3-Methylcrotonyl-CoA Carboxylase deficiency (3MCC)

What is 3MCC deficiency?

It is one of the organic acid disorders due to the deficiency of one of the enzymes that is involved in the catabolism of leucine. This enzyme is called the 3-Methylcrotonyl-CoA Carboxylase which is also important in breakdown the 3-methylcrotonic acid. This leads to the accumulation of harmful substances in the blood.

What causes the disease?

The mutations in MCCC1 or MCCC2 genes are a potential cause of the Methylcrotonyl-CoA Carboxylase enzyme deficiency.

What are the clinical features of the disease?

The presentation of 3MCC deficiency is variable and there may be individuals with this disorder who are asymptomatic or do not develop symptoms until later in life. Occasionally, asymptomatic women who has 3MCC deficiency will have infants who appear to have 3MCC deficiency on the newborn screen but are found later not to be affected. This finding is a transient state in the newborn as it is a reflection of the mother's metabolic status. Some patients presented at few months of life with vomiting lethargy and metabolic crises triggered by URTI or other catabolic state.

How is the diagnosis confirmed?

The diagnosis of 3-MCC deficiency is confirmed by finding specific urine organic acid and plasma acylcarnitine profiles. DNA molecular testing of MCCC1 or MCCC2 gene as well as enzymatic studies may also help in confirming the diagnosis. Furthermore, a blood acylcarnitine profile and urine organic acids analysis should be done for the mother to exclude maternal 3-MCC deficiency.

What is the treatment of the disease?

The mainstay of treatment is to prevent fasting, especially when the child is ill. In an acute symptomatic episode, IV D10% and fluids are given, along with other medications that can help the body to get rid of harmful substances and to decrease the level of acid in the blood. In the long term, a low protein diet is often recommended in children with 3-MCC deficiency. A special medical formula may also be suggested. Supplementation with carnitine may also be considered. Treatment can prevent metabolic crises and their sequelae. A Biochemical genetics specialist and a Metabolic Genetics dietitian should coordinate the treatment.