Tay-Sachs Disease (TSD)

Case Presentation

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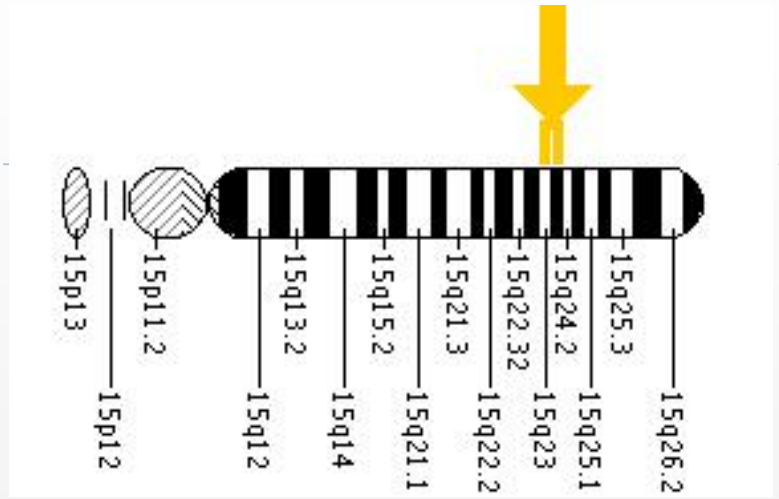
What is it?

- Autosomal recessive, progressive neurodegenerative disorder.



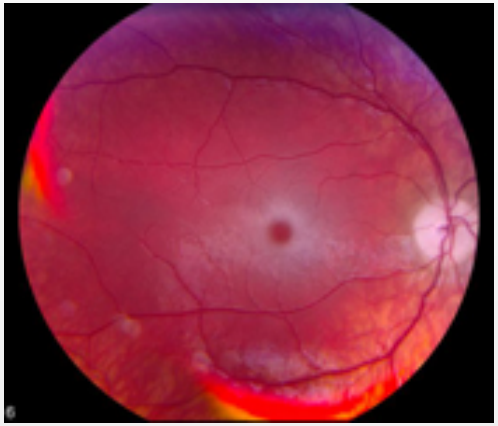
- Deficiency in alpha subunit of beta-hexosaminidase (HEX A) causes an accumulation of GM2 ganglioside.
- Most common among Ashkenazi Jews, but also more frequent among French Canadians of southeastern Quebec, Cajuns of southern Louisiana, and Old Order Amish in Pennsylvania
- Most common form is infantile Tay-Sachs Disease.

Symptoms of Tay-Sachs Disease

- Affected infants appear normal at birth.
- Motor weakness, myoclonic jerks, and exaggerated startle reaction to sharp noise begin at 3-6 months.
- From 6-10 months, stagnation/decline in motor skills and decreasing visual attentiveness associated with the 'cherry-red' spot.
- Seizures common by 12 months, enlargement of the head begins at 18 months.
- Death usually occurs by age two to four, usually from bronchopneumonia

Classical Diagnosis Methods

- A 'cherry-red' spot can be seen in the eye by funduscope due to lipid-laden ganglion cells.



- Presence of ballooned neurons in the central nervous system.
- Early, persistent extension response to sound, known as the "startle reaction"

Classical Treatment

- Treatment is supportive, providing adequate nutrition and hydration, manage infectious disease, protect the airway
- Seizure control can be done with conventional anticonvulsants.
- For adult-onset individuals, conventional antipsychotic or antidepressent therapy is used for psychiatric manifestations.
- Lithium salts and electroconvulsive therapy has been shown to be effective against psychotic depression.

Novel Diagnostics

- Carrier testing can be done by HEX A enzymatic and HEXA mutation analysis.
- Before population-based carrier screening, TSD occurred around one in 3600 Ashkenazi Jewish births (1 in 30 carriers). Genetic counseling and carrier screening programs have reduced this by over 90%.
- In other groups, the disease is about 100 times less common (so around 10% the number of carriers)

Novel Therapies

- Enzyme replacement in the central nervous system and neuronal-corrective gene therapy are only at the theoretical stage.
- Clinical trials with inhibitors of the biosynthesis of glycoshingolipids have been initiated.
- Purified enzyme replacement therapy, cellular infusions, and bone marrow transplants do not have evidence of benefits.

Sources

- Entrez Gene: HEXA hexosaminidase A (alpha polypeptide) [Homo sapiens]
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- Hexosaminidase A Deficiency – GeneReciews – NCBI Bookshelf
  - http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=tay-sachs
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  - http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=272800