A “Bitter” Complaint Leading to an Unusual Diagnosis

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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.

History of Present Illness

- 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

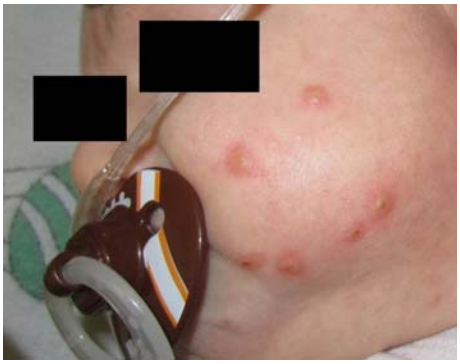
- Afebrile at home.
- No sick contacts. Mom does have a history of cold sores though none since the infant was born.
- Full term without complications. Negative maternal labs and no maternal history of STI.
- Family history significant for maternal 3rd cousin with a death at age 4 from “viral illness”.

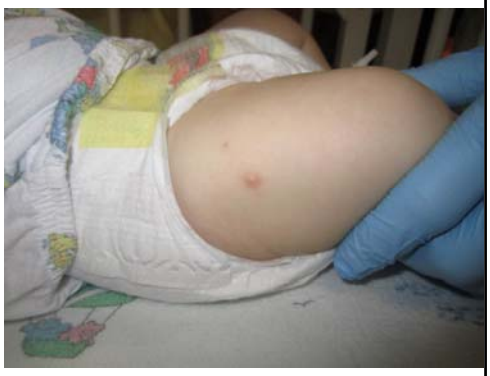
Physical Exam

- 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

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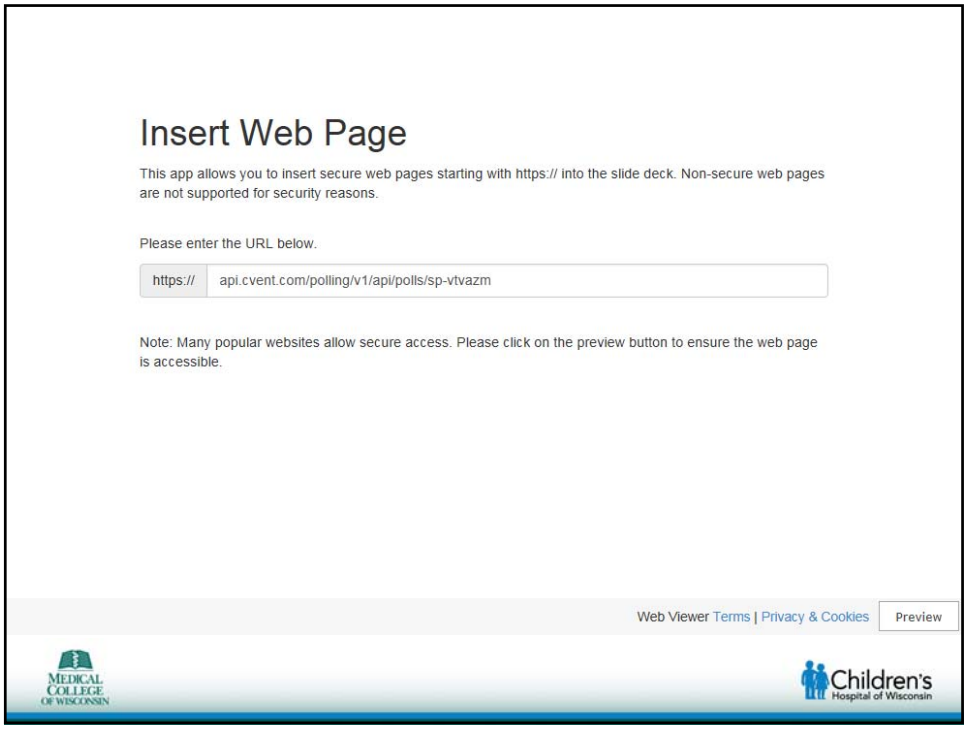

Differential Diagnosis of Infantile Rash

- 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
  - Epidemolysis bullosa
  - Epidermolytic hyperkeratosis
  - Aplasia cutis congenita
  - Incontinentia pigmenti
- Cutaneous mastocytosis
- Autoimmune/Reactive
  - Neonatal lupus
  - Sweet syndrome
- Malignancy

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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
- E. Bacterial culture of the lesions
- F. Viral culture of the lesions
- G. Inflammatory markers (e.g. CRP and/or ESR)
- H. Viral respiratory PCRs
- I. Chest x-ray
- J. Other

