Condition: Ataxia

Inheritance:

Genetically heterogeneous; most forms autosomal dominant; Friedreich ataxia autosomal recessive

Genetic etiology:

More than 20 loci have been identified that are associated with ataxia. Many include a CAG triplet repeat, and the mutations are repeat expansions resulting in a polyglutamine expansion. Friedreich ataxia is due to mutation in the FXN gene, which encodes the protein frataxin. The mutation is a GAA triplet repeat expansion within an intron. Normal alleles contain 5 – 33 repeats; permutation alleles 33 – 65 repeats; borderline alleles 44-66 repeats; full penetrance disease alleles 66-1700 repeats.

Frequency:

Approximately 1/30,000.

Clinical features:

Hereditary ataxia syndromes may manifest as pure ataxia or ataxia in association with other symptoms. Friedreich ataxia usually has onset in late childhood or adolescence, although later onset may occur. Symptoms include ataxia, loss of proprioception, weakness, peripheral neuropathy, spasticity, and autonomic dysfunction. Non-neurological symptoms include hypertrophic cardiomyopathy and diabetes mellitus.

Management:

Supportive care.

Genetic counseling:

Autosomal dominant for most hereditary ataxias; autosomal recessive for Friedreich ataxia. Genetic testing is available for many of these disorders.

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