The Basics of Urticaria Management

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Conflicts of Interest

• None to disclose
Objectives

• Discuss epidemiology & background
• Review the pathophysiology
• Describe the clinical presentation & various types
• Distinguish between acute & chronic urticaria
• Review the differential diagnosis & work-up
• Discuss the basics of management
Epidemiology

- Urticaria may present at any age
- Estimated to have an overall lifetime prevalence of 10-25%
- Chronic urticaria is more common in females (2:1)

Urticaria

• Term used for recurrent whealing of the skin
  – Also encompasses angioedema

Urticaria

- **Wheals**
  - Superficial dermal swelling
  - Pale center
  - Pruritic
  - Individual lesions last < 24 hours

Urticaria

• Angioedema
  – Deep swelling of the skin/mucosa
  – Painful or burning
  – No color change
  – Less well defined
  – Can last 2-3 days
  – Can affect mouth, GI tract, & respiratory tract

Pathophysiology

- Mast cell: primary effector cell
  - Express high affinity IgE receptor (and non-IgE receptors)
  - Various stimuli bind receptors
    - Immunologic
    - Non-immunologic

Pathophysiology

- Immunologic
  - IgE mediated
    - Autoantibodies
    - Type 1 hypersensitivity reaction

- Non-immunologic
  - Cause direct release of mast cell mediators
    - Opiates
    - Polymyxin B
    - Tubocurarine
    - Radiocontrast dye
    - Aspirin & NSAIDs
    - Tartrazine
    - Benzoate
    - Dietary pseudoallergens
    - Vasoactive stimuli (i.e. nettle stings)
Pathophysiology

- Degranulation - release of mediators
- Mediators bind receptors of post-capillary venules
  - Vasodilation
  - Inflammation
  - Increased permeability and leakage of plasma

Acute vs. Chronic Urticaria

- **Acute Urticaria**
  - Repeated appearance of wheals < 6 weeks

- **Chronic Urticaria**
  - ≥ 6 weeks
  - Occurring at least twice a week
Acute Urticaria

- Idiopathic: 50%
- URI infections: 40%
- Drugs: 9%
- Foods: 1%
Chronic Urticaria

- Ordinary: 60%
- Inducible: 35%
- Urticarial Eruptions: 5%
Chronic Urticaria

- Spontaneous “Ordinary” Urticaria
  - Often appear in the evening & are present on waking
  - 60% of chronic urticaria
    - Autoimmune
    - Pseudoallergens
    - Infections
    - Idiopathic

Chronic Urticaria

- **Inducible Urticarias**
  - Induced by exogenous physical stimulus
  - 35% of chronic urticaria
  - Location & history
  - Can occur in association with spontaneous urticaria

<table>
<thead>
<tr>
<th>Causes of Inducible Urticaria</th>
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<tbody>
<tr>
<td>Physical Urticarias</td>
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<tr>
<td>• Mechanical Stimuli</td>
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<tr>
<td>• Temperature Changes</td>
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<tr>
<td>• Sweating &amp; Stress</td>
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<tr>
<td>• Sun (Solar)</td>
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<tr>
<td>• Water (Aquagenic)</td>
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<tr>
<td>Contact Urticaria</td>
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Chronic Inducible Urticaria

• Physical Urticarias
  – Dermatographism
    • Most common of the physical urticarias
      – 10% of the general population
    • Linear wheals at sites of scratching or friction
    • No association with systemic disease, atopy, food allergies, or autoimmunity
    • Test: Gentle stroking of the skin

Chronic Inducible Urticaria

• **Physical Urticarias**
  – Delayed Pressure Urticaria
    • Sites of sustained pressure
      – Waistline, Socks, Shoes
    • Test: 5lb. weight to the thigh or back for 20 min.: wheal occurs in 30 minutes to 8 hours

Chronic Inducible Urticaria

• Physical Urticarias
  – Cholinergic Urticaria
    • Due to increased **body temperature**
      – Within 15 min. of physical exertion, hot bath, emotional stress, alcohol, or spicy food
    • Characteristic monomorphropic papular wheals (2-3mm)
    • Prominent on upper body
    • Test: Increase body temp (i.e. physical exertion)

