U023 – Nursery Tales: Challenging Dermatoses in Newborns

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Objectives
- Develop a differential diagnosis for challenging dermatoses in premature and term infants
- Utilize laboratory testing to diagnose skin disease in neonates
- Formulate management plans for newborn skin eruptions

Case

2 day-old FT girl with grouped vesicles on arms
- Afebrile
- Feeding well
- No seizure activity or abnormal movements
- Maternal labs: RPR NR, rubella- immune, hepB neg, HIV neg; GBS negative; no maternal history of herpes
Patient’s mother

- Hypopigmented thin patches in shape of “Chinese characters” on thighs
- Patchy alopecia
- History of retinal detachment

Incontinentia pigmenti (IP)

- X-linked dominant disorder; IKBKG gene (NEMO)
  - Random X chromosome inactivation -> extent of disease
- Four cutaneous phases (may overlap)
  - Inflammatory vesicles/bullae
  - Verrucous lesions
  - Hyperpigmented streaks
  - Hypopigmented +/- atrophic streaks

Follows Lines of Blaschko

Mane, S. Indian Pediatrics 2006; 43:1005-1014
Bruckner, A. Seminars in Cutaneous Medicine and Surgery, 2004; 23 (2) 116–124
Pacheco, T, et al. JAAAD, 2008; 55(2) 251-255

Full-term baby boy with linear arrays of crusted erosions and vesicles

Biopsy: spongiotic intra-epidermal vesicles with numerous eosinophils

Diagnosis?

Incontinentia Pigmenti (IP)

Incontinentia Pigmenti (IP): X-linked dominant

X-Linked dominant conditions
- Incontinentia Pigmenti
- Focal dermal hypoplasia (Goltz syndrome)
- CHILD (Congenital Hemidysplasia with ichthyosiform erythroderma)
- Conradi-Hünerman
- Oro-Facial-Digital Syndrome
- Albright’s hereditary osteodystrophy
- Bazex syndrome

- IP: X-linked dominant disorder; IKBKG gene (NEMO)
  - 97% - female
  - males born with IP, somatic mosaicism vs. XXY

Incontinentia Pigmenti

Dermatologic ‘clues’
- Alopecia
- Dystrophic nails

Systemic manifestations
- CNS
  - Seizures
  - Developmental delay
  - Microcephaly
  - Ataxia
- Dental
  - Malformed ‘Peg’ teeth

Ophthalmological
- Optic nerve atrophy
- cataracts
- Strabismus
- Retinal detachment

In 2006, Jenna Lyons was diagnosed with Incontinentia Pigmenti (IP), a genetic skin disorder that affects the skin, eyes, and other organs.

Jenna Lyons
Diagnosed with IP
Former President and Executive Creative Designer at J Crew
Case

34 5/7 WGA premature infant born by repeat C-section after PPROM with widespread erosions

- Widespread erosions at birth
- Normal pregnancy and prenatal ultrasound
- Normal prenatal infectious disease blood evaluation
- FMHX:
  - no skin disorders
  - no genetic diseases
- Afebrile, vital signs stable

Epidermolytic Hyperkeratosis

- Mutations in
  - KRT1: encodes keratin 1
  - KRT10: encodes keratin 10
- ~ 50% new mutations
- otherwise usually autosomal dominant

- Presentation at birth may have:
  - Erosions
  - Severe blistering
  - Erythroderma

- Later in life:
  - hyperkeratotic skin especially over joints

Spitz, J.L. Genodermatoses, LW&W, 2005
Naik, N. Dermatology Online Journal. 2003; 9: 4
• 1 day-old Hispanic girl
  – born by C-section
  – 38 WGA
  – APGARS 9/9
• Transferred from a rural hospital
• Stable
• Feeding, voiding, stooling well
• Large erosions at birth
• Deep, membranous shiny plaques (consistent with aplasia cutis congenita)
• Two dark thick fingernails
• Oral mucosa clear

