Inherited metabolic disorders of complex molecules

Inherited metabolic disorders of complex molecules [1] [2] are genetic disorders of the synthesis, transport or catabolism of macromolecules. They affect organelles, in which they are synthesized or degraded, such as lysosomes and peroxisomes, or transport proteins, and then manifest as disorders of cellular transport and processing. These are often **storage** diseases. Macromolecules whose metabolism may be affected include[1] sphingolipids, glycosaminoglycans (mucopolysaccharides), oligosaccharides, myelin, very long chain fatty acids, ether phospholipids (plasmalogens), phytanate and others.

Pathogenesis

A disorder in the catabolism of a complex molecule leads to its **accumulation**, typically **in a cellular organelle**, in which the enzyme responsible for the disease would otherwise be located, which is manifested mainly by a **membrane abnormality**.

For example, a deficiency of the acid beta-glucosidase enzyme in Gaucher's disease as a result of a mutation in the GBA gene leads to accumulation of glucosylceramide, which then manifests as visceral, hematological and bone impairment.[1]

A disorder in the synthesis of a complex molecule leads to its deficiency, and thus to the absence of its function.

Symptoms

The disease has a slow course, the prodromal phase lasts for months, years to decades[2]. The clinical manifestations of these diseases differ significantly from the symptoms of inherited small molecule metabolic disorders; they are permanent, progressive, independent of diet or concomitant diseases (fever and related catabolic conditions have no effect). They often affect more than one organ at a time, and symptoms include, for example, psychomotor retardation, facial dysmorphia, organomegaly, skeletal disorders, cardiovascular system, sight hearing.

The differential diagnosis includes some similar symtoms, such as hematooncological or other cancers, chromosomal aberrations, or neurodegeneraticve diseases of unclear etiology[2].

Therapy

As with other inherited metabolic disorders, there is currently no permanent causal treatment (gene therapy), but for some, depending on their nature, there are approaches that at least temporarily eliminate the cause, or at least slow the progression or alleviate the consequences of the disease[1]:

- **enzyme replacement therapy** (*enzyme replacement therapy*, ERT) – eg. in type I Gaucher disease, Fabry disease or Pompe disease
- **substrate reduction therapy** (*substrate reduction therapy*, SRT) – eg. in Gaucher disease
- **organ transplantation** – eg. allogeneic bone marrow transplantation in some cases in Krabbe disease

In most cases, however, treatment is only symptomatological (eg. treatment of seizures in *GM2-gangliosidosis*[1]).

Links

related articles

- Inherited metabolic disorders
- Inherited metabolic disorders of small molecules

Source

- S laskavým svolením použity materiály doc. MUDr. Viktora Kožicha, CSc.
- MUDr. M. Hřebíček, PhD.: Dědičné poruchy lysosomů a peroxisomů., 8.10.2010 [přednáška z patobiochemie, 1. LF UK]

Reference

1.
2.

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inherited metabolic disorders. 4th edition. Prague: Triton, 2008. 607 pp. ISBN 978-80-7387-096-6 .
- KOŽICH, Viktor and Jiří ZEMAN. Hereditary metabolic disorders in pediatrics. Postgraduate Medicine [online] . 2010, vol. 12, vol. 7, pp. 793–799, also available from < https://zdravi.euro.cz/ >. ISSN 1214-7664.

Kategorie:Patologie Kategorie:Patobiochemie

- ws: Dědičné metabolické poruchy komplexních molekul