Tay-Sachs Disease

A Case Presentation

By Dana Neel

What is Tay-Sachs?

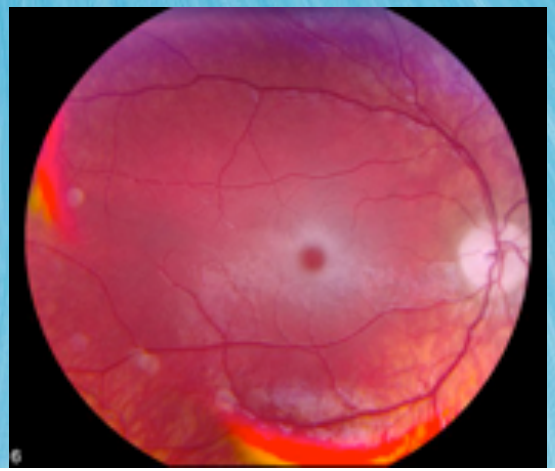
- Autosomal recessive lipid storage disorder
- Incidence high among Ashkanazi Jews, Cajuns, French Canadians
- Lack vital enzyme, ß-Hexosaminidase A (ß-Hex A)
  - Needed to break down lipid, GM2 ganglioside
- Leads to accumulation of GM2 ganglioside in neurons

Symptoms of Tay-Sachs

- Infants initially appear healthy; symptoms appear ~6 months of age
- Development begins to slow
- Loss of motor skills, mental functions
- Child becomes blind, deaf, paralyzed, mentally retarded, and non-responsive
- Fatal, usually by age 4

Classical Diagnosis

- Appearance of aforementioned symptoms
- "Cherry-red" spot on eyes, caused by lipid-laden ganglion cells
- Larger startle reflex to noise
- Before 1970, Tay-Sachs could not be diagnosed at birth



Classical Testing

- In 1969, researchers discovered the biochemical basis for the disease
- Michael Kaback of JHU created an enzyme assay to test for heterozygotes
  - Detects individuals with lower levels of Hex-A
- Can detect all mutations, but with some inconclusive results

Classical Treatment

- There is currently no treatment for Tay-Sachs disease
- Supportive treatment
  - Antiseizure medicine
  - Feeding tube
  - Proper nutrition, hydration

Genetic Testing

- Caused by mutations in both alleles of *HEXA* gene on chromosome 15. Exact location (15q23-q24) determined in 1990.
- PCR tests for actual mutations. Gives definite results, but only for known mutants.

Treatment

- All in experimental stages
- Gene therapy
  - Replace defective *HEXA* genes. Difficult to transport genes to neurons.
- Enzyme replacement therapy by replacing Hex-A.
  - Hex-A is too big to pass through the blood-brain barrier.
  - Neurons are unable to take up Hex-A because it is too big.

Prevention

- Prenatal diagnosis
  - Genetic testing by amniocentesis
- Embryo screening
  - Test embryo prior to *in vitro* fertilization
  - Select embryos without Tay-Sachs

Sources

- Genes and Disease Database
  - http://www.ncbi.nlm.nih.gov/books/bv.fcgi?highlight=tay-sachs&rid=gnd.section.238
- OMIM: Tay-Sachs Disease
  - http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=272800
- National Tay-Sachs and Allied Dieases Association
  - http://www.tay-sachs.org/taysachs.php
- National Institute of Neurological Disorders and Stroke
  - http://www.ninds.nih.gov/disorders/taysachs/taysachs.htm