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Ethylmalonic encephalopathy an early-onset, progressive inborn disorder of sulfide metabolism – report of first Austrian case

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Einleitung: Ethylmalonic encephalopathy (EE) is a severe, early-onset, progressive inborn disorder of sulfide metabolism in the mitochondria. The causative gene is named ETHE1, which encodes for a protein (ETHE1 enzyme) that is crucial for the breakdown of sulfide (H2S) in mitochondria. Sulfide is produced in the body´s tissues as part of normal cell processes. At low levels sulfide is critical for normal cell functioning. At higher levels this molecule becomes toxic, interfering with numerous cell activities. The main problem is the interference with mitochondrial energy production by blocking cytochrome C oxidase (COX). H2S and its metabolites have very strong vasoactive and vasotoxic effects, causing a widespread multisystem endothelial vascular damage mainly located in the brain, skin, muscle and gastrointestinal tract. Prevalence of ethylmalonic encephalopathy is unknown, to our knowledge less than 100 cases worldwide are reported to date (2022).
Ergebnisse: The boy is the first child of Austrian non-consanguineous parents. Pregnancy and birth were uneventful. First signs of developmental delay were seen at age 5 to 6 months. An evaluation for muscular hypotonia (exclusion of spinal muscular atrophy) at that age was negative. First symptoms suggestive of EE were petechiae and reduced level of consciousness at the age of 7 months, in the course of an acute gastroenteritis. In the past medical history, a developmental standstill since the age of 5 to 6 months and a tendency to develop hematomas could be objectified.
The combination of developmental standstill/delay, truncal hypotonia, spastic posture of feet, petechiae and lactic acidosis, led to suspicion of EE, which was confirmed by a marked excretion of ethylmalonic acid in the analysis of organic acids in urine and later also genetically by a homozygous mutation in ETHE1 gene.
Schlussfolgerungen/Diskussion: We report the first known Austrian patient with ethylmalonic aciduria. However rare, it is important to exclude EE in the evaluation of muscular hypotonia / developmental delay, which is easily achieved through the analysis of urinary organic acids.