Metachromatic Leukodystrophy

- Hereditary neurodegenerative disease caused by a deficiency of **arylsulfatase A** (ARSA) causing accumulation of sulfatides (a sphingolipid) in white matter
    - Ccerebroside sulfate is a major lipid component of myelin and in high concentrations causes demyelination
    - sulfatides are metachromatic sediments in the urine
- One of the lysosomal storage diseases
- Marked by progressive motor and neurocognitive dysfunction
- Autosomal Recessive
- Subtypes based on age of onset
    - Late Infantile - onset in first 3 years of life (>50%)
    - Juvenile - onset age 4- sexual maturity (20-30%)
    - Adult- > age 16

Common Features

- Motor dysfunction
    - difficulty walking
    - Muscle wasting, weakness and rigidity
    - Impaired swallowing
    - Paralysis
- Seizures
- Progressive dementia
    - May be preceded by personality changes or mild cognitive dysfunction

Eye Features

- Optic Atrophy
- Cherry-red Spot in macula

Diagnosis

- Serum ARSA enzyme level confirmed by elevated urine sulfatide
- MRI Brain
    - diffuse high signal on T2 or Proton Density
    - diffuse symmetrical anterior leukoencephalopathy sparing the subcortical arcuate U fibers
- Gene sequencing of ARSA gene
    - over 200 mutations known and many mutations may not be pathologic
- Nerve/brain biopsy

Treatment

- Bone Marrow Transplant
- Clinical Trials
    - Gene Therapy
        - with autologous stem cell transplant
        - intracerebral vector delivered genes
    - Intrathecal enzyme replacement therapy

Reference

- GeneReviews
- National Institute of Neurological Disorders and Stroke

syndrome