Cutaneous Hypersensitivity Reactions in Children

Basic Dermatology Curriculum

Content for this module was developed by the Society for Pediatric Dermatology.

Created September 2015
Goals and Objectives

-The purpose of this module is to develop a clinical approach to the evaluation and initial management of cutaneous hypersensitivity reactions in children.

-By completing this module, the learner will be able to:
  - Identify key features of drug induced hypersensitivity syndrome, work-up, and management
  - Identify the classic morphologic findings and triggers for erythema multiforme
  - Distinguish between erythema multiforme and other hypersensitivity reactions in children including serum sickness like reaction and urticaria multiforme
  - Refer patients with serious cutaneous eruptions to dermatology or for inpatient care
Definition: Cutaneous Hypersensitivity Reactions

- Group of conditions mediated by immunologic or hypersensitivity reactions to foreign proteins such as drugs or infectious agents.
- This module is not meant to be comprehensive. We will focus on several hypersensitivity reactions important to pediatrics not highlighted in other modules.
- Please refer to the end of the module for a list of other hypersensitivity disorders and their associated Basic Dermatology Curriculum modules.
Case 1
Case 1

A 4-year-old girl presents to your clinic with new onset oral and skin lesions within the last two days.
Case 1

HPI: Yesterday, itchy red bumps developed on her hands and feet. This morning, she awoke with erosions on her lips and tongue. She had a cold sore several days ago

PMH: Otherwise healthy

Medications: Completed a course of amoxicillin 5 days ago for otitis media

Allergies: NKDA

Social History: Recent camping trip two weeks ago

Family History: Mother reports cold sores several times per year

ROS: Chills, fatigue, joint aches
Question 1: How would you describe this lesion?
Typical Target Lesion

- **3 distinct color zones**
  - Central zone has dusky appearance, reflecting damage/necrosis to the top layer of the skin
- Regular round shape
- Well-defined borders
- Less than 3 cm in diameter
Question 2: What is the most likely diagnosis?

a) Erythema multiforme
b) Herpetic gingivostomatitis
c) Lyme disease
d) Stevens-Johnson syndrome
e) Urticaria multiforme
Case 1 continued

Question 2: What is the most likely diagnosis?

a) Erythema multiforme
b) Herpetic gingivostomatitis
c) Lyme disease
d) Stevens-Johnson syndrome
e) Urticaria multiforme
Erythema Multiforme: Morphology

- Hallmark is the **typical target lesion**
- Sometimes, there may only be several **typical target lesions** intermixed with **atypical papular target lesions** with only 2 distinct color zones
- Skin findings have abrupt onset with majority of lesions appearing within 24 hours
- Remain fixed at the same site for 7 days or longer
Erythema Multiforme: Location

- Eruption is randomly distributed
- Occurs on any part of the body with predilection for:
  - Face
  - Palms/soles
  - Dorsal hands/feet
  - Extensor arms and legs
Erythema Multiforme: Mucosal Lesions

- Oral lesions occur in 25-50% of children
- Typically limited to the buccal mucosa and lips
- Initially vesiculobullous and rapidly evolve into painful erosions
- Infrequently involve the ocular and genital mucosa

Erythema Multiforme: Systemic Symptoms

• Oral involvement is typically accompanied by **systemic symptoms** including:
  – Fever
  – Arthralgias with joint swelling
  – Rarely renal, hepatic and hematologic abnormalities
Case 1 continued

Question 3: What is the most likely cause of erythema multiforme in this patient?

a) Amoxicillin

b) *Borrelia burgdorferi*

c) Herpes simplex virus, type 1

d) Herpes simplex virus, type 2

e) *Mycoplasma pneumonia*
Question 3: What is the most likely cause of erythema multiforme in this patient?

a) Amoxicillin

b) Borrelia burgdorferi

c) Herpes simplex virus, type 1

d) Herpes simplex virus, type 2

e) Mycoplasma pneumonia
Erythema Multiforme: Pathogenesis

- Pathogenesis is not clear, but likely an immune reaction in the setting of an infection.

- **Herpes simplex virus, type 1 is the most common**
  - Many cases follow herpes labialis, but can be concurrent.

- Other causes include Herpes simpex virus (type 2), *Mycoplasma pneumonia* (controversial), Epstein-Barr virus, *Histoplasma*, and parapoxvirus.

