Focus Session U020: Case Based Challenges in Pediatric Dermatology Hospital Consults

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Objectives for this session

• Develop a differential diagnosis and order appropriate tests to manage challenging Pediatric Dermatology inpatient consults

• Identify genodermatoses presenting in the NICU

• Recognize cutaneous manifestations of systemic disease, and treat severe Pediatric dermatoses
Case 1
What tests would you order for this baby?

• MRI/MRA of the head and neck
• eye exam
• echocardiogram
• thyroid function tests
• all of the above
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PHACE(S) Syndrome

P: Posterior Fossa Abnormalities
H: Hemangioma (Segmental) of face
A: Arterial abnormalities - intracranial, extracranial, includes coarctation of the aorta
C: Cardiac anomalies
E: Eye anomalies
S: Sternal cleft, supraumbilical raphe
PHACE Syndrome

- Increased risk of stroke in a subset of patients with intracranial arterial stenosis
- Initiate propranolol as an inpatient for close monitoring of neurovitals
- In general, PHACE workup performed prior to initiating propranolol
- Patients with arterial stenosis should also be followed by neurology
- Risks of strokes and migraines longer term
Case 2
Investigations

• *Chest CT*: patchy bilateral ground glass opacities in upper and lower lung zones.

• *Echocardiogram*: moderate dilation of left ventricle, moderate-severely diminished systolic function.
Investigations

• Positive ANA titer (1:640 homogenous)

• anti-Scl 70, anti-centromere and anti-RNA polymerase III antibodies were negative
This patient meets criteria for juvenile systemic sclerosis

True

False
This patient meets criteria for juvenile systemic sclerosis

True

False
Diagnosis: juvenile systemic sclerosis

- **Major criteria** (required)
  - Proximal sclerosis/induration of skin

- **Minor criteria (need 2/20)**
  - Sclerodactyly
  - Nailfold capillary abnormalities
  - Heart failure/arrhythmia
  - Pulmonary fibrosis
  - Positive antinuclear antibodies
Diagnosis: paraneoplastic scleroderma

First case of juvenile scleroderma developing *concurrently* with hepatoblastoma
Systemic sclerosis & cancer in adults

• Much higher incidence of malignancy than would be expected by chance

• *Increased cancer risk of:*
  – Lung
  – Liver
  – Bladder
  – Lymphoma and leukemia
Juvenile systemic sclerosis & cancer

• Only one previous report:
  – Teenager status-post chemotherapy for thymic carcinoma, developed scleroderma 9 months after completion of therapy
  – No autoantibodies reported

Pediatric hepatoblastoma

• Incidence
  – 1-5 cases/million children
  – 1-4% of all solid pediatric tumors
  – 95% occur in children < 4 years old

• Presentation
  – Failure to thrive/weight loss
  – Rapidly enlarging abdominal mass
Proposed mechanisms for paraneoplastic scleroderma

- Tumor derived growth factors, cytokines, chemokines
  - TGF- Beta1
- Autoantibodies triggered by abnormal tumor
  - 3+ POLR3A gene mutations identified
- Cancer and scleroderma both triggered by an exogenous stimuli such as virus or toxin
Case 3
History

• 2 month old male

• admitted with fever, decreased urine output, tachycardia, purulent umbilical drainage

• blood cultures grew *enterococcus faecalis* and *staph aureus*

• prior to admission his PCP diagnosed eczema due to a scaly rash, believed to be due to a milk allergy
Investigations

- WBC: 49 (6-14 K/uL)
- eosinophils: 10.8
- elevated IgE: 2339
- IgG, IgM, IgA: low
- absence of CD19 positive B cells
- absence of CD45RA cells
- TRECS (T-cell receptor excision circles) absent
Investigations

- due to sepsis, hypogammaglobulinemia, absence of B cells and TRECS:
  - concern for severe combined immunodeficiency
  - complete gene panel sent to evaluate for SCID
Genetic testing

