Congenital Blueberry Muffin Rash: A Case Based Review

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Objectives I

- To present a patient case of neonatal rash
- To review the differential diagnosis of “blueberry muffin rash”
- To explain the initial work up for a patient presenting with “blueberry muffin rash”
Patient Presentation

- 14 day old M presents with rash and fever
- Recently discharged from an OSH NICU for congenital rash/rule out sepsis
Birth History

- Full term
- C-section
- Mother reports “in labor for 24 hours”
- ROM at delivery
- Meconium aspiration
  - Intubated for suctioning
- GBS positive, appropriately treated
- Mother received prenatal care
History of Present Illness

- Recent NICU stay for rule out sepsis
- Congenital rash – now worsening
  - “Blueberry muffin rash”
  - Scattered moles all over body, no blisters
- Fever 102.9° F at home
  - Afebrile during NICU stay
Review of Systems

- Feeding well
  - Breastfeeding and supplementing with Enfamil
- No cough/congestion
- No constipation/diarrhea
- No vomiting
- Normal activity level
- No seizure activity
- + intermittent bloody stool
Medical History/NICU workup

- Torch titers – negative
- Blood and urine cultures - negative
- Received empiric antibiotic treatment
  - Ampicillin and Cefotaxime
- Echo negative for vegetation, revealed PFO and PPS
Family History

- Half brother: premature, Grade IV IVH with shunt, now 15 y/o
- Half sister: allergies
Physical Exam

- General: awake and alert, fussy but consolable

- HEENT: MMM, Bohn’s nodules noted, small ulceration on R buccal mucosa

- CV: RRR, +PPS murmur, 2+ pulses, <2 sec cap refill

- Pulm: CTA B/L, no wheezing or crackles

- GI: soft, + hepatosplenomegaly, liver edge palpable 3-4 cm and spleen palpable 2-3 cm below costal margin
Physical Exam

- GU: petechiae noted on penis and perianally
- Ext: moves all extremities well
- Skin: multiple hyperpigmented palpable purple/red colored papules with some scabbing covering entire body, including palms, soles, penis, perianal region, scalp, and ears, scattered petechiae, no active bleeding from lesions, red scaly lesion across forehead
- Neuro: symmetric moro, plantar/palmar grasp intact, good sucking reflex
Hemorrhagic vesicopustules on the forehead of a 3-day-old newborn.


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Hemorrhagic vesicopustules on the plantar surface.

Physical Exam Continued

- 4 episodes of right arm extension and left arm flexion lasting ~10 seconds each
- Unable to break
IMMEDIATELY TRANSFERRED TO THE PICU
Differential Diagnosis of Hemorrhagic Vesiculopustules in a Newborn
Differential Diagnosis: Infectious

- TORCH Infections
  - Toxoplasmosis
  - Other: syphilis
  - Rubella
  - Cytomegalovirus
  - Herpes Simplex Virus
- Bullous Impetigo
- Congenital Varicella
- Congenital Candidiasis
- Listeriosis
CMV
Rubella
Differential Diagnosis: Noninfectious

- Neonatal pustular melanosis
- Erythema toxicum neonatorum
- Neonatal hemangiomatosis
- Extramedullary hematopoieses
- Incontinentia pigmenti
- Congenital leukemia
- Langerhan’s cell histiocytois
- Juvenile xanthogranulomas
- Generalized eruptive histiocytoma
- Indeterminate cell histiocytoma
- Neuroblastoma
Congenital Leukemia
Juvenile Xanthogranulomas
Neuroblastoma
Initial Work-Up

- Rule out infectious etiology and begin empiric treatment
  - Blood, urine, CSF cultures
  - Ampicillin AND Gentamicin
    - AND Acyclovir
    - +/- Penicillin
- Skin biopsy
# Initial Evaluation and Management of Hemorrhagic Vescicopustules or Papules in a Newborn

## Step 1: Quick Tests

| HSV/VZV DFA ± Tzanck smear; KOH; Gram stain |

## Step 2: “Slow” Tests

| Skin biopsy; RPR; VDRL; viral, bacterial, and fungal cultures |

## Step 3: Empiric Therapy

| Acyclovir; if ill-appearing, use ampicillin + gentamicin; if syphilis is suspected, use penicillin |


Patient’s Initial Workup

- CBC, CMP, PT/PTT/INR, D-Dimer, Fibrinogen, CBG
  - Thrombocytopenia (70,000)
- Blood culture, Urine culture
- Wound culture (from skin lesion)
- LP attempted, desaturated during attempt

Consults:
- Neurology
- Infectious Disease
- Dermatology
Patient’s Clinical Course

- Dermatology biopsied skin → Histiocytes with Birbeck granules
  - consistent with Langerhan’s Cell Histiocytosis

- EGD with biopsy → mild chronic gastritis with superficial erosions noted in left colon
  - staining consistent with LCH

