Refsum Disease

Refsum disease is type IV of the hereditary motor sensory neuropathies. It is an autosomal recessive condition that is characterized by peroxisomal dysfunction. This leads to accumulation of phytanic acid in several tissues. Clinical manifestations include retinitis pigmentosa, hearing loss, anosmia, polyneuropathy, and ataxia. Diagnosis is suspected by the clinical picture and elevated phytanic acid levels in the plasma. Genetic testing is confirmatory. Interventions focus on reducing phytanic acid levels through dietary modification and, in severe cases, plasmapheresis.

PLAY PICMONIC

Pathophysiology

Autosomal Recessive

Recessive-chocolate

Refsum disease is inherited in an autosomal recessive manner, meaning that two copies of the mutated gene are needed to acquire the disease.

Peroxisome Dysfunction

Dead Pear-ox

Refsum disease is caused by different mutations leading to peroxisomal dysfunction. Peroxisomes are organelles that are involved in key metabolic processes including fatty-acid oxidation. In Refsum disease there is a defect in peroxisomal function leading to the accumulation of phytanic acid, a branched-chain fatty acid.

Increased Phytanic Acid

Up-arrow Titanic Acid-lemon

Phytanic acid is normally degraded into pristanic acid through alpha oxidation. In Refsum disease, this pathway is impaired, and there is an accumulation of phytanic acid in plasma, adipose tissue, myelin sheaths, kidneys, and the liver. Phytanic acid accumulation causes damage to the structural integrity of cells, causing varying clinical manifestations.

Clinical Features

Retinitis Pigmentosa

Red-tin-eyes Piggy-bank

Retinitis pigmentosa is a retinal disease caused by dystrophic tissue architecture of the retina and/or retinal pigment epithelium. Clinical manifestations include night blindness (nyctalopia), defects in color and contrast vision, and peripheral visual field loss. In Refsum disease, the accumulation of phytanic acid causes gradual deterioration of the retina.

Hearing Loss

Deaf-guy

Patients with Refsum disease can present with sensorineural hearing loss due to auditory nerve involvement. It most cases, the hearing loss is bilateral.

Polyneuropathy

Polly-nerve

As phytanic acid accumulates in the myelin sheath, patients may present with peripheral polyneuropathy. Both sensory and motor peripheral neurons may be affected. Classically, a chronic, asymmetric, ascending, and progressive polyneuropathy ensues. Patients may initially complain of numbness, tingling, and impaired perception of vibration and position. In untreated individuals, the disease can progress to widespread weakness leading to disability.

Anosmia

Ant-nose-plug

One of the neurologic manifestations in Refsum disease is anosmia, or the complete loss of the ability to smell.

Ataxia

A-taxi

Ataxia is the loss of coordination of voluntary movement, which may manifest as unsteadiness. Patients with Refsum disease may have impaired cerebellar function resulting in cerebellar ataxia.

Diagnosis

Genetic Testing

Jeans and Test-tubes

Refsum disease is associated with defects in different genes that code for enzymes or proteins involved in peroxisome function. This leads to abnormal metabolism of phytanic acid. The most common genetic mutation in classical Refsum disease is in PHYH, also known as PAHX. The genes involved in infantile Refsum disease include PEX1 and PEX6. Once clinical suspicion is raised, confirmation can be achieved by molecular/genetic testing or by enzyme analysis to identify the defects or deficiencies.

Management

Dietary Changes

Diet Changed by Delta

The main goal in the management of a patient with Refsum disease is to decrease phytanic acid levels. The main dietary sources of phytanic acid are green vegetables and animal fat. Dietary restriction of phytanic acid sources is fundamental since it is associated with improvement in clinical manifestations such as ataxia and sensory neuropathy.

Plasmapheresis

Plasma-fairy

Plasmapheresis is used in severe cases to filter and reduce serum phytanic acid. Some indications include acute arrhythmias and extreme weakness.