The Disappearing Rash: Catch Me if You Can! Incontinentia Pigmenti

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History of Presenting Illness

- Patient presented at birth on 6/26/16 with Rash on all 4 extremities seen by nursing staff at time of delivery.

- At delivery, via C-section, the baby had APGARS of 9 and 9. Patient was monitored in the NICU for 2 days due to possible exposure to ESBL E. Coli. She received 2 days of meropenum.
OB History

- Mother had uneventful pregnancy with good prenatal care until the 38th week of gestation when she was diagnosed with cystitis and pyelonephritis caused by ESBL E. coli. Treated with meropenem for 5 days until spontaneous rupture of membranes.
- Placental sample was sent and returned as chorioamnionitis.
Mother of baby has history of blindness in left eye of unknown cause. On ophthalmic examination there is retinal detachment and cataract noted in the left eye. She has normal vision in the right eye.
- **PMH, Surgical History, Allergies:** Negative
- **Social history:** No maternal alcohol, smoking, illicit drug use. No occupational exposures.
Physical Examination

- **Vitals:** Temp: 36.6, HR 127, RR 38, SpO2 99%
- **General:** Healthy appearing, vigorous infant with strong cry
- **CVS:** Regular rate and rhythm, no murmurs, rubs, gallops
- **Neurological:** Easily aroused, good symmetric tone and strength
- **Skin:** Scattered small bullous lesions on both inner thighs, forearms, knees and dorsal aspect of hands.
Differential Diagnosis

- Neonatal Herpes Simplex
- Epidermolysis Bullosa
- Neonatal Pemphigus Vulgaris
- Staphylococcus Scalded Skin Syndrome (SSSS)
- Sucking Blisters
- Erythema Toxicum Neonatorum
Neonatal Herpes Simplex

- Mostly transferred from mother at intrapartum period, but possibly in utero as well.
- Can cause microcephaly, chorioretinitis, hydrocephalus, vesicular skin lesions.
- Few different manifestations:
  1) skin, mouth and eye
  2) encephalitis
  3) disseminated disease
- Complications include: seizures, psychomotor retardation, spasticity, blindness, learning disabilities, death.
Epidermolysis Bullosa

- Blisters occur shortly after birth
- They usually form where there is friction or trauma
- The blistering can involve dermis and mucosal surfaces
- Mild forms can have no scarring.
- Severe forms can cause severe blistering with scarring, contractures, esophageal strictures, squamous cell carcinoma
Neonatal Pemphigus Vulgaris

- Autoimmune condition caused by transfer of maternal IgG autoantibodies to desmoglein 3 when mother has pemphigus
- Can cause transient flaccid blisters and erosions on skin and mucous membranes
- Usually never progresses past the neonatal period
Staphylococcus Scalded Skin Syndrome (SSSS)

- Caused by epidermolytic toxin caused by Staph aureus
- Happens first 2-30 days of life
- Rash starts as erythema that progresses to blisters that easily rupture → denuded skin
- Systemic symptoms: fever, lethargy, poor feeding
- Can lead to decreased thermoregulation, abnormal electrolytes, secondary infection
- Treat with antibiotics
Sucking Blisters

- Vigorous sucking on affected part in utero
- 0.5-2cm bullae mostly seen on fingers, thumbs, wrist, lips, radial forearm
- Spontaneous resolution
Erythema Toxicum Neonatorum

- Most common transient rash in healthy neonates
- Small erythematous macules with or without papules
- Starts at 1-3 days of life
- Spontaneously resolves within 3 days
But in this case ...
Incontinentia Pigmenti

- **Small** blisters present on lower extremities. Also, there were areas of hyperpigmentation along the **lines of Blaschko** where previous healed blisters were present in a **whorled pattern**.

