Urticaria

Basic Dermatology Curriculum

Last updated September 2015
Module Instructions

- The following module contains a number of blue, underlined terms which are hyperlinked to the dermatology glossary, an illustrated interactive guide to clinical dermatology and dermatopathology.
- We encourage the learner to read all the hyperlinked information.
Goals and Objectives

- The purpose of this module is to help participants develop a clinical approach to the initial evaluation and treatment of patients with urticaria.

- After completing this module, the learner should be able to:
  - Describe the morphology of urticaria
  - Distinguish between acute and chronic urticaria
  - Develop an initial treatment plan for a patient with acute or chronic urticaria
  - Recognize the signs and symptoms of anaphylaxis
Urticaria: The Basics

- **Urticaria** (hives) is a vascular reaction of the skin characterized by **wheals** surrounded by a red halo or flare (area of erythema).
- Cardinal symptom is PRURITUS (itch).
- Urticaria is caused by swelling of the upper dermis.
- Up to 20% of the population experience urticaria at some point in their lives.
Angioedema: The Basics

- **Angioedema** can be caused by the same pathogenic mechanisms as urticaria, but the pathology is in the deep dermis and subcutaneous tissue and swelling is the major manifestation.
- Angioedema commonly affects the face or a portion of an extremity.
  - Involvement of the lips, cheeks, and periorbital areas is common, but angioedema also may affect the tongue, pharynx, larynx and bowels.
- May be painful or burning, but usually not pruritic.
- May last several days.
Example of Angioedema
Urticaria & Angioedema

- Urticaria and angioedema may occur in any location together or individually.
- Angioedema and/or urticaria may be the cutaneous presentation of anaphylaxis, so assessment of the respiratory and cardiovascular systems is vital.
Urticaria: Clinical Findings

- Lesions typically appear over the course of minutes, enlarge, and then disappear within hours
- Individual wheals rarely last >12hrs
- Surrounding erythema will blanch with pressure
- Urticaria may be acute or chronic
  - \textbf{Acute} = new onset urticaria < 6 weeks
  - \textbf{Chronic} = recurrent urticaria (most days) > 6 weeks
- Most urticaria is acute and resolves
Common Causes of Acute Urticaria

- Idiopathic
- Infection
  - Upper respiratory, streptococcal infections, helminths
  - Most common cause of urticaria in children is viral illness
- Food reactions
  - Shellfish, nuts, fruit, etc.
- Drug reactions
  - Blood products, contrast agents
Etiology of Chronic Urticaria

- Idiopathic: over 50% of chronic urticaria
- Physical urticarias: many patients with chronic urticaria have physical factors that contribute to their urticaria
  - These factors include pressure, cold, heat, water (aquagenic), sunlight (solar), vibration, and exercise
  - Cholinergic urticaria is triggered by heat and emotion
  - The diagnosis of pure physical urticaria is made when the sole cause of a patient’s urticaria is a physical factor
- Autoimmune Urticaria: possibly a third or more of patients with chronic urticaria
- Other: infections, ingestions, medications
Dermatographism

- Most common form of physical urticaria
- Sharply localized edema or wheal within seconds to minutes after the skin has been rubbed
- Affects 2-5% of the population
Urticaria Multiforme

- A subset of pediatric urticaria with larger polycyclic or annular lesions with dusky and ecchymotic centers along with acral edema.

- We can distinguish from erythema multiforme (EM) because in EM, individual lesions are fixed for at least 7 days. Also, urticaria multiforme improves with antihistamines.
Urticaria: Pathophysiology

- The mast cell is the major effector cell in urticaria
- **Immunologic Urticaria**: antigen binds to IgE on the mast cell surface causing degranulation, which results in release of histamine
  - Histamine binds to H1 and H2 receptors to cause arteriolar dilatation, venous constriction and increased capillary permeability, causing swelling and itch.
Non-Immunologic Urticaria: not dependent on the binding of IgE receptors

• For example, aspirin may induce histamine release through a pharmacologic mechanism where its effect on arachidonic acid metabolism causes a release of histamine from mast cells.

