A “Bitter” Complaint Leading to an Unusual Diagnosis

Danita Hahn, MD
Assistant Professor of Pediatrics, Section of Hospital Medicine
Medical College of Wisconsin and Children’s Hospital of Wisconsin

Financial Disclosures

• I have no financial disclosures to report.
History of Present Illness

• 2 month old previously healthy term male presenting with acute onset of fever and rash.

• In his usual state of health until he developed rhinorrhea several days prior to admission.

• One day prior to admission, parents noted a rash on his cheek.

• He also became fussy and difficult to console.

• Oral intake decreased and parents became concerned for dehydration, prompting presentation to the ED.
Additional Patient History

- Afebrile at home.
- No sick contacts. Mom does have a history of cold sores though none since the infant was born.
- Full term without complications. Negative maternal labs and no maternal history of STI.
- Family history significant for maternal 3rd cousin with a death at age 4 from “viral illness”.

Physical Exam

- Vital Signs: T 39.2C, HR 168, RR 72, BP 91/54, SpO2 87% room air
- General: Fussy but consolable, ill appearing
- HEENT: Fontanel open and flat, no oral lesions, mucus present in nares.
- CV: Tachycardic with hyperdynamic precordium, no murmurs, distal pulses 1+
- Pulm: Tachypneic with prominent subcostal retractions and grunting, lungs clear and with good aeration.
- Ext: Capillary refill time 3 seconds.
Physical Exam

Skin Exam:

What would be highest on your differential diagnosis at this point?

- A. Respiratory virus with viral rash
- B. Invasive bacterial infection (e.g. bacteremia, meningitis, UTI, pneumonia)
- C. HSV or VZV infection
- D. Other viral skin infection (e.g. Enterovirus or Poxvirus)
- E. Bacterial skin infection (e.g. Staph or Strep)
- F. Other

https://api.cvent.com/polling/v1/api/polls/sp-vtvazm
Differential Diagnosis of Infantile Rash

- **Infectious**
  - Viral
    - >HSV
    - >VZV
    - >Enterovirus
    - >Poxvirus
    - >Viral exanthem
  - Bacterial
    - >Staph
    - >Strep
    - >Listeria
    - >Syphilis
  - Fungal
  - Parasitic
    - >Scabies
    - >Bed bugs

- **Benign**
  - Erythema toxicum
  - Transient neonatal pustular melanosis
  - Infantile/neonatal acne
  - Milia
  - Miliaria

- **Congenital**
  - Epidermolysis bullosa
  - Epidermolytic hyperkeratosis
  - Aplasia cutis congenita
  - Incontinentia pigmenti

- **Cutaneous mastocytosis**
- **Autoimmune/Reactive**
  - Neonatal lupus
  - Sweet syndrome

- **Malignancy**
Which of the following would you obtain as part of your initial workup?

- A. CBC
- B. Blood culture
- C. Urinalysis with urine culture
- D. CSF studies with CSF culture
- E. HSV and/or VZV PCRs of the lesions
- F. HSV and/or VZV PCRs of the blood and/or CSF
- G. Bacterial culture of the lesions
- H. Viral respiratory PCRs
- I. Chest x-ray
- J. Other

https://api.cvent.com/polling/v1/api/polls/spzb53wy
## Workup

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UA negative</td>
<td></td>
</tr>
<tr>
<td>CSF:</td>
<td></td>
</tr>
<tr>
<td>Total Nucleated Cells</td>
<td>3</td>
</tr>
<tr>
<td>Glucose</td>
<td>67</td>
</tr>
<tr>
<td>Protein</td>
<td>27</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>12</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>4</td>
</tr>
<tr>
<td>Monocytes</td>
<td>82</td>
</tr>
<tr>
<td>HSV, VZV, Enterovirus PCRs negative</td>
<td></td>
</tr>
<tr>
<td>CRP</td>
<td>21.4 mg/dL</td>
</tr>
<tr>
<td>AST</td>
<td>17</td>
</tr>
<tr>
<td>ALT</td>
<td>37</td>
</tr>
<tr>
<td>Alk phos</td>
<td>155</td>
</tr>
<tr>
<td>68% segs</td>
<td></td>
</tr>
<tr>
<td>5% bands</td>
<td></td>
</tr>
<tr>
<td>22% lymphs</td>
<td></td>
</tr>
<tr>
<td>CSF:</td>
<td></td>
</tr>
<tr>
<td>Total Nucleated Cells</td>
<td>3</td>
</tr>
<tr>
<td>Glucose</td>
<td>67</td>
</tr>
<tr>
<td>Protein</td>
<td>27</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>12</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>4</td>
</tr>
<tr>
<td>Monocytes</td>
<td>82</td>
</tr>
<tr>
<td>HSV, VZV, Enterovirus PCRs negative</td>
<td></td>
</tr>
<tr>
<td>CRP</td>
<td>21.4 mg/dL</td>
</tr>
<tr>
<td>AST</td>
<td>17</td>
</tr>
<tr>
<td>ALT</td>
<td>37</td>
</tr>
<tr>
<td>Alk phos</td>
<td>155</td>
</tr>
<tr>
<td>68% segs</td>
<td></td>
</tr>
<tr>
<td>5% bands</td>
<td></td>
</tr>
<tr>
<td>22% lymphs</td>
<td></td>
</tr>
<tr>
<td>Blood, urine, CSF cultures negative</td>
<td></td>
</tr>
<tr>
<td>Nasopharynx PCRs negative for:</td>
<td></td>
</tr>
<tr>
<td>Mycoplasma</td>
<td></td>
</tr>
<tr>
<td>Human metapneumovirus</td>
<td></td>
</tr>
<tr>
<td>Parainfluenza</td>
<td></td>
</tr>
<tr>
<td>Enterovirus</td>
<td></td>
</tr>
<tr>
<td>Influenza A&amp;B</td>
<td></td>
</tr>
<tr>
<td>RSV</td>
<td></td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td></td>
</tr>
<tr>
<td>Pertussis</td>
<td></td>
</tr>
<tr>
<td>Chest x-ray: Viral peribronchial prominence, no focal infiltrate</td>
<td></td>
</tr>
</tbody>
</table>

