Challenging pediatric skin conditions: what’s new and what’s true

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Contact dermatitis from homemade slime

- **Slime ingredients**
  - Borax (sodium borate): irritant
  - Laundry detergent, glue: irritants + contact allergens such as isothiazolinones (MCI/MI), fragrances

- **Hand dermatitis:** fingertips, proximal fingers/webspaces, palms

- **Onychomadesis**

Heller et al Ped Derm 2018, Anderson et al Ped Derm 2019; Tehrany et al Contact Derm 2019; Salman et al Contact Dermatitis 2019
Chronic hand dermatitis due to slime

• Often more prominent on dominant hand

Kondratuk et al Pediatr Derm 2019; Gittler et al J Pediatr 2018
Allergic contact dermatitis due to “noise putty”

- + Patch testing for isothiazolinones
Chemical burns & acute irritant dermatitis due to garlic

- Garlic has been used in many cultures as natural remedy since ancient times
- Examples shown:
  - Necklace/wreath of freshly peeled garlic for nasal congestion, abdominal discomfort in young children
  - Garlic paste to treat facial pruritus in a teen based on rec from internet

Esfahani et al Pediatr Dermatol 2017
Fick et al Pediatr in Rev 2018
Schimmel Contact Dermatitis 2019
Bullous irritant contact dermatitis with cloth diaper use

- Can mimic impetigo or HSV infection
- Favors toddlers, who have less frequent diaper changes
- Genitals often involved in boys
- Improves with change to disposable diapers and barrier ointment use

Harfman et al Pediatr Dermatol 2017
“Granuloma gluteale infantum” and variants with cloth diaper use

• “Erosive papulonodular dermatosis” spectrum
  – Also includes Jacquet’s erosive dermatosis and pseudoverrucous papules/nodules
  – All are manifestations of irritant contact dermatitis
  – Additional factors may include topical corticosteroid use and candidiasis

Ramos Pinhiera et al Pediatrics 2018
Robson et al JAAD 2006
Toilet seat dermatitis

- **Irritant contact etiologies**
  - Harsh bathroom cleansers
- **Allergic contact etiologies**
  - Polypropylene in plastic seats
  - Rosin and other components of wooden seats
  - Polyurethane (contains isocyanates), e.g. in exposed foam
- **Use paper toilet seat covers, or change suspect home seat/cleansers**

Turan et al. Pediatr Derm 2011
Helig et al. Pediatr Derm 2011
Litvinov et al. Pediatrics 2010
Potty seat dermatitis

Dorfman et al Pediatr Derm 2018
www.amazon.com/Prince-Lionheart-weePOD-Basix-Poppy/dp/B005ZBI04M#customerReviews
Pediatric positional sitting dermatitis

- Localized dermatitis in areas of repetitive irritation due to seating positions
  - Shoes contact posterior thighs/buttocks at sites of dermatitis
What about oils? – “*I only use natural products*”

- **Coconut oil**: ~90% saturated FAs, 60% medium-chain FAs – especially lauric acid/monolaurin $\rightarrow$ ↓ TEWL, antimicrobial

- **Olive oil**: ~20% saturated FAs, high oleic acid $\rightarrow$ ↓ stratum corneum integrity, may induce inflammation, “feeds” *Malassezia*
  - X Irritant contact dermatitis with “ozonated” form

- **Sunflower seed oil**: high linoleic acid $\rightarrow$ ↑ stratum corneum integrity and hydration

- **Mineral oil**: (cyclo)alkanes $\rightarrow$ ↓ TEWL, no “food” for *Malassezia* (and actually “natural” – from fossils of algae/plankton)

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Aerts et al Contact Derm 2016; Siegfried & Glenn Arch Ped Adol Med 2012
Allergic contact dermatitis to “natural” products

- “Natural” and “botanical” products are popular and perceived as safer by the public
  - Used by ~50% of respondents in recent survey at the Minnesota State Fair
- Many components of “natural” topicals are potential allergens
  - Most common: propolis, tea tree oil, Compositae extracts
  - 79 essential oils have been reported to cause ACD
- >80% of topical cannabinoid preparations contain NACDG allergens
  - e.g. lavender & peppermint oils, fragrance

De Groot & Schmidt Dermatitis 2016
Goodier et al Contact Dermatitis 2019
Corazza et al Contact Dermatitis 2014
Adler & DeLeo J Am Acad Dermatol 2019
Allergic contact dermatitis in pediatric patients

