Inherited metabolic disorders of small molecules

Inherited metabolic disorders of small molecule [1] [2] are genetic metabolic disorders leading to acute or progressive **intoxication**, caused by the accumulation of toxic substances **before the metabolic block**, or **acute deficiency** of intermediates of energy metabolism, caused by the lack of products **behind the metabolic block**.

They include:

- Aino acid catabolism disorders (phenylketouria, homocystinuria, tyrosinemia, maple syrup disease);
- certain organic aciduria (methylmalonic aciduria, propionic aciduria, isovaleric aciduria);
- carbohydrate intolerance (galactosemia, inherited fructose intolerance);
- fatty acid metabolism disorders;
- urea cycle disorders;
- porphyria;
- metal intoxication (Menkes'disease, Wilson's disease, hemochromatosis);
- disorders of neurotransmitter synthesis and degradation (GABA, glycine, monoamines);
- inherited disorders of amino acid synthesis (serine, glutamine, proline).

Pathogenesis

The presence of a metabolic block casues **the accumulation of toxic substances**, most often metabolites of proteins, carbohydrates or fatty acids supplied by food, which do not have or cannot use an alternative metabolic pathway in a given situation. In other cases, after starvation, **metabolites are missing**, that the individual is unable to synthesize on his own due to the enzyme deficiency and only accepts them through food.

Symptoms

The prodromal phase is typically short, with symptoms often appearing in young children or infants, but not interfering with embryonic or fetal development. They appear as acute metabolic attacks following food intake or, on the contrary, starvation, they are exacerbated by fever, intercurrent illnesses, intensive catabolism. Manifestations of intoxication are usually **acute** (disorders of consciousness to coma, acetonemic vomiting, liver failure, thrombolic complications, metabolic acidosis) or **chronic** (failure to thrive, delayed psychomotor development, cardiomyopathy, visual disturbances), unless the accumulating metabolite is toxic enough to be acute. Attacks recur in many cases depending on the circumstances that tend to cause them (ingestion of food, infection, starvation, muscle strain).

The differential diagnosis includes sepsis, intoxication or meningoencephalitis[1].

Therapy

For the treatment of acute causes of symptoms:

- Urgent removal of toxins in the form of diet, extracorporeal elimination methods, „cleansing“ drugs (carnitine, sodium benzoate, penicillamine and others).
- Urgent supplementation of missing intermediates of energy metabolism (glucose), either orally or parenterally with constant vomiting.

For long-term treatment:

- **Diet adjustment** (restriction of intake of substances that the patient cannot process, supplementation of substances that the patient cannot produce)
- In some cases, the administration of vitamins involved in a given enzymetiv reaction as cofactors may be beneficial[1]

Links

related articles

- Inherited metabolic disorders
- Inherited metabolic disorders of complex molecules

Reference

1.
2.

KOŽICH, Viktor a Jiří ZEMAN. Dědičné metabolické poruchy v pediatrii. Postgraduální medicína [online]. 2010, roč. 12, vol. 7, s. 793–799, dostupné také z <https://zdravi.euro.cz/>. ISSN 1214-7664.

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- ws:Dědičné metabolické poruchy malých molekul