• Physical stimuli may induce histamine release through direct mast cell degranulation.
Case One

Mrs. Ila Cook
Case One: History

- HPI: Mrs. Cook is a 46-year-old woman with a 3-day history of a widespread pruritic rash. Individual lesions last approximately 8hrs and then fully resolve.
- PMH: hip replacement 6 weeks ago
- Allergies: none
- Medications: oxycodone (for pain, s/p hip replacement) and aspirin
- Family history: no history of atopic dermatitis or allergies
- Social history: lives with her husband in the city
- ROS: negative
Case One: Exam

- Vital signs: afebrile, HR 74, BP 120/70, RR 16, \( \text{O}_2 \) sat 98% on RA
- Skin: diffuse erythematous papules coalescing into plaques (wheals)
- No associated bruising
Case One, Question 1

What other part(s) of the exam are essential?

a. Musculoskeletal
b. Neurologic
c. Psychiatric
d. Respiratory
e. Cognitive
Case One, Question 1

Answer: d

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a. Musculoskeletal
b. Neurologic
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e. Cognitive
Clinical Evaluation

- Ask about symptoms of anaphylaxis, including: chest tightness or difficulty breathing, hoarse voice or throat tightness, nausea, vomiting, abdominal pain, lightheadedness

- In addition to the skin exam, the physician should obtain a set of vital signs and evaluate for respiratory distress (dyspnea, wheeze, bronchospasm, stridor) and hypotension

- For acute urticaria, no lab testing is required
  - Laboratory testing is generally driven by associated signs and symptoms (e.g. C1 esterase deficiency only causes angioedema, not hives)
Case One, Question 2

What important feature(s) are revealed in the history?

a. The lesions fully resolve
b. She recently began new medications
c. The lesions last 8 hours
d. Three-day history of rash
e. All of the above
Case One, Question 2

Answer: e

What important feature(s) are revealed in the history?

a. The lesions fully resolve (characteristic of urticaria)
b. She recently began new medications (likely etiology)
c. The lesions last 8hrs (individual wheals rarely last over 12 hrs.)
d. Three-day history of rash (this is acute urticaria)
e. All of the above
Diagnosis: Medication-induced Urticaria

- Medications are a common cause of urticaria and angioedema
  - Penicillin and related antibiotics are common via the IgE-mediated mechanism
  - Aspirin is a common cause via a non-IgE-mediated mechanism
  - 30% of chronic urticaria is exacerbated by aspirin/NSAID use
- Many patients ask about detergent use. However, it generally causes irritant or allergic contact dermatitis, not urticaria.
Case Two
Ms. Sandra Jennings
Case Two: History

- HPI: Ms. Jennings is a 55-year-old woman who presents to the dermatology clinic with a 6-month history of periodic swelling on her body. The swelling started with localized itching followed by raised lesions that disappear within minutes to hours. She finds these lesions embarrassing and would like treatment or a cure.
- PMH: no hospitalizations or major illnesses
- Medications: occasional NSAID, daily fish oil, Vitamin D
- Allergies: no known drug allergies
- Family history: no history of skin disease
- Social history: married, works as a nurse
- Health-related behaviors: no tobacco or alcohol; has used marijuana and cocaine in the past
Case Two Continued

- Further questioning reveals that Ms. Jennings’s urticaria is worse with exercise, rubbing of the skin, pressure (e.g. develops lesions at the site of her purse strap on her shoulder), and embarrassment.
- She also describes that most of the time she does not notice an association with any potential triggers.
- Her lesions appear 2-3x/week, often in public. She is particularly embarrassed when lesions appear on her face while taking care of patients.
Case Two: Skin Exam

- Vital signs within normal limits
- Full skin exam reveals:
  - No wheals or erythema
  - Multiple benign appearing nevi on the trunk
Case Two, Question 1

Which of the following medications may be contributing to her urticaria?

a. Fish oil  
b. Ibuprofen  
c. Vitamin D  
d. Marijuana  
e. Cocaine
Case Two, Question 1

Answer: b

Which of the following medications may be contributing to her urticaria?