• In atopic dermatitis (AD) patients, consider patch testing if recalcitrant, unusual distribution, or new-onset in older child/teen
  – Relevant + reactions most common with eyelid or hand dermatitis
  – ACD more frequent in adolescents with AD (up to 70%) than in children with AD (<30%)
  – Especially components of skincare products

• Important allergens
  – 38-allergen pediatric patch test series recently developed
  – TRUE test misses ~40% of top 40 pediatric allergens
  – Topical antibiotics, fragrances, lanolin, cocamidopropyl betaine, corticosteroids, isothiazolinones, propylene glycol, formaldehyde, nickel
  – Consider activities/sports, equipment, toys, products, caregivers

Yu et al Dermatitis 2018
Jacob et al Pediatrics 2017
Lagrelius et al Br J Derm 2018
Pap et al Pediatr Dermatol 2018
Simonsen et al Br J Dermatol 2018
Recurrent blistering in a baby

- **Perinatal history**
  - Born full term via C-section for failure to progress
  - Back and right thigh became swollen soon after birth
  - Diagnosed clinically with subcutaneous fat necrosis, calcium levels have been monitored

- **Now presents at age 4 months**
  - Parents very concerned that these areas continue to blister ~weekly
  - Seen in ED twice for seizure-like activity and decreased responsiveness, with normal baseline EEG
A “mole” that swells up, or recurrent blistering in the same location?

mastocytoma
Pediatric mastocytosis

- Accumulation of clonal mast cells
  - Somatic activating *KIT* mutations: codon 816 (~35%) or other (~45%)
- Unlike adults, usually limited to the skin in children
- Rare involvement of the bone marrow, GI tract, liver/spleen, and lymph nodes
- Revised cutaneous mastocytosis classification in 2016
  - Consensus from international group

Matito et al Immunol All Clin N Am 2018
Small, monomorphous “maculopapular” lesions

- Resembles conventional adult mastocytosis
  - Typical “urticaria pigmentosa”
- Usual codon 816 \( KIT \) mutation
- Histo: spindle-shaped atypical mast cells (“sausages”)
  - \( \text{CD25}^+ \) in bone marrow
- Higher tryptase levels
- Later onset: \( \sim 60\% \) >24 mos
- Longer duration: \( \sim 60\% \) \( \geq 15 \) y

Weichers et al J All Clin Immunol 2015
Matito et al Immunol All Clin N Am 2018
Large ± polymorphic “maculopapular” lesions

- “Well differentiated” mastocytosis
- Lesions ≥1 cm
- Other KIT mutations
  - Occasionally familial
- Histo: round typical mast cells (“eggs”)
  - CD25-negative in bone marrow
- Lower tryptase levels
- Earlier onset: ~80% age ≤6 mos
- Shorter duration: ~70% <8 y, 95% <15 y
  - Frequent fading/shrinking of lesions
Large/polymorphic “maculopapular” mastocytosis: fading/resolving over time

Weichers et al 2015
Uzzaman et al
Ped Bl Cancer 2009
Diffuse cutaneous mastocytosis

- Generalized thickening of the skin without discrete lesions
  - Peau d’orange texture
- Frequent blistering, flushing, GI symptoms
- Other KIT mutations
  - Sometimes familial (AD): persists, more often internal involvement
- High tryptase levels, ↓ over time
- At birth or develops in early infancy
- Duration usually <8 y

Weichers et al J All Clin Immunol 2015
Matito et al Immunol All Clin N Am 2018
Jenkinson et al Pediatr Dermatol 2019
Cutaneous mastocytomas

- Current definition: up to 3 lesions
- $KIT$ mutations common
  - 1/3 codon 816, 1/3 other, 1/3 none
- Histo: entire dermis packed with mast cells
  - Be careful eliciting Darier sign in larger lesions
- Flushing can occur; rarely hypotension with large lesions

Ma et al Histopathol 2014
Blistering in mastocytosis

- Infants with large, thick lesions or diffuse involvement
  - Triggered by friction/irritation
  - Likely role of mast cell proteases
- Tendency usually remits by age 3 y
Mast cell mediators and mastocytosis symptoms

Preformed mediators:
- Histamine
- Heparin
- Neutrophil chemotactic factors
- Eosinophil chemotactic factors
- Tryptase/chymase