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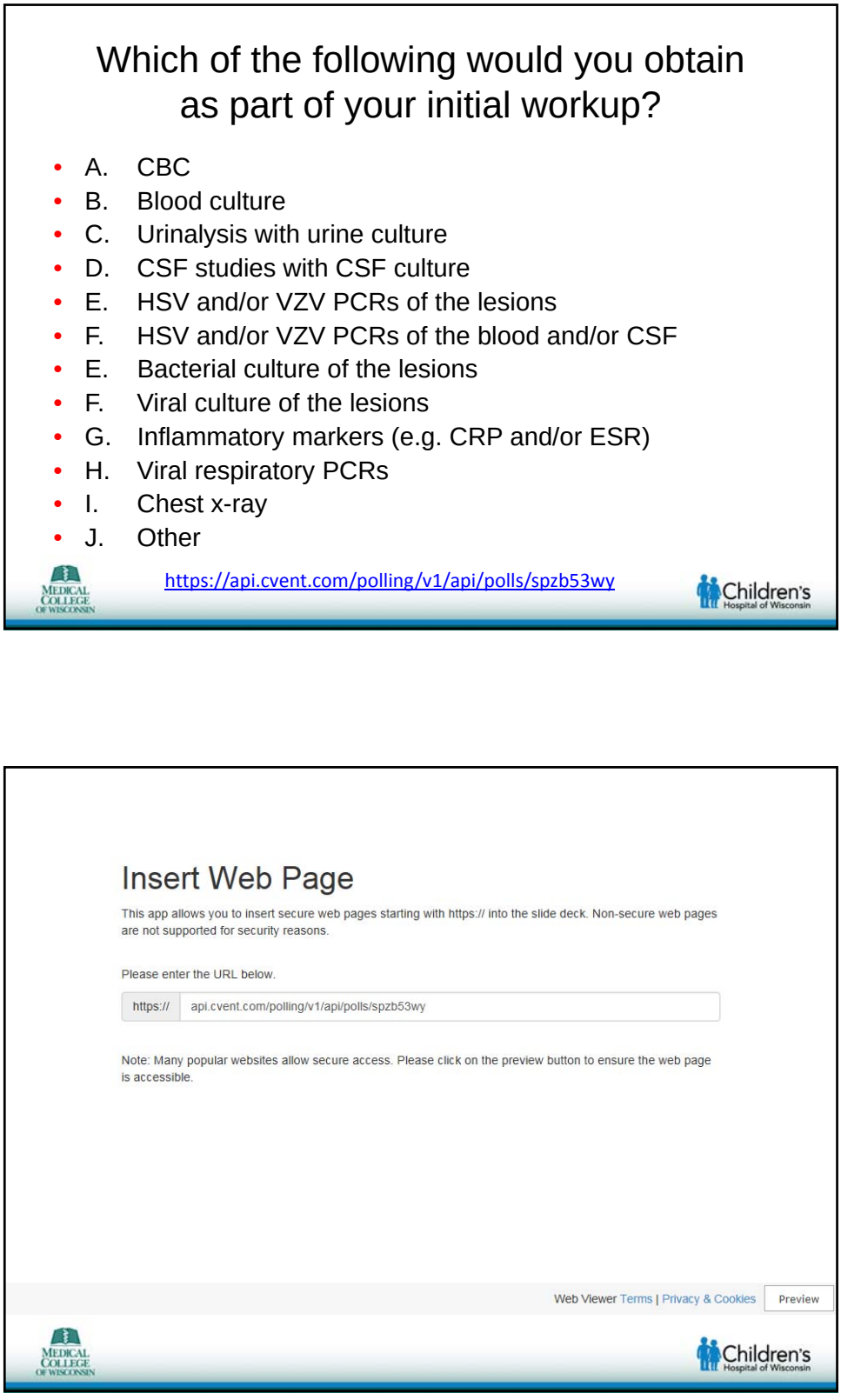
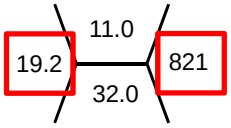


Workup



68% segs
5% bands
22% lymphs

CRP 21.4 mg/dL

AST 17
ALT 37
Alk phos 155

UA negative

CSF:
Total Nucleated Cells 3
Glucose 67
Protein 27
Neutrophils 12
Lymphocytes 4
Monocytes 82
HSV, VZV, Enterovirus PCRs negative

From lesion:
HSV PCR negative
VZV PCR negative
Viral culture negative

Blood, urine, CSF cultures negative

Nasopharynx PCRs negative for:
Mycoplasma
Human metapneumovirus
Parainfluenza
Enterovirus
Influenza A&B
RSV
Chlamydia pneumoniae
Pertussis

Chest x-ray: Viral peribronchial prominence, no focal infiltrate

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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

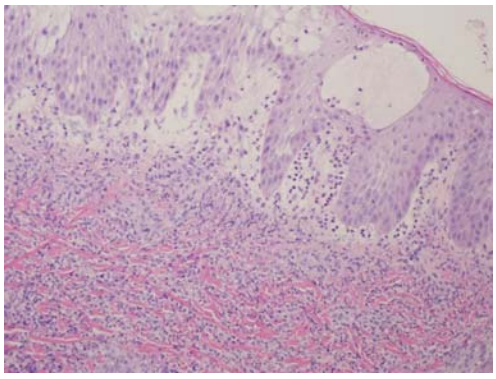
- Major criteria (need both)
  - Abrupt onset of painful erythematous nodules or plaques
  - Histopathologic evidence of a dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis

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

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Questions?