Pyruvate Dehydrogenase Deficiency

Pyruvate dehydrogenase deficiency is a metabolic disorder caused by a deficiency of the pyruvate dehydrogenase enzyme complex. This complex consists of three enzymes that transform pyruvate to acetyl CoA via pyruvate decarboxylation. Acetyl CoA then enters the citric acid cycle. Deficiency of this enzyme causes a backup of pyruvate, which is commonly converted to alanine. Because acetyl CoA cannot be produced to enter the Kreb cycle, aerobic metabolism is severely impaired and the body uses anaerobic pathways to produce ATP. This causes a severe elevation of lactic acid. This condition can be inherited genetically following an X-linked inheritance pattern. Because this enzyme complex requires thiamine as a cofactor, a pyruvate dehydrogenase deficiency can also be acquired from a thiamine deficiency. Individuals can present with severe neurologic defects due to a large energy deficit. Severe enzyme deficiencies can also lead to congenital brain malformation due to lack of ATP during neural development. Treatment includes thiamine supplementation and ketogenic diets including amino acids like lysine and leucine to limit lactic acidosis.

PLAY PICMONIC

Characteristics

X-Linked

X-suit

Pyruvate Dehydrogenase Deficiency is typically inherited in an X-linked manner due to mutations in the PDHA1 gene, where males are more frequently affected, and females may be carriers or show milder symptoms.

Acquired from Thiamine Deficiency

Thigh-man Tied-up

Because this enzyme complex requires thiamine as a cofactor, a pyruvate dehydrogenase deficiency can also be acquired from a thiamine deficiency.

Backup of Alanine and Pyruvate

Backup of Aladdins with Pie-roots

The pyruvate dehydrogenase enzyme complex consists of three enzymes that transform pyruvate to acetyl CoA via pyruvate decarboxylation. Deficiency of this enzyme causes a backup of pyruvate, which is commonly converted to alanine.

Symptoms and Complications

Neurologic Defects

Neuron

Individuals can present with severe neurologic defects due to a large energy deficit. Severe enzyme deficiencies can also lead to congenital brain malformation due to lack of ATP during neural development.

Lactic Acidosis

Lake Acidic-lemon

Because acetyl CoA cannot be produced to enter the Kreb cycle, aerobic metabolism is severely impaired and the body uses anaerobic pathways to produce ATP. This causes a severe elevation of lactic acid.

Interventions

Ketogenic Nutrients

Ketone-key

Treatment includes thiamine supplementation and ketogenic diets including amino acids like lysine and leucine to limit lactic acidosis.

Lysine and Leucine (Ketogenic Nutrients)

L icing cake and Lucy

Lysine and leucine are the only purely ketogenic amino acids, which are used in the treatment of individuals with pyruvate dehydrogenase deficiency to limit lactic acidosis.