Newly formed mediators:
- PGD₂
- LTB₄, LTC₄, LTD₄, LTE₄
- Platelet activating factor

Cytokines:
- TNF-α
- IL-6
- IL-4
- IL-8
- IL-5
- SCF
- GM-CSF, IL-13

Symptoms:
- Headaches
- Cognitive disorganization
- Fatigue
- Bullae
- Flushing
- Pruritus
- Urticaria
- Cramping
- Nausea
- Diarrhea
- Vomiting
- Epigastric pain
- Weight loss
- Chest pain
- Palpitations
- Dizziness
- Syncope
- Dyspnea
- Bone pain
  (Osteoporosis/osteosclerosis)
Symptoms in pediatric mastocytosis

• Systemic symptoms can result from skin MC mediator release
• Severe reactions from bee stings, anesthesia, or meds are rare
• Most common with extensive or diffuse skin lesions
  – Frequency of systemic sx correlates with # of skin lesions and skin sx

Symptoms in children with mac-pap mastocytosis, n=110 (%)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Itch</td>
<td>50</td>
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<tr>
<td>Flushing</td>
<td>40</td>
</tr>
<tr>
<td>Blistering</td>
<td>20</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>20</td>
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<tr>
<td>Abd pain</td>
<td>20</td>
</tr>
<tr>
<td>Bone pain</td>
<td>10</td>
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<tr>
<td>HA</td>
<td>10</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>10</td>
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</tbody>
</table>
Pediatric mastocytosis: evaluation

- Serum tryptase level
  - Correlates with total mast cell burden and risk of severe symptoms
  - >20 ng/ml is minor criterion for systemic disease diagnosis
  - Measure (not during event) baseline and if elevated Q6-12 mos

- Assess for hepatosplenomegaly (clinical ± abdominal US)

- Bone marrow biopsy if hepatosplenomegaly
  - In NIH study, of 53 children who had BM bx, all 19 with HSM had systemic disease, vs none of the 34 without HSM (all with ↑ tryptase &/or severe sx)

- KIT mutations in the skin do not predict prognosis

- Clinical diagnosis is routine for mastocytomas

Carter et al J All Clin Immunol 2015
Matito et al Immunol All Clin N Am 2018
Meni et al Br J Dermatol 2018
Chan & Clark Clin Exp Dermatol 2018
Pediatric mastocytosis: avoiding triggers

- Emphasize to families: mastocytosis does **not** cause allergies, although may have more severe reactions if you have an allergy
- Physical triggers
  - Friction, heat > cold
- Alcohol, hot beverages, spicy foods, other foods/additives
- Mast cell degranulating medications
  - Include NSAIDs, aspirin, narcotics, dextromethorphan
  - Some systemic anesthetics (local lidocaine injection OK)
- ? EpiPen®
  - If history of hypotension/severe reactions or high mast cell burden

Hermans et al Ann Allergy Asthma Immunol 2017
Pediatric mastocytosis: treatment

- **Antihistamines for symptoms**
  - **Scheduled long-acting H1-antihistamine** if frequent flares (±↑ dose, multiple agents)
  - H2-antihistamines for GI sx or as adjunct
- **Oral cromolyn (low absorption)** for GI sx
- **Topical therapy**
  - **Cromolyn sodium 4% cream/lotion**
    - www.mastokids.org/magic-masto-lotion
  - **Class 1-3 corticosteroid** in 2-6 week cycles
    - • ± occlusion; intraleisonal TAC
  - **Pimecrolimus cream** can induce mast cell apoptosis, decrease mediators
  - **Hydrocolloid dressing** for larger mastocytomas with frequent flares
- **Narrowband UVB**
- **Kinase inhibitors (systemic dz)**: midostaurin, imatinib

Liu et al J All Immunol Clin Prac 2019
Matito et al Immunol All Clin N Am 2018
Mashiah J et al Clin Exp Dermatol 2018
Patrizi et al Dermatol Ther 2015; Edwards BMJ Case Rep 2011
Take home points on pediatric mastocytosis

- Mastocytomas are underrecognized and may have systemic symptoms.
- Mastocytosis prognosis depends on the clinical pattern:
  - Large/polymorphic lesions predict shorter duration.
- Hepatosplenomegaly is a marker of systemic disease.
- Treatment depends on symptoms, with multiple options available.