- Hepatosplenomegaly → liver and spleen involvement

- Pancytopenia → bone marrow involvement

- PET scan → Diffuse disease
  - Soft tissue and bony involvement of the skull/L3
  - Pulmonary involvement
  - Diffuse lymph node involvement
Patient’s Diagnosis

CONGENITAL MULTISYSTEM LANGERHAN’S CELL HISTIOCYTOSIS
Objectives II

- To recognize potential presenting symptoms of Langerhans Cell Histiocytosis (LCH)
- To be aware of the appropriate work up of a patient diagnosed with LCH
- To know the difference between single-system and multi-system LCH
Histiocytic Disorders

- Derived from mononuclear phagocytic cells and dendritic cells
- Classified as Langerhans Cell Histiocytosis and Non-langerhans histiocytosis

Langerhans Cell Histiocytosis:
- Rare histiocytic disorder most commonly characterized by single or multiple osteolytic bone lesions
- Morphology and immunophenotype of the abnormal cells is similar to Langerhans cells
- Same antigens: CD1a, CD207, S100
LCH: Pathogenesis

- Proliferation of a single clone
- Overall – pathogenesis largely unknown
Presentation: Skin Involvement

- Generalized or localized
- Manifests as seborrheic dermatitis of the scalp
- Purpuric or necrotic lesions
- Diffuse candidal diaper dermatitis
Presentation: Lytic Bone Lesions

- Can involve the skull, vertebral bodies, ribs, scapula, and femur
- Occur in 80% of patients
- Usually asymptomatic
- Can present as raised, soft, tender areas
- Lesions in the periorbital region may cause proptosis
- Lesions in the skull determine risk of CNS involvement
Presentation: CNS Manifestations

- Seizures
- Nystagmus
- Paresis
- Ataxia
- Headache
Presentation: Endocrine Abnormalities

- Encroachment on the pituitary gland -> Growth Retardation and Diabetes Insipidus
Presentation: Other PE Findings

- Dental abnormalities: floating teeth
- Ulcers of the palate, buccal mucosa, tongue, or lips
- Chronic otitis externa
- Localized or disseminated lymphadenopathy
- Hepatosplenomegaly
“Floating Teeth”
Presentation: Lab Findings

- Pancytopenia
- Increased liver enzyme values
- Hypoalbuminemia
- Hyperbilirubinemia
- Clotting factor deficiencies
Diagnosis

- Based on the histiologic findings of a skin, lymph node, or bone biopsy
- Presence of CD1a surface marker
- Characteristic raquet-shaped bodies in the cytoplasm in the lesional cells that are visible on electron microscopy
  - Birbeck granules
- Bean shaped nuclei
  - Reniform nuclei
Work Up of Patient with LCH

- Physical exam → lymphadenopathy/skin findings
- Abdominal ultrasound → hepatosplenomegaly
- CBC and CMP → liver function abnormalities, pancytopenia
- Skeletal Survey → lesions within skull or long bones
- Urine osmolality → diabetes insipidus
- +/- bone marrow biopsy
- +/- Endoscopy with biopsy
Single vs Multi-system LCH

- **Single-system LCH**
  - Usually good outcome with no or only local therapy

- **Multi-system LCH**
  - Less than 15% of all cases of LCH
  - Can have poor response to the initial 6 weeks of chemotherapy and have poor outcomes
Approach to congenital skin-only LCH. CBC indicates complete blood count; LFTs, liver function tests (including alanine aminotransferase, aspartate aminotransferase, total bilirubin, albumin, and total protein); CT, computed tomography.

LCH

**Initial evaluation for systemic involvement**

- Lymph nodes: Physical examination
- Bones: Skeletal survey, Urine osmolality (skull)
- Hematologic: CBC +/- bone marrow biopsy
- Liver/spleen: Physical examination, LFTs, abdominal ultrasound

**Multisystem LCH**

Oncology evaluation to determine if systemic therapy is indicated

**Skin-only LCH**
Skin-only LCH

Follow-up

History and physical: With emphasis on:
- symptoms (bone pain, abdominal pain, polyuria, polydipsia)
- examination (skin, lymphadenopathy, hepatosplenomegaly)
  Monthly for first year of life, then
  Annually for 5 y, then every other year thereafter

Screening laboratory tests: CBC, LFTs, urine osmolality
  Monthly for 1 y, then
  Annually for 5 y, then every other year thereafter

Abdominal ultrasound, CT scan, radiographs, and bone marrow biopsy as clinically indicated
Patient’s Clinical Course

- **ID**: ID consulted upon admission. Amp and Claf were given. Repeat blood/urine cultures: negative. TORCH titers reviewed and confirmed as negative.

- **Neuro**: No further seizure activity noted.

- **Onc**: Treated with a 28 day course of prednisolone; VCR and Ara-c (x 4 days).

- **Skin lesions and lymphadenopathy** showed vast improvement.
References

- McClain K. Clinical Manifestations, pathologic features, and diagnosis of Langerhans cell histiocytosis. UpToDate. October 2014
Questions?

SEPTEMBER HISTIOCYTOSIS AWARENESS MONTH

Thank you
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