Huntington's disease

Huntington's disease (HD - Huntington's Disease, also Huntington's chorea) is a disorder first described in 1872 by the American doctor *George Huntington*. It is a neurodegenerative autosomal dominantly inherited disease belonging to the polyglutamine disorders (see below). It has an incidence of 4–10 per 100,000. It manifests most often in middle age. Symptoms are dominated by motor impairment, personality changes, progressive dementia and in the end, death.

Genetics

HD is a disease with an autosomal dominant type of inheritance, but we can trace several special features in the family trees:

- HD is a typical **late onset** of the disease. Most carriers of the mutated allele become ill around the age of 40, but rarely, symptoms can appear at virtually any time (at 2 or 80).
- During the transmission of the disease in the family, the progression of the dynamic mutation can occur - i.e. the increase of the already pathological number of triplets. This phenomenon is called **anticipation**.

The disease is caused by a mutation in the HTT gene, which was discovered in 1993. It is an increased repeat of CAG triplets, which is the codon for glutamine (hence polyglutamine disorders). The gene encodes the **huntingtin protein**. The exact function of the protein is still unknown, it is predominantly expressed in the CNS. It interacts with a number of transcription factors, so its important role in the normal development of the CNS is likely, and its importance for the normal course of mitosis in the CNS has also been demonstrated. Normal individuals carry 9-35 CAG repeats in their gene, affected individuals have more than 40. The higher the number of repeats, the earlier the onset of the disease.

The expanded repetiton is inherited from the affected parent. During transmission, however, there is sometimes a further expansion of this repeat during meiosis. A situation may therefore arise when the parent has the number of repetitions at the upper limit of the norm (premutation), i.e. is healthy, but the offspring acquires an expanded allele, so that the disease breaks out in him. The expansion occurs more frequently in HD during male gametogenesis, which is why the severe, early-onset forms with repeat counts of 70–120 are inherited from the father.

New mutations can also appear - about 25% of patients have a negative family history.

Manifestations of the disease

HD is characterized by the **selective loss of neurons** in the basal ganglia, which are involved in the coordination of movements.

Therefore, patients suffer from: chorea - involuntary rapid movements that affect different parts of the body. Other parts of the brain are also affected, such as the cortex. Depression, psychosis, paranoia and progressive dementia appear. The disease lasts 10-30 years.

Causes of death include *aspiration pneumonia, falls, or suicide*.

Pathogenesis

The mechanism of neuronal damage is not entirely clear. Overloading of neurons by glutamate neurotransmission, reduction of antiapoptotic effects of normal huntingtin or mitochondrial dysfunction (patients have lower metabolic activity in the affected areas) are considered.

Therapy

There is currently no cure for HD. Substances that could have a neuroprotective effect due to the aforementioned pathogenetic mechanisms are being investigated. However, most of them did not yield significant results.

Transplantation of new sources of neurons looks promising. However, the fact that HD affects multiple areas of the brain is problematic, and there are also many ethical questions related to this topic.

Diagnostics

Direct **genetic testing** is available for the presence of a mutation in the relevant gene. It is performed for the purpose of confirming or excluding the disease, ascertaining the status of the patient at genetic risk and in prenatal or pre-implantation diagnosis.

Due to the lack of treatment, testing is associated with psychological and ethical problems - there is a risk of psychological traumatization of the patient, depression, and in extreme cases, even suicide. Therefore, the testing should be approached with caution and the patient should be carefully informed about all aspects of the testing.

Before a predictive (presymptomatic) molecular genetic examination for HD, a special protocol is followed, which, in addition to repeated consultations with a clinical geneticist, also includes neurological, psychiatric and psychological examinations. Examination of children and minors at risk based on the interest/request of their parents is inadmissible (preserving the right not to know).

Video

What is Huntington disease? Huntington disease is a type of autosomal dominant disorder involving a triplet repeat of CAG, leading to an abnormal protein that results in neuronal cell death, and various movement and cognitive-related symptoms. This video covers the pathophysiology, as well as major clinical signs and symptoms of Huntington disease.

Links

External links

- Huntingtonova choroba (česká wikipedie)
- Huntington's disease (anglická wikipedie)

References

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