid
Idiopathic nephrotic syndrome

From Table 142-1: Environmental Control of Allergen Exposure. *Nelson's Textbook of Pediatrics*. 20th ed. Elsevier; 2016.

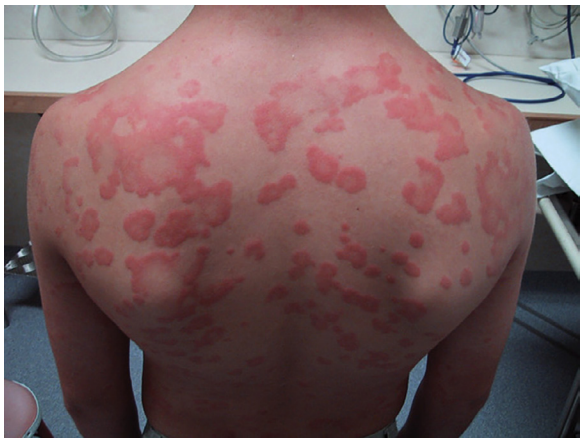

Fig. 4.1 Clinical presentation of urticaria. (Photograph courtesy of Pete Smith, MD, Griffith University, Brisbane, Queensland, Australia.)

immunosuppression (cyclosporin, tacrolimus), biologics (omalizumab)
- Prognosis is good with resolution in up to 50% within 1 year of onset

Hereditary Angioedema (HAE)

Basic Information

- Most often an autosomal dominant disease due to a deficiency in C1-esterase inhibitor, leading to dysregulation of the complement pathway and intermittent episodes of swelling of various body parts
  - Type 1: 85% of patients, quantitative defect in C1-esterase inhibitor
  - Type 2: 15% of patients, qualitative defect in C1-esterase inhibitor

Clinical Presentation

- Tissue swelling (most commonly skin, upper respiratory tract, GI tract) *without* urticaria or pruritus
  - Majority of patients experience abdominal pain
  - Laryngeal swelling can be fatal
- Episodes may be preceded by trauma
- Untreated, symptoms can last for several days

Diagnosis and Evaluation

- Diagnosis based on clinical history and physical exam during episodes
- Labs: C4 as initial screening test (generally decreased when asymptomatic, absent during attacks), C1 esterase inhibitor protein level and function

Treatment

- First-line therapy: replacement of C1 esterase inhibitor is needed
- Second-line therapy (if above not available): fresh frozen plasma
- Symptoms DO NOT improve with antihistamines, steroids, or epinephrine
- In the acute setting of an attack: consult allergist on-call and protect airway, with supportive management for dehydration and pain if present

Mastocytosis

Basic Information

- Two forms:
  - Cutaneous mastocytosis (predominantly children), three subcategories:
    - Urticaria pigmentosa (also maculopapular cutaneous mastocytosis, MPCM), most common form of cutaneous mastocytosis in children
    - Diffuse cutaneous mastocytosis (DCM)
    - Mastocytoma of the skin
  - Systemic mastocytosis (predominantly adults)
    - Majority of patients will have cutaneous involvement

Clinical Presentation

- Cutaneous mastocytosis
  - Eighty percent of patients will have brown or red skin lesions. See Fig. 4.2
  - Darier's sign (wheal or reddening of the skin with mechanical stroking or rubbing). See Fig. 4.3
  - Less than 10% of patients develop systemic symptoms
- Systemic mastocytosis
  - Previously mentioned cutaneous symptoms
  - Systemic symptoms: idiopathic anaphylaxis, flushing, hives, angioedema, diarrhea, fatigue, bone pain, wheezing

Diagnosis and Evaluation

- Cutaneous mastocytosis
  - Clinical diagnosis: skin biopsy if diagnosis is unclear
  - No bone marrow biopsy needed in children
- Systemic mastocytosis
  - Bone marrow biopsy and biopsy of the affected organs
  - Serum tryptase level, KIT D816V mutation analysis

Treatment

- Cutaneous mastocytosis
  - Topical corticosteroids for pruritic lesions
  - Oral second-generation antihistamines for pruritus
- Systemic mastocytosis
  - Management per hematologist

