Hemoglobinopathies in Pregnancy

Pregnancy ECHO

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Hemoglobin structure

- 4 interlocking polypeptide chains with attached heme molecules
  - Hemoglobin A = 2 alpha + 2 beta
  - Hemoglobin F = 2 alpha + 2 gamma
  - Hemoglobin A₂ = 2 alpha + 2 delta

- Hemoglobinopathies = single-gene disorders
  - Structural hemoglobin variants
  - Thalassemias
Sickle cell disease – pathophysiology

• A group of autosomal recessive disorders of beta globin structure
  • Hb S
  • Hb C
• Under conditions of decreased oxygen tension, red blood cells become distorted
  • Vaso-occlusion
  • Hemolysis
Sickle cell disease – complications

- **Pain**: distinguish acute painful episode from life-threatening crisis
- **Infection**: bacteremia, meningitis, pneumonia
- **Multiorgan failure**: requires prompt exchange transfusion
- **Anemia**: chronic compensated hemolysis, crises
- **Neurologic**: stroke, TIA, epilepsy, PRES
- **Pulmonary**: acute chest syndrome, pulmonary hypertension
- **Renal**: chronic kidney disease, hypertension, renal infarct
- **Skeletal**: dactylitis, osteoporosis, osteomyelitis, avascular necrosis
- **Cardiac**: cardiomyopathy, myocardial infarction, dysrhythmia
- **Hepatobiliary**: acute ischemia, transfusional iron overload
- **Pregnancy**: IUGR, IUFD, preeclampsia
Thalassemias

• Reduced synthesis of globin chains* leading to microcytic anemia
• Classified according to globin chain affected
  • Alpha
  • Beta
• Different molecular mechanisms arose in different parts of the world

*Can also have structural changes in alpha globin chains (Hb Constant Spring, Hb Qong Sze), but these are much less common.
Alpha thalassemia

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<th>Condition</th>
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<th>Functional genes</th>
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<td>Alpha-thal trait</td>
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Beta thalassemia

• Mutation in beta globin gene causing either absent or deficient beta chain production
• Heterozygotes have beta-thalassemia minor
  • Often seen in association with Hb S
  • If no normal beta chain production, results in clinically severe sickle cell-beta thalassemia with no production of Hb A
• Homozygotes have either beta-thalassemia major or beta-thalassemia intermedia
  • Depends on the degree of beta chain production associated with the specific mutation
Genetic counseling

• Hemoglobinopathies are heritable conditions
  • Autosomal recessive, with some caveats
• Ethnicity not always a good predictor of risk
Screening

- Start with CBC/MCV
  - Part of routine prenatal labs
- Hemoglobin electrophoresis
  - African descent
  - Microcytic anemia with normal ferritin
  - Solubility testing inadequate
- DNA-based testing for alpha globin gene deletions
  - Microcytic anemia with normal ferritin AND normal hemoglobin electrophoresis
Summary of clinical pearls

- Offer carrier screening to individuals at increased risk for being hemoglobinopathy carriers
- CBC and hemoglobin electrophoresis are appropriate initial lab tests for hemoglobinopathy screening
  - NOT solubility testing
- Offer genetic counseling to couples at risk for having a child with sickle cell disease or thalassemia
- Pregnant women with sickle cell disease or thalassemia should be co-managed with hematology and MFM
Questions?