Leucinosis

Leucinosis or **maple syrup urine disease** (MSUD) is a disease with **autosomal recessive inheritance**. The gene is located on 19q13.1-q13.2 (E1α), 6p21-p22 (E1β), 1p31 (E2), 7q31-q32 (E3). It is caused by a disorder in the processing of branched-chain amino acids (leucine, isoleucine and valine) due to a dehydrogenase deficiency of branched α-keto acids. Incidence: 1: 185,000 births (worldwide), at least **7 cases** are diagnosed in the Czech Republic. [1]

Patogenesis

It is caused by a **deficiency of branched-chain α-ketoacid dehydrogenase** (BCKD), a **multienzyme complex** loosely associated with the inner membranes of the mitochondria. In leucinosis, the branched-chain amino acids leucine, isoleucine and valine **cannot be** break down to their **α-keto acid derivatives**. Amino acids and related organic acids accumulate and lead to **severe toxicity**. MSUD is an organic aciduria. [1]

The organism is flooded with toxic metabolites at **each load** with an increased amount of branched-chain amino acids, for example when:

- normal weight loss in the neonatal period,
- breaking down of the child's body proteins during fever and starvation ,
- common infections,
- after surgery and in similar stressful situations.[1]

Klinical signs

Leucinosis most often manifests itself in newborns, some slower forms appear later, but usually by the second year of age.[1]

At birth, the children appear normal and the development of clinical symptoms begins between **4-7th day of life**. The first signs are **lethargy** and poor sucking, followed alternatively by hyper- or hypotonia, **irritability and dystonia** (reminiscent of boxing or cycling). **The smell of urine**, sweat, breath and earwax after maple syrup (caramel, dried pears, or maggi) is typical. The disease further progresses to **severe ketoacidosis, hyperammonaemia** with convulsions and coma (and without treatment to death due to cerebral edema). [1]

Screening

Since October 1, 2009, it has been a part of nationwide neonatal screening in the Czech Republic. Elevated leucine / isoleucine levels indicate the presence of MSUD. Leucinosis screening is characterized by a relatively high number of false-positive findings because it is not possible to distinguish leucine / isoleucine from hydroxyproline when screened by tandem mass spectrometry. Confirmation of the diagnosis is possible by analysis of amino acids in plasma and urine - in leucinosis, plasma analysis shows elevated levels of leucine, isoleucine, **alloisoleucine** and valine (branched chain amino acids) and analysis of organic acids in urine of abnormal branched chain hydroxy- and keto acids; for hydroxyprolinemia, the analysis will only show an increased level of hydroxyproline. [1]

Therapy

Diet with **reduced leucine** and **limited valine and isoleucine** (paid for by the patient) and special nutrition containing amino acids necessary for the growth and healthy development of the patient (fully or partially covered by public health insurance). In any disease, **prevent starvation** and reduce protein intake - replace energy in the form of glucose.[1] Intensive treatment of acute metabolic episodes (eg elimination methods).

Prognosis

Course of the disease without treatment: The classic untreated form progresses to coma and death. The milder form develops neurological impairment (mental retardation, hyperactivity) and attacks of metabolic decompensation. Intermittent patients have a normal development with occasional episodes of metabolic decompensation. Chronically higher levels of branched-chain amino acids cause demyelination even without metabolic decompensation. [1]

Course of the disease with treatment: Age at diagnosis and initiation of treatment is the most important factor in the long-term development of the patient. In patients with the classic form, whose treatment is started after the 14th day of life, a completely normal intellect is rarely achieved. The timeliness of treatment improves its outcome, but complications must be taken into account. Even with proper treatment, the patient may die of cerebral edema in acute decompensation. The neurological consequences of the disease are different, depending on the intensity of metabolic episodes. [1]

Examination of relatives

In other children who have the same father and mother as the affected child, the risk of this disease is 1/4 (25%). Prenatal diagnosis is possible by enzyme examination or, in the case of a known mutation, by molecular examination.[1]

Links

Related articles

- Neonatal screening
- Isovaleric aciduria
- Glutaric aciduria

References

1.

External links

- OMIM #248600 (https://omim.org/entry/231670)

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