Tay-Sachs disease

Tay-Sachs disease *(TSD, GM2 gangliosidosis)* is a rare autosomal recessive inherited disease. Its progress is usually early lethal.

Occurrence and heredity

This disease is rare in most populations, the exception being the Ashkenazi (Central European Jewish branch). This disease affects 1 in 3600[1] births in this population, every 30th[1] adult is heterozygous for the mutant allele.

Pathogenesis

The cause of the disease is a defect in the *HEXA* gene, which codes the lysosomal enzyme hexosaminidase-A. The role of the enzyme is to split ganglioside G_{M2} into smaller parts : ganglioside G_{M3} and N-Acetyl-D-galactosamine. Ganglioside G_{M2} is a complex of lipids that normally protects nerve cells and isolates them from surrounding stimuli, thus accelerating the transmission of nerve impulses. Hexosaminidase-A enables its dynamic recovery. The absence of the enzyme causes the accumulation of G_{M2} on the surface of nerve cells, blocking their functions and thus the gradual degeneration of the nervous system.

Clinical picture

Newborns are normal at birth, hypersensitivity to loud sounds appears during the first months of life. A red spot is formed on the retina (as a result of accumulation of gangliosides). These initial symptoms are often not registered by parents or doctors. Between six months and one year of life, gradual neurological degeneration occurs. Mental retardation, deafness, blindness and total loss of control of bodily functions (paralysis) develop. During the second year of life, individuals cease to be able to move, they suffer from frequent respiratory tract infections, which later develop into a chronic form. Death usually occurs during the third to fourth year of life.

Classification

- **Infantile TSD** appears between six months and four years of age and is fatal. This is the most common form of this disease, the clinical picture was described above.
- **Juvenile TSD** is the rarest form. It develops between the second and tenth year of life. Patients have impaired locomotor system, motor skills and cannot swallow (or with difficulty). The death of these patients occurs between the fifth and fifteenth year of life.
- **Adult (late) TSD** appears between 20–30th year of life. Individuals usually have poor locomotor functions, slow development and suffer from psychological disorders, the most common is schizophrenia. TSD at this time of life is not fatal. Disabled people are mostly confined to a wheelchair, mental disorders can be suppressed with medication, which allows them to lead a relatively normal life.

Diagnosis

Tay-Sachs disease is diagnosed using targeted molecular genetic diagnostics. The disease can be diagnosed as part of prenatal diagnosis from materials obtained by CVS or aminocentesis. After birth, targeted diagnostics from peripheral blood is performed.

There is also the possibility of pre-implantation genetic diagnosis, which is linked to in vitro fertilization, when we can examine the relevant gene in blastomeres taken from individual embryos. Subsequently, only embryos that are not homozygous for the Tay-Sachs disease gene are implanted.

Therapy

There is currently no effective therapy for this disease. Replacement treatment (delivery of a functional enzyme) is unfortunately not possible, because the enzyme does not pass through the blood-brain barrier.

Summary video

https://www.youtube.com/watch?v=2z3nSnBe8Vg

Links

Related articles

- Autosomal recessive inheritance

- Lysosomal Metabolism Disorders/Treatment
- Lipidosis
- Cherry spot

Used literature

- SNUSTAD, D. Peter – SIMMONS, Michael J. *Genetika.* 1. edition. Masarykova univerzita, 2009. ISBN 978-80-210-4852-2.

References

1.
    - SNUSTAD, D. Peter – SIMMONS, Michael J. *Genetika.* 1. edition. Masarykova univerzita, 2009. ISBN 978-80-210-4852-2.