Eswaran V.S.

BIOCHEMICAL DIFFERENTIAL DIAGNOSIS OF FATTY ACID METABOLIC DISORDERS

Tutor: associate professor Khotko E.A.
Department of Biological Chemistry
Belarusian State Medical University, Minsk

Biochemical differential diagnostic methodologies are important to understand the disease caused as it outlines the specific characteristic of that disease through biochemical experiments. This document details the differential diagnosis for four inherited metabolic disorders: Sandhoff's disease, Wolman's disease, Refsum's disease, and Medium-chain acyl-CoA dehydrogenase MCAD deficiency.

Sandhoff's disease is caused by the mutation in the gene located in chromosome 5 resulting the deficiency of hexoaminidase A and B. The fluorimetric method which has the ability to detect these enzymes activity is used to diagnose this disease. The accumulation of these enzymes causes cherry red spots due to the damage of neurons leading to neuroregression.

Wolman's disease and Refsum's disease is caused by the mutation in the gene located in chromosome 10. The cause of Wolman's disease is the deficiency of enzyme lysosomal acid lipase (LAL) that can be detected clinically through cell-free acid lipase activity assay. Absence of lysosomal acid lipase(LAL) results in fat accumulation in the liver leading to hepatosplenomegaly. The hallmark feature of the Refsum's disease is the significant elevation of the plasma phytanic acid levels which can exceed to 200 μmol/L, is measured by Gas Chromatography-Mass Spectrometry (GC-MS).The phytanic acid is identified through it's unique fragmentation pattern allowing its quantification in μmol/L. Presence of this acid results in the olfactory nerve damage causing anosmia in patients.

Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency is caused by the deficiency of mitochondrial medium-chain acyl-CoA dehydrogenase enzyme due to mutation in the gene in chromosome 1. The biochemical diagnosis of this disorder involves acylcarnitine profiling from dried blood spot samples, the extracted samples contain stable isotope-labelled internal standard which is subsequently analyzed by Tandem Mass Spectrometry through flow injection method. This detects specific charged ions corresponding to acylcarnitines, with elevated levels of C6, C8, C10, and C10:1. Acylcarnitines serves as diagnostic markers for Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency. This enzyme deficiency disrupts normal fatty acid metabolism leading to hypoketotic hypoglycemia and clinical manifestations such as lethargy and vomiting.

Together, these diagnostic approaches enables early and precise diagnosis of a disease which is essential for patient care and treatment.