Hemophilia A (F8)

“Classic Hemophilia”

Hoa Mai
BIOC 118Q: “Genomics & Medicine”
Winter 2011
Hemophilia A

 Symptoms:

 - Slow blood clotting process
 - Prolonged, excessive bleeding after injury, surgery, or tooth extraction
 - Easy bruising
 - Spontaneous heavy bleeding
 - Hematuria
 - Internal bleeding in joints and muscles
  - Swelling, pain, and decreased function in joints
  - Hemorrhage in joints → necrosis, contractures, and neuropathy
Mendelian Sex-Linked Trait

- HEMA F8 gene
- Altered protein coagulation factor VIII
- X-linked, recessive trait

Heterozygous females: 1 normal allele can offset effects by altered allele.

Gene inherited from a carrier mother.

Males: 1 altered allele is enough to cause the disease

Primarily affects males $\rightarrow$ 1/1,500 male newborns
Traditional Diagnostic Methods

- Diagnosed when symptoms appeared (1st episode of unusual bleeding)
- Blood tests used to detect:
  - platelet count and function analysis
  - Bleeding time tests
  - Factor VIII assays
- Time of diagnosis depends on severity
  - Severe → first 2 years of life
  - Moderate → 5-6 years
  - Mild → later in life
Traditional Treatment

- mid-1960s: infusion of factor VIII concentrations from donor plasma

Complications:
- 1979 to 1985: many individuals contracted HIV and hepatitis C
- 30% develop alloimmune inhibitors for factor VIII
- infusion of processed plasma with recombinant Factor VIII concentrate
- Desmopressin (dDAVP): synthetic analog
Novel Diagnostics

- PCR or Southern blotting → an F8 intron 22-A or intro 1 in 50% of severe cases
- Others: large deletions, insertions, frameshift, nonsense and missense mutation
- Identification of the specific F8 mutation can determine severity and the likelihood of inhibitor development
- Genetic counseling
Novel Treatments

- 140 federally funded hemophilia treatment centers (HTCs)
- Prophylactic treatment
- Longer-acting factor VII concentrates still under clinical trials
- More research on immune tolerance therapy to avoid alloimmune inhibitors
- Use retroviral vector systems to insert Factor VIII gene into DNA of cells
- Clinical trials for gene replacement therapy has been discontinued
Sources

- NCBI

- Genetics Home Reference
  </ghr.nlm.nih.gov/condition/hemophilia>

- OMIM
  <www.omim.org/entry/306700>

- Images
  - Google.com