Maple syrup urine disease

MAPLE SYRUP URINE DISEASE An inherited disorder of amino acid metabolism Maple syrup urine disease is an autosomal recessive inborn error due to defective activity of branched-chain -ketoacid dehydrogenase complex (Fauci et al, 2008: 2472; Leucine mildly to moderately elevated). This enzyme participates in the metabolism of branched-chain amino acids (BCAAs) namely leucine, isoleucine and valine. These amino acids have carbon arrangements not synthesized naturally by humans thus these are included in the list of essential amino acids. Because they are not fully metabolized, this leads to accumulation of these amino acids and their corresponding -ketoacids (Laygo, 2007: 28).

Branched-chain -ketoacid dehydrogenase complex (BCKD)

This enzyme complex is composed of three catalytic components E1, E2, and E3 and two regulatory enzymes, BCKD phosphatase and BCKD kinase. The E1 component is further divided into two subunits, E1 and E1 (Bodamer, 2008). The defect in maple syrup urine disease lies in the E1, E1, E2, and E3 components (Fauci et al, 2008: 2472). In addition, E3 component is also associated with pyruvate dehydrogenase and -ketoglutarate dehydrogenase, thus, this defect in BCKD with specific mutation in E3 causes additional deficit in pyruvate and -ketoglutarate dehydrogenases (Bodamer, 2008).

The Metabolic Pathway

The catabolism of BCAAs involves the same enzymes in the first two steps (Laygo, 2007: 28). The first enzyme utilized is BCAA aminotransferase which converts leucine, isoleucine and valine to their -ketoacids: -ketoisocaproic acid, -keto--methylvaleric acid, and -ketoisovaleric acid respectively. The branched-chain -ketoacid dehydrogenase complex catalyzes the decarboxylation of these -ketoacids so that they are degraded to short fatty

acids, isovaleryl-CoA, -methylbutyryl-CoA and isobutyryl-CoA (Leucine mildly to moderately elevated). Further metabolism should yield acetyl-CoA, acetoacetate, and succinyl-CoA (Bodamer, 2008).

Clinical Findings

Among the clinical manifestations of maple syrup urine disease are lethargy, vomiting, encephalopathy, seizures, mental retardation, " maple syrup" odor and protein intolerance (Fauci, 2008). As mentioned earlier, the result of impaired metabolism is the accumulation of leucine, isoleucine, and valine and their -ketoacids. These -ketoacids are toxic in the body and the initial manifestation of this toxicity is encephalopathy. On the other hand, the characteristic " maple syrup" or " burnt sugar" odor is detectable in the cerumen in the ear or in the urine (Leucine mildly to moderately elevated). Specifically, this odor is also attributed to accumulation of isoleucine in the plasma (Bodamer, 2008).

Due to impaired catabolism of BCAAs initiated in muscles, acetyl-CoA, acetoacetate, and succinyl-CoA become also lacking. This leads to decreased NADH2 and FADH2 utilized for ATP generation (Laygo, 2007: 28). Consequently, with lesser ATP production, the inflicted individual becomes lethargic.

Particular neurological abnormalities and deficits are primarily caused by elevation of leucine. The blood brain barrier is highly permeable to leucine, and this amino acid is metabolized in specific pathways to ultimately yield glutamate and glutamine (Bodamer, 2008). In addition, poor formation of myelination was caused by abnormal development of CNS secondary to lack of these essential amino acids (Laygo, 2007: 28).

Works Cited

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