## Differential Diagnosis of Infantile Rash

- **Infectious**
  - Viral
    - HSV
    - VZV
    - Enterovirus
    - Poxvirus
    - Viral exanthem
  - Bacterial
    - Staph
    - Strep
    - Listeria
    - Syphilis
  - Fungal
  - Parasitic
    - Scabies
    - Bed bugs
- **Benign**
  - Erythema toxicum
  - Transient neonatal pustular melanosis
  - Infantile/neonatal acne
  - Milia
  - Miliaria
- **Congenital**
  - Epidermolysis bullosa
  - Epidermolytic hyperkeratosis
  - Aplasia cutis congenita
  - Incontinentia pigmenti
- **Cutaneous mastocytosis**
- **Autoimmune/Reactive**
  - Neonatal lupus
  - Sweet syndrome
- **Malignancy**
Clinical Course

- Placed on empiric IV cefotaxime and acyclovir.
- He had persistent fevers, increasing inflammatory markers, development of new skin lesions, and worsening respiratory status.
- Dermatology consulted and skin biopsy was performed.
- Pathology showed a dermal neutrophilic infiltrate consistent with acute febrile neutrophilic dermatosis, or Sweet syndrome.

Sweet Syndrome:
Acute Febrile Neutrophilic Dermatosis
Clinical Presentation

- Characterized by sudden appearance of tender skin lesions.
- Accompanied by fevers, leukocytosis, and elevated inflammatory markers.

Epidemiology

- Usually presents in adults but can occur in children.
- Rarely occurs in infancy.
  - Mean age in pediatric cases is 5 years old.
Pathogenesis

- Etiology unknown.
- Viral trigger is felt to be the most likely and common cause.
- In older children and adults, it is associated with inflammatory bowel disease and pregnancy.
- It has also been associated with malignancy, autoimmunity, or immunodeficiency.
- There have also been reports of drug-induced Sweet syndrome.

Diagnosis

- Major criteria (need both)
  - Abrupt onset of painful erythematous nodules or plaques
  - Histopathologic evidence of a dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis
Diagnosis

• Minor criteria (need two of four)
  ➢ Fever > 38 degrees
  ➢ Association with underlying malignancy, inflammatory disease OR preceded by viral infection
  ➢ Abnormal laboratory values (3 of 4)
    › Elevated ESR
    › Elevated CRP
    › Elevated leukocytes
    › Elevated neutrophil percentage
  ➢ Excellent response to systemic corticosteroids

Diagnosis

• Biopsy shows edema and neutrophilic infiltration of the dermis.
Treatment

• Systemic corticosteroids are considered first-line treatment in children.
  ➢ 1-2 mg/kg/day followed by slow taper.
  ➢ Usually leads to swift improvement in symptoms.
  ➢ Recurrences are common as steroids are tapered.

• Alternative therapies include colchicine, dapsone, potassium iodide, and intravenous immunoglobulin.

Back to Our Patient

• Infectious trigger strongly suspected, though oncologic and immunodeficiency workup was performed and was negative.

• Started on systemic corticosteroids.

• Fevers, rash, inflammatory markers, and respiratory status all improved and he was discharged to home.

• Steroids were slowly weaned without signs of relapse.

• He is now a healthy 3-year-old!
Lessons Learned

- Pediatric hospitalists often encounter children with fever and rash, and the differential diagnosis for this set of symptoms is broad.

- While rare in the pediatric population, Sweet syndrome should be considered in patients with clinical courses of persistent fevers and atypical rash with an otherwise negative workup.

- Skin biopsy should be sought for definitive histologic diagnosis, which allows for appropriate treatment and workup for underlying pathology.

References


Questions?