P-136 - CLINICAL, BIOCHEMICAL AND MOLECULAR CHARACTERISTICS OF MALONYL-COA DECARBOXYLASE DEFICIENCY AND LONG TERM FOLLOW-UP OF NINE PATIENTS

Chapel-Crespo C¹, Gavrilov D², Sowa M¹, Myers J³, Day-Salvatore D⁴, Lynn H⁴, Regier D⁵, Steenari M⁶, Abdenur JE¹


BACKGROUND: Malonyl-CoA decarboxylase deficiency (MLYCD) is a rare autosomal recessive disorder caused by defects in MLYCD gene. MS-MS newborn screening (NBS), has allowed pre-symptomatic diagnosis of more patients. Since its first description in 1984, >40 patients with MLYCD have been published, most as single case reports. Not much is known about the effect of early treatment on the natural history or long-term outcomes. AIMS: To report clinical, biochemical, molecular characteristics and long term outcome of nine patients with MLYCD. METHODS: This is a retrospective multi-site study of 9 patients, eight previously unreported. Diagnosis was based on biochemical, enzymatic and/or molecular data. Information was collected using a standardized data sheet. Brain MRI data were reviewed by the same neurologist and nutritional treatment was reviewed by the same metabolic dietitian. RESULTS: All patients who had NBS test had elevated C3DC. Four patients had neonatal presentation, including hypoglycemia, acidosis, respiratory distress, hypotonia and seizures. Enzyme activity was extremely low (n=4). Most families were of Mexican descent and molecular testing revealed 8 novel mutations. One patient died of cardiac failure, the remaining 8 have a median age of 6.5 y (r1.3-14). Common disease manifestations included neurodevelopmental delay, hypotonia and microcephaly. Most patients had dilated cardiomyopathy, one had left ventricular non-compaction, all of them improved/resolved with treatment. MRI abnormalities were present in 4/6 patients, being the most prevalent cystic lesions in basal ganglia and periventricular white matter changes. Seven patients had a total of 23 admissions with an average of 28 hospital-days per admission. Long-term treatment included fasting precautions, carnitine supplementation and a fat restricted diet (20-37% of total calories) with medium chain triglyceride supplementation. No essential fatty acid deficiencies were reported. CONCLUSION: Our findings significantly expand the number of reported cases and molecular spectrum of MLYCD. Additionally, we provide important information about long term manifestations and response to treatment. NBS can detect most MLYCD cases, however newborns can be symptomatic prior to the availability of NBS results. Early diagnosis and treatment appear to improve outcome and cardiac disease. However, current treatment modalities do not prevent neurodevelopmental manifestations.