Isobutyryl-CoA dehydrogenase deficiency: About two Tunisian Cases

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Background:
Isobutyryl-CoA dehydrogenase deficiency (IBDHD) is a rare autosomal recessive metabolic disorder related to valine metabolism and results from variants in ACAD8 gene. We present clinical, biochemical and genotypes in two siblings with IBDHD in North Africa (Tunisia).

Case Presentation:

Case 1: A 4 years old girl (Fig.1), from Tunisian consanguineous parents, was seen for neurological symptoms since the age of 15 months: bilateral nystagmus, developmental delay, difficulties for walking and speaking with spasticity and cerebellar syndrome. PEV and PEAp: Bilateral involvement of auditory and visual pathways in brainstem with demyelination. Brain MRI showed cerebral leukodystrophy with global hypomyelination. Hb: 9.76 g/dl The diagnosis was raised by detection of increased concentrations of C(4)-carnitine levels by tandem mass and on spectrometry. On LC MS/MS: valine was slightly decreased: 70 µmol/l (NV: 73-329). By CentoXome® Solo (including NGS-based CNV analysis) we identified a homozygous mutation in ACAD8 gene c.184C>G p.(Pro62Ala) and was classified as variant of unknown significance. She was treated by L-carnitine and riboflavin.

Case 2: Her older sister was seen at 7 years-old when she developed difficulty walking and learning at school. She has an increased concentrations of C(4)-carnitine levels by tandem mass : 1.76µmol/l NV:0.01-0.92) and on spectrometry. In urine organic acid tests no increased concentration of isobutyrylglycine excretion were found.

Conclusions: This is the first report, in Tunisia of clinical, biochemical and genetic analysis of this rare disease. More cases are needed to better understand the clinical and biological spectrum of this rare disease.