Chronic Inducible Urticaria

• Physical Urticarias
  – Adrenergic Urticaria
    • Distinguished from cholinergic urticaria by the presence of halos of blanched vasoconstricted skin surrounding small pink wheals
    • Induced by sudden stress
      – Increased serum catecholamines
    • Tx: Propanolol
    • Test: Intradermal injection of norepinephrine

Chronic Inducible Urticaria

- **Physical Urticarias**
  - **Cold Urticaria**
    - Occurs within minutes of exposure
    - AD familial variant
    - Avoid cold baths & swimming - potential risk of anaphylaxis
    - May be assoc. with cryoglobulinemia
    - Test: Ice cube on arm
      - 30 seconds to 20 minutes

Chronic Inducible Urticaria

• Physical Urticarias
  – Aquagenic Urticaria
    • Contact with water of any temperature
    • Resembles cholinergic urticaria
    • Upper body and last less than 1 hour

www.thegnac.com/sports/wwimdiv/2012-13/releases/20121119j85nny; accessed 8/24/17
Chronic Inducible Urticaria

• **Physical Urticarias**
  – **Solar Urticaria**
    • Within minutes of UV exposure
    • Exact mechanism is unknown
    • May be triggered by exogenous substance (i.e. medications)
    • Test: Phototesting
Chronic Inducible Urticaria

- **Contact Urticaria**
  - Percutaneous penetration of the urticant
  - Development of urticaria at the site of contact within minutes
    - Resolve within 2 hours
  - Can lead to anaphylaxis
  - Tx: NSAIDS (Prostaglandins)

<table>
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<tr>
<th>Immunologic (i.e. IgE dependent)</th>
<th>Non-Immunologic (i.e. Irritant)</th>
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<tbody>
<tr>
<td>• Environmental allergens (i.e. grass, foods)</td>
<td>• Due to direct effects of urticants on blood vessels</td>
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<td>• Latex glove allergy</td>
<td>• Usually plant toxins containing histamine</td>
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Differential Diagnosis

- Urticarial dermatoses
  - Urticarial vasculitis
  - Urticarial drug eruptions
  - Eosinophilic cellulitis
  - Bullous pemphigoid
  - Schnitzler’s Syndrome
  - Periodic fever syndromes

- Think of alternative diagnosis if:
  - Lesions last >24 hrs
  - Associated fevers or arthritis
  - Associated pain/burning
  - Resolve with pigmentation changes
Urticarial Vasculitis

- Immune complexes
- Lesions last longer than 24 hours
- Painful/burning sensation
- Evidence of leukocytoclastic vasculitis on biopsy

Diagnosis of Urticaria

• History: Duration, frequency, occupation/leisure activities
  – Duration
    • > 24 hours: Consider biopsy (urticarial vasculitis)
    • <1 hour: Consider physical challenge
    • < 2 hours and localized: Consider contact challenge

• Review of Systems: Symptoms of anaphylaxis
  – i.e. respiratory distress, nausea, abdominal pain
Diagnosis of Urticaria

• Episodes occurring less than 6 weeks
  - Acute urticaria does not warrant lab testing
  - Majority of patients have mild disease that responds to antihistamines
Diagnosis of Urticaria

• **Chronic Urticaria** Laboratory Work-up
  - Complete Blood Count (CBC)
    • Eosinophilia
  - Elevated Sedimentation Rate (ESR)
    • Elevated in periodic fever syndromes & urticarial vasculitis
  - Thyroid stimulating hormone (TSH) & Thyroid autoantibodies
    • Treatment does generally not affect the course
Diagnosis of Urticaria

- **Further Investigations**
  - Complete Metabolic Panel (CMP)
  - Antinuclear antibody (ANA)
  - Epstein-Barr virus (EBV)
  - Hepatitis B Surface Antigen/ Hepatitis C
  - Urinalysis
  - Cryoglobulins
Diagnosis of Urticaria