- Rarely drug induced and should consider alternative diagnoses such as Stevens-Johnson syndrome and urticaria.
Erythema Multiforme: Treatment

Acute episodes

- Supportive care with topical emollients, topical corticosteroids, magic mouthwash, and oral antihistamines is cornerstone
- Oral antiviral treatment has minimal impact if given after the appearance of an acute episode
- Systemic corticosteroids are controversial and are typically not given due to risk of longer and more frequent episodes
- Referral to inpatient should be considered for hydration and pain management
Erythema Multiforme: Treatment

• Recurrent episodes
  - Given association with herpes simplex virus, prophylactic therapy with oral acyclovir for 6-12 months should be considered
  - Episodic therapy with acyclovir is not useful
Case 2
Case 2

A 12-year-old boy presents to your office with a one week history of cough, malaise, and fever. Yesterday, he developed purulent conjunctivitis, oral erosions, and acral pink papules with central vesiculation.

Case 2 continued

- Lung auscultation was positive for bilateral fine crackles
- Chest X-ray showed bilateral interstitial infiltrate
- Laboratory values show a mild leukocytosis with neutrophilia and elevated ESR
Case 2

**Question 1**: What is the most likely cause of these symptoms?

- a) *Borrelia burgdorferi*
- b) Coxsackievirus
- c) Herpes simplex virus, type 1
- d) Herpes simplex virus, type 2
- e) *Mycoplasma pneumonia*
Case 2

Question 1: What is the most likely cause of these symptoms?

a) *Borrelia burgdorferi*

b) Coxsackievirus

c) Herpes simplex virus, type 1

d) Herpes simplex virus, type 2

e) *Mycoplasma pneumonia*
Mycoplasma-induced rash and mucositis

- Previously categorized under erythema multiforme or SJS/TEN
- Appears to have distinct clinical morphology
- Recently termed *Mycoplasma*-induced rash and mucositis (MIRM)
- Overall, excellent prognosis when compared to SJS/TEN
• Oral mucositis is the predominate feature (94%) presenting as vesiculobullous lesions, ulcerations of the lips and buccal mucosa.
MIRM mucosal morphology

- Ocular involvement (82%) presents as a purulent conjunctivitis, photophobia, eyelid edema
- Urogenital involvement (63%) presents with vesiculobullous, erosions and ulcerations

MIRM cutaneous morphology

• Absent in around 30% of cases

• Typical pattern:
  – Sparse and scattered
  – Acral distribution
  – Vesicobullous lesions
  – Not typical target lesions
  – Some might be target-like with central vesicle

MIRM Management

• Supportive care is currently cornerstone:
  – Analgesia
  – Hydration
  – Early ophthalmology, oral medicine, and urology consultation

• No evidence to favor immunosuppressants such as prednisone and IVIG

• Unclear if systemic antibiotics decrease incidence or severity
Case 3
Case 3

**HPI:** A 15-month-old girl presents to your office with this widespread skin eruption. She is happy and playful.

**PMH:** Otherwise healthy, recent URI

**Medications:** None

**Allergies:** NKDA

**Social History:** Lives with parents and one older sibling

**Family History:** Unremarkable

**ROS:** Rhinorrhea, mild acral edema
Physical Exam Findings:

- Erythematous to violaceous, large, serpiginous and annular plaques
- Slightly dusky center
- Duration > 24 hours
- Mild edema hands and feet
Case 3 continued
Case 3

Question 1: What is the diagnosis?

a) Viral exanthem
b) Erythema multiforme
c) Chronic urticaria
d) Acute hemorrhagic edema of infancy
e) Urticaria Multiforme
Case 3

Question 1: What is the diagnosis?
   a) Viral exanthem
   b) Erythema multiforme
   c) Chronic urticaria
   d) Acute hemorrhagic edema of infancy
   e) Urticaria multiforme
Urticaria Multiforme

• New terminology given to variant of urticaria resembling erythema multiforme and formerly called ‘annular urticaria’ or ‘giant urticaria’
• Polycyclic, annular plaques with dusky centers lasting > 24 hours
• Associated with mild edema of face and extremities in some cases
• Children are otherwise well, though fever and viral prodrome +/- exposure to oral antibiotics often precede skin findings
• Skin findings typically self-resolve within 2 weeks
• Treatment is supportive. If needed, oral antihistamines can be helpful
Case 4
Case 4

HPI: A 19-month-old boy is seen in your office with a history of recurrent otitis requiring numerous courses of oral antibiotics over the past several months. He has had this rash for 48 hours following recent exposure to cefdinir (third generation oral cephalosporin). He is irritable, but afebrile.