- Fish oil
- **Ibuprofen**
- Vitamin D
- Marijuana
- Cocaine
Clinical Evaluation

- Urticaria is generally a clinical diagnosis
- A detailed history and physical exam should be performed
- Many times patients will not present with urticaria during their clinic visit
  - You can show patients photographs of urticaria and ask if their lesions appear similar
  - Patients can take photos of their skin lesions and bring them to their office visit
Clinical Evaluation

- In most cases of chronic urticaria, no external cause can be identified
- If a physical urticaria is suspected, a challenge test with the respective trigger may be performed
- Patients will often ask about food allergies
  - IgE-mediated food allergy is far more likely to present with **acute** urticaria
  - A detailed food diary or dietary modification may reveal foods (or additives) that cause fluctuations in symptoms of chronic urticaria
Allergy testing is not routinely performed in patients with chronic urticaria.

- Skin prick testing may reveal sensitivities to a variety of allergens that may not be relevant to the patient’s urticaria.
- Laboratory tests may identify the 1/3 of patients with chronic urticaria who have an autoimmune pathogenesis. This adds additional costs and may not change the management.
Natural History and Prognosis

- Symptoms of chronic urticaria can be severe and impair the patient’s quality of life (QOL)
- In most patients, chronic urticaria is an episodic and self-limited disorder
- Average duration of disease is two to five years
- In patients with idiopathic chronic urticaria, there is a rate of spontaneous remission at one year of approximately 30 to 50 percent
- However, symptoms extend beyond five years in nearly one-fifth of patients
Ms. Jennings was recommended to avoid tight clothing, stop ibuprofen, and start a first-generation antihistamine (e.g. hydroxyzine).

During a follow-up visit, Ms. Jennings reports she stopped the hydroxyzine because it made her too sleepy and she worried it was beginning to affect her work performance. She became teary-eyed and shared her frustration with her skin condition and fear that she would not be cured.
Case Two: Follow-up Visit

- Patients with chronic urticaria are often frustrated and fearful. Validation and reassurance are important components of successful management.

- Sharing the following information may help:
  - Chronic urticaria is rarely permanent. Approximately 50% of patients undergo remission within one year.
  - While acute urticaria and angioedema may be manifestations of allergic reactions that can be life-threatening, chronic urticaria is a different disorder that rarely puts the patient at any acute risk.
  - The symptoms of chronic urticaria can be successfully managed in the majority of patients.
Case Two, Question 2

Which of the following treatments would you recommend for Ms. Jennings?

a. Daily oral 2nd generation H1 antihistamine
b. Daily topical retinoid to the face
c. No need to continue with an antihistamine; stopping the NSAID should resolve the urticaria
d. Oral 2nd generation H1 antihistamine taken when the itching begins
e. Mid-potency topical corticosteroid to the urticaria
Case Two, Question 2

Answer: a

Which of the following treatments would you recommend for Ms. Jennings?

- **a. Daily oral 2nd generation H1 antihistamine**
- **b. Daily topical retinoid to the face (not used for urticaria)**
- **c. No need to continue with an antihistamine; stopping the NSAID should resolve the urticaria (treatment should be initiated in addition to removing potential triggers)**
- **d. Oral 2nd generation H1 antihistamine taken when the itching begins (less practical and will not help prevent the initial lesions)**
- **e. Mid-potency topical corticosteroid to the urticaria (unhelpful for urticaria)**
Treatment: Antihistamines

- Oral H1 antihistamines are the first-line treatment for acute and chronic urticaria
- 1st-generation H1 antihistamines are less well-tolerated due to sedation, so are often taken at bedtime
  - e.g. 10-50 mg hydroxyzine 1-2 hours before bedtime
  - Can start with smaller doses (10 mg) to allow the patient to manage the sedative effects
  - Remember to warn patient not to drive a car or operate other dangerous machines within 4-6 hours of taking this medication
  - Do not take with other sedating medications
2nd-generation H1 antihistamines (e.g. Loratadine) are better tolerated with fewer sedative and anticholinergic effects and may be used in patients intolerant of or inadequately controlled by 1st-generation agents

Certain populations, including children, the elderly, and patients with renal or hepatic impairment may require dosage calculation or adjustments when using H1 antihistamines

Also used with caution in patients with glaucoma, prostatic hyperplasia, and respiratory disease