• Referral for Further Studies:
  – Skin prick testing & Serum Radioallergosorbent Test (RAST)
    • IgE-mediated reactions to environmental allergens
  – Autologous serum skin test (ASST)
    • Autoantibodies
    • Negative test
      • Good negative predictive value
Diagnosis of Urticaria

• Angioedema without urticaria
  – C1 esterase inhibitor (C1 inh) deficiency
    • Hereditary: Activation mutation in C1 inh
    • Acquired: Persistent activation of C1q
      - B-cell lymphoproliferative disorders, plasma cell dyscrasias, connective tissue disease
  – Medication induced (i.e. ACE-I)

http://www.medicalook.com/Skin_diseases/Urticaria.html
Initial Management

• **Antihistamines**

  – Non-sedating H1 antihistamines (i.e. fexofenadine 180mg)
    • A European consensus paper has recommended increasing the daily dose of second-generation H1 antihistamines up to **fourfold**
    • Scheduled dosing

  – May add sedating H1 antihistamine at night
    (i.e. diphenhydramine 10-25mg or doxepin 10-50mg)
Initial Management

• May add H2 antagonist
  – **Ranitidine** is preferable to cimetidine
    – Does not interfere with hepatic metabolism of other drugs &
      does not bind androgen receptors

• Leukotriene inhibitors- Montelukast
  – May play a role in delayed pressure urticaria
Initial Management

- Antipruritic lotions (i.e. calamine or 1% menthol)
- Avoid common aggravating factors:
  - NSAIDS, aspirin, opiates
- Systemic corticosteroids should be avoided
  - Rebound effect
  - Prolonged duration not recommended due to numerous side effects
    - Hypertension, glucose intolerance, osteoporosis, femoral head necrosis
If Refractory

- Refer to dermatology or allergy & immunology
  - Mycophenolate mofetil
  - Methotrexate
  - Cyclosporine
  - Dapsone
  - Colchicine
  - Omalizumab
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Omalizumab

- Anti-IgE monoclonal antibody
- Indicated for chronic idiopathic urticaria
  - 12 years of age and older
  - Symptomatic despite antihistamine treatment
- 70% of patients significantly improve

http://www.usnon.com/focus-on-omalizumab-xolair.htm
Omalizumab

• Risks & Warnings:
  – Anaphylaxis (2 hours)
  – Malignancies
  – Acute Asthma Symptoms
  – Do not abruptly discontinue corticosteroids upon initiation
  – Serum sickness-like Rxn: Stop if patient has fever, arthralgia, and rash
  – Eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy
The Role of Diet in Urticaria

• Most Allergenic foods:
  – Chocolate
  – Shellfish
  – Nuts
  – Tomatoes
  – Strawberries
  – Melons
  – Pork
  – Cheese
  – Garlic
  – Onions
  – Eggs
  – Milk
  – Spices
The Role of Diet in Urticaria

- Latex Cross-Reaction
  - Avocado
  - Bananas
  - Chestnuts
  - Kiwi

- Preservatives: yeast, salicylates, citric acid, azo dyes, benzoic acid, sulfite, penicillin
The Role of Diet in Urticaria

- Pseudoallergen free diet
  - Substances that induce hypersensitivity
  - Avoidance of fermented foods
    - i.e. cheese, wine
  - Will work quickly (1-3 weeks) if going to make a difference
- Generally not high yield
Prognosis of Chronic Urticaria

• Average duration of chronic urticaria is 2-5 years
  – 50% of patients clear within a year
  – May persist for many years
Summary

• Urticaria are pruritic superficial dermal swellings
• Individual lesions last less than 24 hours
• Acute Urticaria
  – < 6 weeks
  – Idiopathic, infections, medications, foods
  – Does not warrant lab testing
Summary

• Chronic urticaria
  – ≥ 6 weeks (2 or more episodes per week off treatment)
  – Labs: CBC, ESR, TSH/Thyroid autoantibodies
• First line treatment is non-sedating H1 antihistamines
• Oral corticosteroids should be avoided
• Immunosuppressive agents for refractory cases
  – i.e. Omalizumab
References


Thank You

• Stephen Purcell, D.O.
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• Fellow Residents