Hypereosinophilia

Basic Information

- Hypereosinophilia: absolute eosinophil counts (AEC) >500 cells/μL

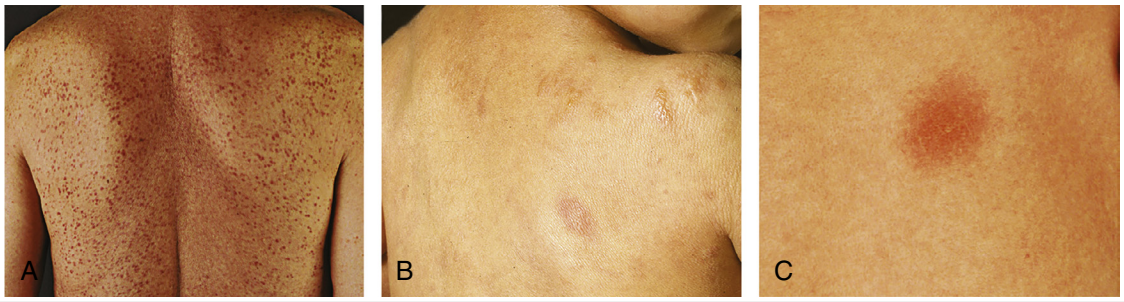

Fig. 4.2 Subforms of CM. Cutaneous manifestations in mastocytosis are categorized into MPCM, presenting with disseminated brown lesions (A); DCM, presenting with generalized erythema and thickened skin (B); and mastocytoma, presenting with a brown or red elevated lesion (C). (From Hartmann K, Escribano L, Grattan C, et al. Cutaneous manifestations in patients with mastocytosis: consensus report of the European Competence Network on Mastocytosis; the American Academy of Allergy, Asthma & Immunology; and the European Academy of Allergology and Clinical Immunology. *J Allergy Clin Immunol*. 2016;137(1):35–45. https://doi.org/10.1016/j.jaci.2015.08.034.)

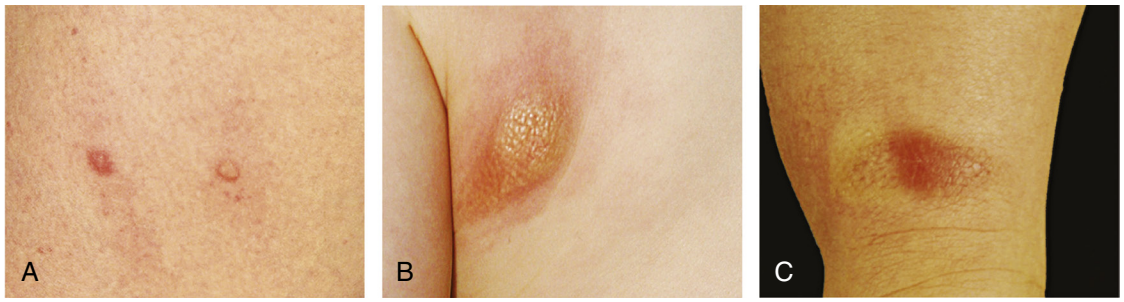

Fig. 4.3 Darier's sign. (A–C) A wheal-and-flare reaction develops upon stroking of a CM lesion with a tongue spatula. Darier's sign is a highly specific diagnostic feature of CM. (From Hartmann K, Escribano L, Grattan C, et al. Cutaneous manifestations in patients with mastocytosis: consensus report of the European Competence Network on Mastocytosis; the American Academy of Allergy, Asthma & Immunology; and the European Academy of Allergology and Clinical Immunology. *J Allergy Clin Immunol*. 2016;137(1):35–45. https://doi.org/10.1016/j.jaci.2015.08.034.)

- Hypereosinophilic syndrome: hypereosinophilia plus organ dysfunction due to eosinophilia
- Mild, transient eosinophilia common in pediatric population
  - Severity
    - Mild: AEC 500–1500 cells/μL
    - Moderate: AEC 1500–5000 cells/μL
    - Severe: AEC >5000 cells/μL
- Primary causes:
  - Hypereosinophilic syndrome (HES): types include myeloproliferative, lymphocytic, overlap (hypereosinophilia with eosinophilic disease of one organ system), familial (autosomal dominant), idiopathic
- Secondary causes (more common in children)
  - Infections: parasites (e.g., strongyloides, toxocariasis, hookworm, scabies), fungal infections (e.g., coccidiomycosis), mycobacterial infection, HIV
  - Allergic disorders:
    - Atopic disease (asthma, atopic dermatitis, allergic rhinitis)
    - Drug-induced, DRESS
    - Allergic bronchopulmonary aspergillosis
  - Eosinophilic disorders
    - Eosinophilic gastrointestinal disease
    - Eosinophilic granulomatosis with polyangiitis
  - Primary immunodeficiencies
    - Autosomal dominant hyper-IgE syndrome (Job syndrome), Omenn syndrome
  - Malignancy-related (leukemia or lymphoma, some solid tumors)
  - Other: autoimmune disorders (e.g., sarcoidosis), adrenal insufficiency, graft-versus-host disease

Clinical Presentation

- Primary HES: usually insidious with skin rash, respiratory (cough, shortness of breath), GI, cardiac and/or neurologic symptoms
- Secondary HES: eosinophilia may be incidental finding during workup for underlying condition

Diagnosis and Evaluation

- Repeat CBC to determine whether eosinophilia is transient, persistent, or rising
- Physical examination and lab testing (e.g., CBC and smear, electrolytes, liver function tests) to evaluate for end-organ involvement
- Primary HES: bone marrow biopsy may be necessary for diagnosis
- Secondary HES: testing for secondary causes is disease specific, will depend on history and physical examination
- IgE may be elevated for certain diseases associated with eosinophilia (see Table 4.1)

Treatment

- Primary HES is treated only if there is end-organ involvement
- Secondary causes are treated for the underlying disorder

W

X

Y

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