- Dermatology consult was obtained

- **The clinical diagnosis of Incontinentia Pigmenti was made**

- Blood test was sent to confirm the diagnosis
Epidemiology

- Prevalence 1/40,000 – 50,000. **As of 2015, 1200 cases are reported.**
- Caucasians > African, Asians
- **Predominantly Females are affected. 20 males in literature**
- Males typically do not survive past the first few months gestation (except if XXY (Klinefelter syndrome) or mosaicism)
- Patients will develop symptoms in the first weeks of life 90% of the time
Genetics

- Inherited in a X-linked Dominant pattern.
- IKBKG gene mutations present in 85% of patients.
- Penetrance very high and most will exhibit the phenotype in early life.
- Expressivity is highly variable. Symptoms can range from near asymptomatic to fatal abnormalities.
Clinical Course

**Rash**

- 4 stages of evolution:
  - **Stage 1: Bullous stage**
    - Blistering-like eruptions on trunk and extremities
    - Appear within first 6 weeks and can be present at birth and disappear by 18 months
  - **Stage 2: Verrucous stage**
    - Hypertrophic warty rash on extremities and trunk
    - Usually appears within first few months of life and lasts for a few months.
  - **Stage 3: Hyperpigmentation stage**
    - Macular grey pigmentation in a swirled pattern
    - Usually starts at 6 months and not present at birth. It can present into adulthood
  - **Stage 4: Atretic stage**
    - Linear hypopigmentation more on extremities.
    - Not all have this
Extracutaneous Manifestations

Ocular

- 35-40% of patients; 20% experience significant vision loss.
- **Retinal:** All mechanisms can lead to retinal detachment.
- **Non-retinal:** Can include cataracts, uveitis, strabismus, optic atrophy, nystagmus, astigmatism and possibly pthisis bulbi.
Extracutaneous Manifestations

**CNS**
- Abnormalities have been noted in up to 30% of patients
- **Seizures:**
  - Range from single episode to lifetime epilepsy
- **Intellectual delay:**
  - Intellectual disability and developmental delays reported in ~25% of patients.
- **Hemorrhagic stroke:**
  - Reported in 1-2% which is fatal. Usually in first few months.

**Cardiovascular**
- Increased chances of structural heart disease
- Increased incidence of pulmonary hypertension.
Extracutaneous Manifestations

Teeth
- microdontia
- hypodontia
- abnormally shaped teeth (coned shape)

Hair
- alopecia usually at site of rash, but also on scalp
Follow up and Testing

**Skin, Nails**
- Dermatology referral
- Mainly for diagnosis
- Follow up as needed
- No treatment for any of the skin lesions other than symptomatic treatment as needed

**Teeth**
- Pediatric dentist referral
- At 6 months of age or when there is tooth eruption
- Dental implants may be placed
- If delayed eruption may benefit from nutritionist
Follow up and Testing

**Neurological**
- Pediatric Neurology referral
- Monitor for seizures, developmental delays
- Schedule
  - every 6 months for the first 2 years
  - After the first 2 years there will be yearly follow ups until age 6
  - Then as needed
- If seizures
  - MRI, EEG
- If developmental delay
  - Early intervention
  - special education
  - speech therapy
**Follow up and Testing**

**Ophthalmic**
- Pediatric Ophthalmology referral
- Monitor of retinal and non-retinal changes
- Schedule
  - **monthly dilated eye exams** for first 4 months
  - then every 3 months until 1 year of age
  - every 6 months between 1 and 3 years
  - then yearly thereafter
- Recommended that **intravenous fluorescence angiography** is completed at ~6 months age
- If changes are seen in the retina, treatment should be aggressive using **cryotherapy and/or laser photocoagulation**
Follow up and Testing

**Cardiovascular**
- Evaluate for structural heart disease of pulmonary hypertension
- Transthoracic Echocardiogram required
- Pediatric cardiology referral may or may not be required
Teaching Points

1) Newborn blisters may not be normal. Be suspicious of rare disorders.

2) Incontinentia Pigmenti is a multiorgan systemic disorder that requires a multidisciplinary team.

3) Strict follow up schedule is required for prevention of sequelae.
VisualDx.com


- NIH, US National Library of Medicine, Genetics Home Reference, Lister Hill National Center for Biomedical Communications Web: January 20, 2017


