Variant non-ketotic hyperglycinemia caused by a mutation in GLRX5 Report of a case

Havva Yazıcı1, Ebru Candı2, Esra Işık2, Hüseyin Onay2, Sema Kalkan Uçar1, Mahmut Çoker1
1Division of Pediatric Metabolism, Ege University, Izmir, Turkey
2Department of Genetic, Ege University, Izmir, Turkey

Background
Nonketotic Hyperglycinemia (NKH) (OMIM # 605899) is a rare genetic defect in glycine metabolism caused by a defective glycine cleavage system (GCS) due to mutations in the GLDC, AMT, GCSH, and GCSE genes. The defect of GCS causes a considerable accumulation of glycine in all tissues, notably in the central nervous system. Lipoic acid (LA) is an essential cofactor required for the activity of five enzymatic complexes that play a central role in the mitochondrial energy metabolism. GLRX5 is one of the genes involved in the lipoic acid synthesis.

Case Report
• The male patient was born from consanguineous parents following an uneventful pregnancy and delivery.
• He had a normal birth and developmental history until three years of age, when he developed status epilepticus and then hypotonia and vision loss.
• Lactic acid measurements were between 54-10 mg/dl.
• His fibroblast pyruvate dehydrogenase complex activity was 7.4 MU/UCS (Controls: 9.7 – 36), mildly decreased.
• His plasma glycine, cerebrospinal fluid, and CSF/plasma glycine ratio were 54 µmol/L, 780 µmol/L, and 0.06. (N <20).
• His cranial MRI revealed signal abnormalities involving deep white matter. He had increased lactate on magnetic resonance spectroscopy.
• Echocardiography was normal.
• GLRX5 gene analysis was homozygous for c.151_153delAAG (p.Lys51del) small deletion.

Discussion
Glycine elevation can be observed with defects in lipoic acid synthesis due to the defective lipoylation of the H-protein of the GCS. Therefore, when high glycine levels are detected in body fluids, lipoic acid biogenesis defects should be included in the differential diagnosis.