Canavan Disease

Genetics

-ASPA (Aspartoacylase; 17pter-p13)

-AR

Clinical findings/Dysmorphic features

-Neurodegenerative disorder associated with spongy degeneration of white matter of brain

-Neonatal/Infantile (Severe) Canavan Disease most common

-Infants normal early in life; by 3-5 mths --> hypotonia --> spasticity, head lag (inability to support head is constant feature of this disorder), macrocephaly, DD ; HC grows

-DD more obvious with increasing age; delayed in motor skills; not able to sit, stand, walk, talk

-Optic atrophy develops in the second year of life; normal hearing

-Progression: irritable, sleep disturbance, seizures, feeding difficulties, swallowing deteriorates, joint stiffness

-Prognosis: die in first decade of life; with improved medical and nursing care a larger number of children survive beyond the first decade

Etiology

-Carrier frequencies from 1:40 to 1:82 in AJ

Pathogenesis

-Aspartoacylase catalyzes conversion of N-acetyl-L-aspartic acid (NAA) to aspartate and acetate --> deficiency leads to build up of NAA in brain --> demyelination

Genetic testing/diagnosis

-Typical clinical findings + elevated N-acetylaspartic acid (NAA) in urine using gas chromatography-mass spectrometry (UOA) and/or biallelic pathogenic variants in ASPA

-3 common mutations account for 99% of disease-causing alleles in AJ (p.Tyr231Ter, p.Glu285Ala, and p.Ala305Glu), 50-55% in Non-Jewish populations (mainly p.Ala305Glu)