Alabama Begins Newborn Screening for SCID

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What is Severe Combined Immune Deficiency (SCID)?

- A severe defect in adaptive immunity caused by essentially absent T cell function
- B cell function (antibody production) is also severely impaired even if the defect only directly affects the T cell compartment

Case Presentation:

- A 4.0 kg full-term male neonate has an uneventful delivery and perinatal course
- Two weeks after delivery, the mother notices a generalized erythematous maculopapular rash and the infant develops diarrhea

Case Presentation:

- The pediatrician diagnoses a viral gastroenteritis and prescribes a temporary formula change
- The diarrhea and rash continue and three weeks later the infant develops a loose cough and mucopurulent rhinorrhea
- In the office he is tachypneic with diffuse rales and oximetry reveals 89% saturations on room air

Case Presentation:

- He is referred for admission
- Two days after admission his respiratory status deteriorates and he is transferred to PICU
- Physical exam discloses bilateral otitis media
- The tonsils are small and no cervical adenopathy can be appreciated
- Thrush and a Candida diaper dermatitis are present

Common Features of Severe Combined Immunodeficiency

- Failure to thrive
- Onset of infections in the neonatal period
- Opportunistic infections
- Chronic or recurrent thrush
- Chronic rashes
- Chronic or recurrent diarrhea
- Paucity of lymphoid tissue

SCID Common Laboratory Features

- Low lymphocyte count (usually)
  - Low or absent T cells and low T-cell Receptor Excision Circles (TRECs)
  - Often low or absent B cells
- Low serum immunoglobulin levels
- Absent mitogen responses
- Absent antibody responses to immunizations

Treatment of Confirmed SCID

- Bone marrow transplantation, preferably from a histocompatible sibling
- Gene therapy (?)

History of Newborn Screening for SCID

- 1963: Initial population-based screening begins for PKU
- 2008: First state to initiate screening for SCID: Wisconsin
- 2010: SCID added to nationally recommended uniform panel for newborn screened disorders

History of Newborn Screening for SCID

- 2014: First commercial assay marketed for SCID screening
- 2015 status: 23 states, District of Columbia, Navaho nation include SCID in their screening panel

How Cost-Effective is Newborn Screening for SCID?

- Data still inconclusive but generally favor at least neutral cost:
  - $4.25 per test x 58,000 births annually in Alabama = $246,500
  - Expected patients detected annually in Alabama: 1

Modell et al 2014

How Cost-Effective is Newborn Screening for SCID?

- Cost of transplant + 5 years transplant costs for a patient diagnosed at ≤ 3.5 months estimated at $120,000 + $200,000 respectively (Hospital Cost and Utilization Project (AHRQ) and CMMS Hospital Accounting Records 2010)

Modell et al 2014

How Cost-Effective is Newborn Screening for SCID?

- Cost of treatment/transplant of an infant diagnosed after 3.5 months of age estimated at least $2,000,000

Modell et al 2014

Screening Sensitivity and Specificity: The Wisconsin Experience

- 207,696 infants screened in the first three years
- 0.19% required rescreening because of prematurity or poor sample quality
- 72 classified abnormal (0.035%) and underwent flow cytometry testing
- Of these, 38 ultimately proved normal (false positive rate 0.18%, specificity 99.98%)

Verbsky & Routes 2014

Summary

- Newborn screening for SCID is practical and cost-effective.
- Problems remain – screening does not detect all types of SCID and does not cover severe B cell, phagocyte, or complement deficiencies.
- Timeline should permit initial screening to begin in Alabama by the end of 2016