Glycine Encephalopathy (Nonketotic hyperglycinemia)

Genetics

-Genes: GLDC (80%; Glycine Dehydrogenase), AMT (20%; Aminomethyltransferase)

-AR

Clinical findings/Dysmorphic features

-Inborn error of glycine metabolism; defect of glycine cleavage enzyme system (GCS)

-Majority with onset in neonatal period; manifest as progressive lethargy evolving into profound coma and marked hypotonia; 85% have severe NKH and 15% attenuated NKH

-Neonatal hypotonia, seizures, apnea and hiccups

Etiology

-1:76,000

Pathogenesis

-Accumulation of large quantities of glycine in all body tissues including brain

-Glycine is major neurotransmitter: activates inhibitory glycine receptors; co-agonist for excitatory glutamatergic NMDA receptors

Genetic testing/diagnosis

-GLDC: Seq 80%, InDel 20%; AMT: Seq >99%

-Elevated isolated glycine in plasma and CSF by quantitative amino acid analysis + abnormal CSF/plasma glycine ratio (nl ≤0.02; ratio > 0.08 is diagnostic)

-Diffusion-weighted imaging: diffusion restriction in the posterior limb of the internal capsule, anterior brain stem, posterior tegmental tracts, cerebellum

-Corpus callosum can be thin and shortened but is not absent

Others

-Nonketotic hyperglycinemia vs ketotic hyperglycinemia (MMA/PA)

-Urine organic acid profile is expected to be normal