Gaucher Disease

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What is Gaucher Disease?

- Inherited disorder caused by a gene mutation
  - Autosomal recessive pattern
- Lacks enzyme called glucocerebrosidase
  - Needed to break down glucocerebroside
    - Fat build up in liver, spleen, and bone marrow
- Many types
- Possible link to Parkinson’s Disease
- Affects 1 in 100,000
Classical Diagnosis

- Blood test
  - enzyme activity
  - white blood cell count
- enlarged organs
  - spleen
  - liver
- Bone marrow test
  - Look for Gaucher cells
Gaucher: Type 1

- Also called non-neuronopathic Gaucher disease
  - Central nervous system usually not affected
- Symptoms appear anytime from childhood to adulthood
  - Symptoms include:
    - hepatosplenomegaly (enlargement of liver and spleen)
    - Anemia
    - Thrombocytopenia (decrease in blood platelets)
    - Lung disease
    - Bone abnormalities
- Range from mild to severe
More Types

TYPE 2

- neuronopathic form
  - Affects the central nervous system
- In addition to symptoms from type 1, type 2 also includes:
  - Seizures
  - Brain damage
  - Abnormal eye movements
- usually life-threatening medical problems
  - Start from infancy

TYPE 3

- Also a neuronopathic form
  - Affects nervous system
- Progresses more slowly than type 2
- Also has symptoms from type 1
More Types

PERINATAL LETHAL FORM

- Most severe type
- Life-threatening complications
  - Start before birth or in infancy
- Symptoms:
  - Hydrops fetalis: extensive swelling caused by fluid accumulation before birth
  - Ichthyosis: dry, scaly skin
  - Hepatosplenomegaly
  - Distinctive facial features
  - Severe neurological problems
- Most infants survive only a few days after birth

CARDIOVASCULAR TYPE

- Affects the heart
  - Causes heart valves to calcify
- People with this form also usually have:
  - splenomegaly
  - eye abnormalities
  - bone disease
Multisystem Involvement in Type 1 Gaucher Disease
Can Manifest at Any Age

- Pathological Fracture
- Hepatomegaly
- Collapsed Vertebrae
- Bone Pain and Bone Crisis
- Erlenmeyer Flask Deformity
- Splenomegaly
- Thrombocytopenia
- Anaemia
- Osteonecrosis
- Bone Marrow Infiltration
- Osteopenia
**Enzyme Replacement Therapy (ERT)**
- Consists of a modified form of the glucocerebrosidase enzyme -> given intravenously
  - stops and often reverses the symptoms
- Can also have symptomatic treatments if don’t take ERT
  - Such as splenectomy, transfusion of blood products, and analgesics for bone treatment
Substrate Reduction Therapy
- Treatment with N-butyldeoxynojirimycin (NB-DNJ) = an inhibitor of glucosylceramide synthase
  - Treatment over 24 months
  - decreased liver and spleen volumes

Bone Marrow Transplantation
- Gaucher cells disappeared from bone marrow
- Liver size back to normal
Gene Therapy (future)
- Introduction of GBA into hematopoietic stem cells
- Enzyme production does not appear to be sustained

Genetic counseling
- Targeted Mutation Analysis
  - Used to detect carriers in high risk populations (4 common mutations)
    - Can be insufficient

Sequence Analysis
- Nucleotide sequence is determined for a segment of DNA,
  - Done in the GBA coding
References