Diagnostic Studies

• HSV and VZV cultures and PCRs negative
• Offered biopsies for H&E and EB immunomapping
  – family declined
• Offered genetic testing
  – GeneDx EB panel- results: 6 weeks
    • Tests the following known EB causing genes:
      – CD151, CDSN, CHST8, COL17A1, COL7A1, CSTA, DSG1, DSG2, DSG3, DSG4, DSP, DST, EXPH5, FERMT1, GRIP1, ITGA3, ITGA6, ITGB4, KLHL24, KRT1, KRT10, KRT14, KRT5, LAMA3, LAMB3, LAMC2, MMP1, NID1, PKP1, PLEC, TGM5
  – Trio Whole Exome Sequencing- results: 3 weeks
    • Analyses the exons/coding regions of thousands of genes simultaneously using next-generation sequencing techniques
    • Exome of a patient and their parents and then comparing it to normal reference sequence

Diagnosis: Epidermolysis Bullosa Simplex

• Genetic testing results
  – KLHL24 mutation
    • Heterozygous c.1441T>A (p.S481T) variant
    • Both parents negative for above variant
  – KLHL24
    • Encodes a cullin 3–RBX1 ubiquitin ligase substrate receptor
    • KLHL24 interacts with keratin 14
    • AD mutation: epidermolysis bullosa simplex

Case

• 3-month-old healthy infant
• Spreading blistering x 2 days
• Previously with 1 localized blister on shin about 3 weeks ago, diagnosed as impetigo
• No FMHx blistering disorders
• No pregnancy complications
• Morphine for pain in ED
  – ? More blisters per parents
Bullous Mastocytosis

- Form of Diffuse Cutaneous Mastocytosis
- Mast cell infiltration of skin
  - Thick and leathery skin ("peau d’orange" skin appearance)
  - Plaques and nodules
  - Bullae can be the first presentation
  - Suspected etiology of bullae: serine protease release from mast cells

Laboratory Work Up

- CBC/Diff- within normal limits
- LFTs- within normal limits
- Tryptase – 283 mcg/L (range < 10.9 mcg/L)
- Bone marrow biopsy
  - no abnormal mast cell proliferation
- C-KIT mutation analysis- negative

Pediatric Mastocytosis: screening for systemic disease

Cohort of 105 children:
- Most children experienced major or complete disease resolution (57%)
- Partial improvement was observed among remaining children
- Tryptase trends down over time
- Enlargement of liver or spleen (hepatosplenomegaly):
  - strong indicator of systemic disease

Treatment

- Antihistamines: "around the clock"
  - Cetirizine (H1 antihistamine)
  - Ranitidine (H2 antihistamine)
- Breakthrough: diphenhydramine as needed for flushing/itch
- Good skin moisturization
- Topical corticosteroids:
  - triamcinolone 0.1% ointment
- "Magic Masto Lotion": cromolyn

Cutaneous Mastocytosis: Revised Consensus Classification 2016

- Diffuse cutaneous mastocytosis
  - Diffuse skin thickening and erythema
  - Pronounced dermatographism
  - Bullae in some infants ("bullous mastocytosis")
- Maculopapular cutaneous mastocytosis
  - Polymorphic
  - Monomorphic
- Cutaneous mastocytoma
  - No longer recommended: telangiectasia macularis eruptiva perstans (TMEP)

Summary: Pediatric Mastocytosis

- Revised cutaneous mastocytosis nomenclature (2016):
  - Diffuse cutaneous mastocytosis
  - Maculopapular cutaneous mastocytosis
    - Polymorphic (urticaria pigmentosa)
    - Monomorphic— with onset in childhood may be more likely to persist into adulthood
  - Cutaneous mastocytoma
  - No longer recommended category: telangiectasia macularis eruptiva perstans (TMEP)
- Among children with cutaneous mastocytosis
  - Organomegaly appears to be the most sensitive predictor of systemic disease
  - Antihistamines (H1&H2)
  - +/- topical corticosteroids or "magic masto lotion" helpful
  - Prognosis good with most children improving over time