Lafora Disease

Other names:

Lafora Progressive Myoclonic Epilepsy

Introduction:

Lafora disease is a hereditary epilepsy that is considered to be one of the progressive myoclonic epilepsies.

Progressive myoclonic epilepsies are characterized by the following:

1. Myoclonus
2. Tonic-clonic and/or mycolonic seizures
3. Progressive mental deterioration
4. Cerebellar ataxia and/or involuntary movements

Epidemiology

Transmitted in an autosomal recessive fashion. Onset is in late childhood to adolescence (age 11 to 18 with a mean age of 14).

Clinical Course

Tonic-clonic and/or myoclonic seizures are the usual initial features. The myoclonus progresses and may be very pronounced. Seizures and/or myoclonus are often stimulus induced. Mental retardation begins early in the course and progresses as well. Hallucinations are common and are likely secondary to occipital lobe seizures. Ataxia, spasticity, involuntary movements, impulsive behavior, and personality changes occur later in the course of the disease. Death occurs 5 to 6 years after the initial onset of symptoms.

Pathophysiology

A mutation in the EPM2A gene is the culprit in a majority of cases (80%). This gene encodes laforin, which is a tyrosine kinase inhibitor that plays a significant role in the regulation of glycogen metabolism.

Differential diagnosis

Other epilepsies initially (especially other progressive myoclonic epilepsies). Later in the course, this disease mirrors Unverricht-Lundborg Disease (Lafora bodies are not present on autopsy in this disease, and the mutation is in the cystatin B gene which causes defective functioning of a cysteine protease inhibitor).

How to diagnose

Clinical diagnosis with genetic testing to confirm. EEG is initially normal, and later develops nonspecific generalized polyspike discharges during the awake state. Overtime, the background becomes disorganized and epileptiform activity becomes more constant, and photosensitive discharges are regular late features. On brain biopsy (usually at autopsy if done), large basophilic cytoplasmic bodies within neurons are found (these can be found in other organs as well). These bodies are composed of a glucose polymer (likely secondary to dysregulation of glycogen metabolism, given the dysfunctional laforin protein). See slide of Lafora body in the brain at this link: (http://www.pathology.vcu.edu/education/WirSelfInst/image/014lafora.jpg). Hepatic and skin cells often reveal homogenous PAS-positive bodies that displace the nuclei.

Basic Science Correlates

Basophilic describes the appearance of structures seen in histological sections that take up basic dyes. In H&E sections, basophilic dyes appear purple.

Periodic acid-Schiff (PAS) is a staining method used to detect glycogen in tissues. The reaction of periodic acid selectively oxidizes glucose residues which creates aldehydes that react with the Schiff reagent, which creates a purple color.

Treatment

Not available for the underlying disease. Use AED's to treat seizures (VPA, clonazepam, and phenobarbital are commonly used on brief review of literature).

Odd tid bits and such:

Lafora disease was identified in 1911 when this someone named Lafora identified the large basophilic cytoplasmic bodies in the brain.

References:

Fenichel, Adams and Victors, Epilepsy Continuum, The internet (for pictures and basic science stuff)