Arylsulfatase A Deficiency (Metachromatic Leukodystrophy)

Genetics

-Gene: ARSA (Arylsulfatase A) or Saposin B (Activator of ARSA)

-AR

Clinical findings/Dysmorphic features

-Late-infantile: onset < 30 mths; weakness, hypotonia, clumsiness, frequent falls, toe walking, dysarthria --> language, cognitive, motor skills regress --> spasticity, pain, szs, compromised vision and hearing --> tonic spasms, decerebrate posturing, unawareness of surroundings

-Juvenile: onset 30 mths – 16y; decline in school performance and behavioral problems; gait disturbances; progression similar but slower than in late-infantile

-Adult: onset > 16 years; problems in school/job performance, personality changes, emotional lability, psychosis, neurologic symptoms (weakness and loss of coordination progressing to spasticity and incontinence), seizures initially predominate; peripheral neuropathy is common

Etiology

-Prevalence between 1:40,000 and 1:160,000

Pathogenesis

-Lysosomal Sphingolipidosis; arylsulfatase A (ARSA) enzyme deficiency --> defect breakdown of sulfatides (3-O-sulfogalactosylceramide),

-Sulfatides: sulfate-containing lipids; throughout body; greatest abundance in nervous tissue, kidneys, testes; approximately 5% of the myelin lipids

-Sulfatide accumulation in nervous system --> myelin breakdown (leukodystrophy) and progressive neurologic disorder

Genetic testing/diagnosis

-Progressive neurologic dysfunction --> MRI evidence of leukodystrophy

-Abnormally high sulfatides in urine

-ARSA: Seq 90-95%; In/Del <1%

Others

-Pseudodeficiency (5-15% of normal activity) in ~2% of European Caucasian alleles