Condition: Niemann-Pick, types A, B, & C

Inheritance:

Autosomal recessive.

Genetic etiology:

Types A & B due to mutation in *SMPD1* gene encoding sphingomyelin phsphodiesterase, required to break down sphingomyelin in the lysosome. Type C due to mutation in either *NPC1* or *NPC2*, which encode Niemann-Pick C1 protein and epididymal secretory protein E1, respectively.

Frequency:

Type A & B: 1/250,000, with increased frequency of type A mutations in Ashkenazi Jewish population (carrier frequency 1/100); Type C: 1/150,000.

Clinical features:

The feature common to all forms is the accumulation of glycosphingolipids in lysosomes. Types A & B result from deficiency of acid sphingomyelinase, leading to accumulation of sphingomyelin. Type A is the neuronopathic form, which presents with hepatosplenomegaly, progressive neurological deterioration, a cherry-red spot in the macula of the eye, and interstitial lung disease. Type B is later in onset and less likely to involve fulminant neurological deterioration. Type C is a defect in intracellular lipid trafficking, with failure of transport of lipids and cholesterol to the cell membrane. It may present in infants with hepatic failure and infiltration of the lungs, or with neurological signs. More often, presentation is in later childhood, with ataxic gait, impaired vertical gaze, cognitive impairment, seizures. Adults may present with dementia.

Management:

Supportive care.

Genetic counseling:

Based on autosomal recessive inheritance; molecular genetic testing available.

Human Genetics and Genomics, Fourth Edition. Bruce R. Korf and Mira B. Irons.