Urticaria

UCSF Dermatology

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Module Instructions

- The following module contains a number of green, 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 medical students develop a clinical approach to the initial evaluation and treatment of patients with urticaria.

- After completing this module, the medical student will 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
  - Distinguish between 1\textsuperscript{st} and 2\textsuperscript{nd} generation H1 antihistamines with regard to sedation
  - Recognize the signs and symptoms of anaphylaxis
  - Discuss when to refer to a dermatologist
Urticaria: The Basics

- **Urticaria** (hives) is a vascular reaction of the skin characterized by *wheals* surrounded by a red halo or flare.
  - Cardinal symptom is *PRURITUS* (itch)
- Up to 20% of the population experience urticaria at some point in their lives
- **Angioedema** is caused by swelling of the subcutaneous tissue whereas urticaria is caused by swelling of the dermis
- Angioedema and/or urticaria may be the cutaneous presentation of anaphylaxis, so assessment of the respiratory and cardiovascular systems is vital!
Urticaria: The Basics

- 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
  - Acute = new onset urticaria < 6 weeks
  - Chronic = recurrent urticaria (most days) > 6 weeks
- Most urticaria is acute and resolves
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

- Chronic autoimmune
  - 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: 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.

- 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 itchy rash. Individual lesions last approximately 8hrs. Recently started a new laundry detergent.
- PMH: hip replacement 6 weeks ago
- Allergies: none
- Meds: recently started oxycodone and aspirin
- FH: no history of atopic dermatitis or allergies
- SH: lives with her husband in the city
- ROS: negative
Case One: Exam

Vital signs: afebrile, HR 74, BP 120/70, RR 16, 02 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. Respiratory
  b. Musculoskeletal
  c. Neurologic
  d. Psychiatric
  e. all of the above
Case One, Question 1

Answer: a

- What other part(s) of the exam are essential?
  - a. Respiratory
  - b. Musculoskeletal
  - c. Neurologic
  - d. Psychiatric
  - e. all of the above
Clinical Evaluation

- Remember to 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.
- Laboratory testing is generally driven by associated signs and symptoms (i.e. C1 esterase deficiency only causes angioedema, not hives).
  - Random testing tends to be low yield and rarely cost-effective
Case One, Question 2

What is the important feature(s) of the history revealed in this case?

a. She recently began new medications
b. The lesions last 8hrs
c. She recently began a new detergent
d. all of the above
e. a and b
Case One, Question 2

Answer: e

- What is the important feature(s) of the history revealed in this case?
  a. She recently began new medications
  b. The lesions last 8hrs
  c. She recently began a new detergent
  d. all of the above
  e. a and b
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 causes irritant or allergic contact dermatitis not urticaria
Acute Urticaria: Common Causes

- Idiopathic
- Drug reactions
- Food reactions
  - Chocolate, shellfish, nuts, eggs, etc.
- IV administration
  - Blood products, contrast agents
- Infection
  - Streptococcal infections, helminthes
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. She describes the swelling starts with localized itching followed by raised lesions that will 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 for pain relief, daily fish oil, and Vitamin D
- **Allergies:** NKDA, bee stings
- **Family history:** no history of skin disease
- **Social history:** married, works as a nurse
- **Health-related behaviors:** no tobacco, alcohol or drug use
Further questioning reveals that Ms. Jennings’s urticaria is worse with exercise, rubbing of the skin, pressure (i.e. 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. Vitamin D
  b. Ibuprofen
  c. Fish oil
  d. None of the above
  e. All of the above
Case Two, Question 1

Answer: b

- Which of the following medications may be contributing to her urticaria?
  a. Vitamin D
  b. Ibuprofen
  c. Fish oil
  d. None of the above
  e. All of the above
Which of the following recommendations do you agree with?

a. Wear loose fitting clothing
b. Create a food diary
c. Try aspirin rather than ibuprofen for pain relief
d. Get allergy tested with skin prick testing
Case Two, Question 2

**Answer: a**

- Which of the following recommendations do you agree with?
  
  a. Wear loose fitting clothing *(Avoidance of aggravating factors is recommended. In this case, Ms Jennings reported pressure and rubbing as a trigger for her urticaria)*
  
  b. Create a food diary *(Often not helpful unless food is initially suspected)*
  
  c. Try aspirin rather than ibuprofen for pain relief *(Aspirin is another NSAID, would recommend acetaminophen instead)*
  
  d. Get allergy tested with skin prick testing *(May be useful, but not often part of the initial evaluation)*
Clinical Evaluation

- Urticaria is a clinical diagnosis
- A detailed history and physical exam should be performed
- Many times patients will not present with urticaria during their clinic visit
  - 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
- 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.
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 (i.e. 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.

What might you say to Ms Jennings?
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 Ms Jennings:
  - Chronic urticaria is rarely permanent. Almost 50 percent 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 3

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

a. Daily topical retinoid to face
b. Daily oral 2\textsuperscript{nd} generation H1 antihistamine
c. Oral 2\textsuperscript{nd} generation H1 antihistamine, take when the itching begins
d. No need to continue with an antihistamine, stopping the NSAID should resolve the urticaria
Answer: b

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

- a. Daily topical retinoid to face (not used for urticaria)
- b. **Daily oral 2\textsuperscript{nd} generation H1 antihistamine**
- c. Oral 2\textsuperscript{nd} generation H1 antihistamine, take when the itching begins (less practical and will not help prevent the initial lesion)
- d. No need to continue with an antihistamine, stopping the NSAID should resolve the urticaria (treatment should be initiated in addition to removing potential triggers)
Treatments: 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
- 2nd-generation H1 antihistamines 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 adjustments when using H1 antihistamines
- Also used with caution in patients with glaucoma, prostatic hyperplasia and respiratory disease
Urticarial Lesions

- 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 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 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
Case Three: History

- **HPI:** Mrs. Walker is a 25 year-old woman who was brought in to the emergency department by her husband after she began feeling short of breath with a new and expanding rash.
- **PMH:** asthma, occasional use of inhaler, no history of intubations.
- **All:** aspirin (causes a rash) & shellfish (reaction at a young age of facial swelling).
- **Meds:** occasional use of albuterol, otherwise no daily medications.
- **FH:** not contributory.
- **SH:** recently started cooking school.
- **ROS:** short of breath, anxious.
Case Three: Exam

- Vitals: T 98.6°F, HR 110, BP 90/50, RR 34
- Gen: women sitting upright with difficulty breathing, unable to speak in full sentences
- Respiratory: tachypneic, using accessory muscles, bilateral rhonchi
- Skin: periorbital edema, scattered erythematous papules and plaques on the trunk
Case Three, Question 1

- What is the next course of action in this patient?
  a. Make a food diary
  b. Administer IV metoprolol
  c. Assess ABC’s (airway, breathing, circulation)
  d. Give systemic corticosteroids
Case Three, Question 1

Answer: c

- What is the next course of action in this patient?
  a. Make a food diary
  b. Administer IV metoprolol
  c. Assess ABC’s (airway, breathing, circulation)
  d. Give systemic corticosteroids
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
- 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.
- Oral H1 antihistamines are first-line treatment for acute and chronic urticaria.
- 1st generation H1 antihistamines can cause sedation.
The presence of systemic symptoms should signal the possibility that an urticarial rash is not ordinary urticaria.

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.
End of Module