3-hydroxyisobutyryl-CoA hydrolase deficiency

3-hydroxyisobutyryl-CoA hydrolase deficiency (HIBCH) is a neurodegenerative disease characterized in most patients by a continuous decline in psychomotor abilities or a secondary regression triggered by febrile infections and metabolic crises. Spitz et al. described two Paroxysmal Dyskinesia (PD) patients from two pedigrees, both carrying a homozygous c.913A > G, p.Thr305Ala mutation in the HIBCH gene, associated with an unusual clinical presentation. The first patient presented in the second year of life with right paroxysmal hemidystonia lasting for 30 minutes, without any loss of consciousness and without any triggering factor. The second patient has presented since the age of 3 recurrent exercise-induced PD episodes which have been described as abnormal equinovarus, contractures of the lower limbs, lasting for 1 to 4 hours, associated with choreic movements of the hands. Their neurological examination and metabolic screening were normal, while brain magnetic resonance imaging showed abnormal signal of the pallidi.We suggest that HIBCH deficiency, through the accumulation of metabolic intermediates of the valine catabolic pathway, leads to a secondary defect in respiratory chain activity and pyruvate dehydrogenase (PDH) activity and to a broad phenotypic spectrum ranging from Leigh syndrome to milder phenotypes. The two patients presented herein expand the spectrum of the disease to include unusual paroxysmal phenotypes and HIBCH deficiency should be considered in the diagnostic strategy of PD to enable adequate preventive treatment [1)].

1)

Spitz MA, Lenaers G, Charif M, Wirth T, Chelly J, Abi-Warde MT, Meyer P, Leboucq N, Schaefer E, Anheim M, Roubertie A. Paroxysmal Dyskinesias Revealing 3-Hydroxy-Isobutyryl-CoA Hydrolase (HIBCH) Deficiency. Neuropediatrics. 2021 Jan 27. doi: 10.1055/s-0040-1722678. Epub ahead of print. PMID: 33506479.