PMH: Recurrent/chronic otitis media

Medications: Cefdinir

Allergies: NKDA

Social History: Lives with mother and partner. There are no other caregivers or sick contacts

Family History: Unremarkable

ROS: Irritability, possible arthralgias with decreased walking
Case 4
Case 4
Question 1: What is your diagnosis?

a) Erythema Multiforme
b) Henoch Schonlein purpura
c) Acute Hemorrhagic Edema of Infancy
d) Serum Sickness Like Reaction
e) Medium vessel vasculitis
Case 4

Question 1: What is your diagnosis?
   a) Erythema Multiforme
   b) Henoch Schonlein purpura
   c) Acute Hemorrhagic Edema of Infancy
   d) Serum Sickness Like Reaction
   e) Medium vessel vasculitis
Serum Sickness Like Reaction

• Rare adverse drug reaction characterized by fever, rash (often annular, purpuric) and arthralgias
• Seen in the setting of infection and exposure to oral antibiotics
• Classically described following exposure to cefaclor though many different agents associated
• Elevated ESR/CRP and leukocytosis are common
Serum Sickness Like Reaction

• Vasculitis, immune complex deposition or renal failure as seen in true serum sickness is absent.
• Children improve with withdrawal of the antibiotic, usually only requires supportive care. Some patients might require a short course of oral corticosteroids and/or antihistamines.
• Re-exposure can lead to recurrence.
• Allergy testing for the implicated antibiotic is not useful in predicting recurrence.
Case 5
Case 5: History

**HPI:** A 15-year-old otherwise healthy male was started on minocycline for acne 3 weeks ago. A few days ago, he started to have fevers, sore throat, and malaise. This was followed by facial swelling and a rash that started on the face, but has now spread to the entire body. He presents to the ER for further evaluation.

**PMH:** Acne vulgaris, otherwise healthy

**Medications:** Minocycline 100mg PO BID

**Allergies:** NKDA

**Social History:** Lives with parents and older sister. He is in the 10th grade. Denies tobacco, alcohol, or drug use. Denies sexual activity.

**Family History:** Mom and sister both with acne

**ROS:** As above
Case 5: Physical Exam

- Vital signs: T: 102.5 F, HR 110, BP 110/70, RR 18, O2 sat 99% on RA
- General: Ill appearing male in NAD
- Skin: Facial edema, diffuse erythematous morbilliform eruption without mucosal involvement
Case 5: Laboratory Data

- CBC with differential
  - 12.4>36/12<350
  - Eosinophils 10%
  - Atypical lymphocytes 20%
- AST 180, ALT 150
- Creatinine 0.6
Question 1: What is the most likely diagnosis?

a) Drug-induced hypersensitivity syndrome
b) Stevens-Johnson syndrome
c) Group A streptococccocal pharyngitis
d) Viral exanthem
e) Toxic Epidermal necrolysis
Case 5

**Question 1:** What is the most likely diagnosis?

a) Drug-induced hypersensitivity syndrome

b) Stevens-Johnson syndrome

c) Group A streptococcal pharyngitis

d) Viral exanthem

e) Toxic Epidermal necrolysis
Drug Induced Hypersensitivity Syndrome (DIHS)

- Also known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
- Delayed type drug reaction
  - Presents 2 to 6 weeks (range 1 to 12 weeks) after starting initial dose of medication or with dose changes of the medication
- Presents with rash, systemic symptoms, and internal organ inflammation
  - Liver most common
  - CNS, kidneys, lungs, heart
  - Thyroid (late onset occurring 2-3 months later)
DIHS Signs and Symptoms

• Morbilliform eruption
  – Spreads in cephalad to caudal direction
• Facial and periorbital edema
  – Hallmark feature of this condition
• Often with lack of mucosal involvement
  – Distinguishing feature from SJS, TEN, EM
• Symptoms
  – Fever, malaise, cervical adenopathy and pharyngitis
• Laboratory findings
  – Eosinophilia is seen in >70% of patients
DIHS Clinical Course

• Signs and symptoms may relapse and remit or persist for months after cessation of medication

• Prognosis is generally favorable in children, but fatality rate has been reported up to 10% overall
Medications implicated in causing DIHS

- Anticonvulsants
  - Phenytoin
  - Phenobarbital
  - Carbamazepine
  - Lamotrigine
- Aspirin
- Isoniazid
- Anti-HIV medications
  - Abacavir
  - Nevarapine
- Allopurinol
- Antibiotics
  - Sulfonamides (aromatic amine form)
  - Penicillin
  - Minocycline
  - Metronidazole
  - Dapsone
- NSAIDS
DIHS Management and Treatment

• Topical corticosteroids and antihistamines
  – Possible in mild cases without organ involvement

• Oral corticosteroids
  – When there is any evidence of organ inflammation, may require prolonged course
  – Taper over 2 to 3 months

• IVIG in refractory cases
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- Refer patients with serious cutaneous eruptions to dermatology or for inpatient care
Additional Core Curriculum Resources

- Below is a list of additional pediatric hypersensitivity reactions reviewed in the Basic Dermatology Curriculum and their associated modules

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To take the quiz, click on the following link: