Ataxia with Oculomotor Apraxia Type 1 and Type 2

Genetics

-Gene: APTX (AOA1; Aprataxin; 9p13.3), SETX (AOA2; Probable Helicase Senataxin; 9q34)

-AR

Clinical findings/Dysmorphic features

-Childhood onset: slowly progressive cerebellar ataxia --> oculomotor apraxia (defect of controlled, voluntary, purposeful eye movement); severe primary motor peripheral axonal motor neuropathy

-First manifestation: progressive gait imbalance (mean age of onset: 4.3 yrs) --> dysarthria (slurred or slow speech) --> upper-limb dysmetria with mild intention tremor

-Oculomotor apraxia: few years after onset of ataxia, progresses to external ophthalmoplegia (paralysis of the muscles surrounding the eye)

-All affected individuals: areflexia followed by a peripheral neuropathy and quadriplegia (paralysis --> partial or total loss of use of all four limbs and torso) with loss of ambulation

-Intellect remains normal in some individuals

Etiology

-0.5 in 100,000 for AOA1

Pathogenesis

-Aprataxin plays role in DNA-single-strand break repair and double-strand break repair --> enhanced sensitivity to agents that cause DNA breaks

Genetic testing/diagnosis

-Sequencing APTX (increased incidence in Portugal and Japan) and SETX

-Mutation detection rate unknown

Others

-AOA2: onset 3-30 years with cerebellar atrophy, axonal sensorimotor neuropathy, oculomotor apraxia, elevated serum concentration of AFP