H2 antihistamines have mixed data on their efficacy for urticaria and are generally not used as first-line therapy
Antihistamines

The following are examples of H₁ antihistamines:

- **1<sup>st</sup> Generation**
  - Diphenhydramine (OTC)
  - Hydroxyzine (Rx, generic)
  - Chlorpheniramine (OTC)

- **2<sup>nd</sup> Generation**
  - Cetirizine (OTC)
  - Loratadine (OTC)
  - Fexofenadine (OTC)
Not all patients with urticarial eruptions have urticaria. Which of the following patients has ordinary urticaria?
Urticarial Lesions

- Urticarial Vasculitis
- Ordinary Urticaria
- Bullous Pemphigoid
Beyond Ordinary Urticaria

- The appearance of the hives does not tell you the underlying cause.
- The presence of systemic symptoms should signal the possibility that an urticarial rash is not ordinary urticaria but rather a systemic syndrome with urticaria-like skin lesions.
Referral to Dermatology

- Referral to a dermatologist and biopsy should be performed in patients with one or more of the following features:
  - Individual lesions that persist beyond 48 hours, are painful or burning rather than pruritic, or have accompanying petechial characteristics
  - Systemic symptoms
  - Lack of response to antihistamines
  - Lesions that leave pigmentation changes upon resolution
Case Three

Mrs. Julie Walker
HPI: Mrs. Walker is a 25-year-old woman who was brought to the emergency department by her husband after she began feeling short of breath with a new and expanding rash.

PMH: asthma, no history of intubations

Allergies: aspirin (causes a rash) & shellfish (reaction at a young age of facial swelling)

Medications: occasional use of albuterol

Family history: noncontributory

Social history: recently started cooking school

ROS: short of breath, anxious
Case Three: Exam

- Vitals: T 98.6F, HR 110, BP 90/50, RR 34
- General: anxious-appearing woman sitting upright with difficulty breathing, unable to speak in full sentences
- Respiratory: tachypneic, using accessory muscles, bilateral rhonchi
- Skin: periorbital edema, scattered erythematous wheals on the trunk
What is the next course of action in this patient?

a. Administer IV metoprolol
b. Assess ABC's (airway, breathing, circulation)
c. Give systemic corticosteroids
d. Make a food diary
e. Apply super-potent topical corticosteroid
What is the next course of action in this patient?

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Anaphylaxis

- Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death
- Patients with anaphylaxis may have no skin lesions, lesions of angioedema, and/or typical urticarial wheals
- Morphology of the skin lesion does not matter
  - Patients with angioedema are not more likely to have anaphylaxis compared to patients with urticaria
- ABC’s first!
- Recruit more help. May need to triage to higher level of care (in clinic this means calling 911).
Anaphylaxis: Treatment

- First-line therapy for anaphylaxis includes epinephrine, IV fluids and oxygen
- Administer 0.3-0.5ml in 1:1000 epinephrine dilution IM repeating every 10-20min as necessary; for children <30kg, the dose is 0.01mL/kg/dose.
- Make sure airway is patent or else intubation may be emergently necessary
- Patients who have severe reactions requiring epinephrine should be monitored in the hospital
Take Home Points

- Urticaria (hives) is a vascular reaction of the skin characterized by wheals surrounded by a red halo or flare.
- Urticaria is classified as acute or chronic. Acute urticaria is defined as periodic outbreaks of urticarial lesions that resolve within six weeks.
- Over 50% of chronic urticaria is idiopathic.
- The most common cause of urticaria in kids is a viral illness.
- Oral H1 antihistamines are first-line treatment for acute and chronic urticaria.
- The presence of systemic symptoms should signal the possibility that an urticarial rash is not ordinary urticaria.
Take Home Points

- Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death.
- Remember to ask about symptoms of anaphylaxis, including: chest tightness or difficulty breathing, hoarse voice or throat tightness, nausea, vomiting, abdominal pain, lightheadedness.
- The 1st step in management of a patient with signs and symptoms of anaphylaxis is to assess airway, breathing, circulation, and adequacy of mentation.
- Call for help if you suspect a patient has anaphylaxis.
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To take the quiz, click on the following link:

https://www.aad.org/quiz/urticaria-learners