- positive for RAG 2 mutation
- consistent with diagnosis of Omenn syndrome
Omenn syndrome

- deficiency of RAG

- *Recombination Activating Gene* proteins

- mediate DNA double strand breaks that allow immunoglobulin diversity

- T cell dysregulation with humoral and cellular defects
Omenn syndrome

- 98% show extensive cutaneous inflammation
- hepatosplenomegaly
- lymphadenopathy
- alopecia
- eosinophilia
- high serum IgE
Infantile Erythroderma Treatment

• wet wraps

• topical triamcinolone 0.1%

• topical petrolatum
Treatment: Omenn syndrome

- hematopoietic stem cell transplant

- received unrelated bone marrow transplant from a 10/10 unrelated male donor
Case 4
NICU consult

• 32 week GA female infant
• birthweight 1170 grams
• born with thick, dry, grey-colored scales all over
• no collodion membrane
What is your diagnosis?

A. KID syndrome
B. Ichthyosis Prematurity Syndrome
C. Lamellar Ichthyosis
D. Sjogren- Larson syndrome
What is your diagnosis?

A. KID syndrome
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Further investigation

- no ectropion or eclabium
- normal eye exam
- mild conductive hearing loss due to scaling within ear canals
- scales became more plate-like and hyperkeratotic over the next few days, but then less obvious
Further investigation

• karyotype 46 XX, no abnormalities on FISH
  • hematopathology microscopic exam unremarkable:
    • normochromic RBCs
    • normal platelets
    • monocytes without prominent vacuolization of WBCs
  • an ichthyosis panel was sent
Genetic testing

• positive for *ABCA12 heterozygous mutation*

• consistent with autosomal recessive congenital ichthyosis - lamellar ichthyosis

• unusual to be born without a collodion membrane
Lamellar ichthyosis

- type of autosomal recessive congenital ichthyosis (ARCI)
- about 5% have mutations in ABCA12
- other mutations: TGM1, ALOXE3, ALOX12B, CERS3, CYP4F22, NIPAL4/ICHTHYIN and PNPLA1
- usually born with collodion membrane
- phenotype varies from ectropion, eclabium, to milder scaling
KID syndrome

• Keratitis Ichthyosis Deafness Syndrome

• Autosomal dominant, GJB2 gene encoding connexin 26

• congenital deafness, nail dystrophy, hypotrichosis, natal teeth and progressive keratitis
Ichthyosis Prematurity Syndrome

- autosomal recessive
- mutations in FATP4
- typically premature infants at 30-34 weeks similar to our patient
- significant skin improvement over time to mild folliculocentric ichthyosis
Ichthyosis: NICU Management

- 70% humidified incubator
- Application of petroleum jelly q.i.d
- Dilute bleach baths to prevent infection
- Keep eyes lubricated to prevent keratitis
Case 5
Case 5

• 11 day old term infant
• blue nodules on skin
• several present at birth
• developing new lesions
Case 5

- normal pregnancy & delivery
- normal CBC
- no fever
- feeding well
Diagnosis?

a. leukemia cutis
b. neuroblastoma
c. langerhans cell histiocytosis
d. neonatal lupus
e. cytomegalovirus infection
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Congenital Leukemia Cutis

- Bone marrow biopsy showed monocytic myeloid lines
- Acute Myeloid Leukemia
- MLL (mixed lineage leukemia) gene rearrangement
Leukemia Cutis

- 60% of patients with congenital leukemia
- skin lesions may be only sign “aleukemia cutis”
- this baby had a normal CBC
- tends to have poor prognosis
Congenital leukemia

- rare: 4.7 cases/million births
- <1% of pediatric leukemia cases
- MLL gene (11q23) seen in 24% of cases of congenital AML
Treatment

• treatment protocol per COG AAML1031:

• cytarabine, daunorubicin, etoposide, and study drug bortezomib

• off chemotherapy and doing well