Hereditary ATTR (hATTR) Amyloidosis Backgrounder U.S. Version

Disease Overview

Hereditary transthyretin-mediated (hATTR) amyloidosis is a rapidly progressive and life-threatening disease. The condition is caused by a mutation in the transthyretin (TTR) gene.[1,2,3] TTR protein is produced primarily in the liver and is normally a carrier of vitamin A.[4] The mutation results in the accumulation of amyloid deposits in multiple organs of the body, including the nerves, heart, and gastrointestinal (GI) tract.[1,2,3] The condition can have a debilitating impact on a patient's life and may lead to premature death within 4.7 years following diagnosis.[5]

Cause

hATTR amyloidosis is an autosomal dominant disease caused by a mutation in the TTR gene, meaning a person needs only one copy of the mutant gene to manifest the disease, therefore, it can be inherited from one parent.[4,6] More than 120 different TTR gene mutations have been identified, with predominant symptom presentation varying by genotype.[7] The most common mutations in the US are V122I, T60A and V30M.[8] Some mutations are more common in certain populations, including those of Portuguese, Swedish, Japanese, African, and Irish descent.[6,9]

Symptoms

hATTR amyloidosis is a multisystem disease with heterogeneous symptom presentation, meaning the types and severity of symptoms and onset vary from person to person.[3] Common symptoms include:[2]

Peripheral sensory-motor neuropathy
Neuropathic pain
Paresthesia
Weakness

Autonomic dysfunction
Orthostatic hypotension
Recurrent urinary tract infections

GI manifestations
Diarrhea
Nausea
Vomiting

Cardiovascular manifestations
Conduction abnormalities
Arrhythmias
Heart Failure

Symptoms of hATTR amyloidosis can progress quickly, leading to significant disability and dysfunction, including:[6,10]

Decreased ambulation[11]
Inability to walk unaided
Wheelchair-bound or bedridden

Decline in daily function[12,13,14]
Impairment in self-care
Impairment in ability to perform usual activities
Pain/discomfort

Social burden[15]
Anxiety
Depression

Diagnosis

Accurate diagnosis of hATTR amyloidosis is often delayed for years due to its constellation of symptoms, which may overlap with other more common diseases.[6] Multiple specialists are often seen prior to diagnosis. Since the etiology of hATTR amyloidosis is different from that of other diseases with polyneuropathy and cardiomyopathy, a misdiagnosis could lead to ineffective or possibly detrimental treatment.[16] hATTR amyloidosis should be considered in patients with progressive polyneuropathy or cardiomyopathy, especially in those with a family history of hATTR amyloidosis.

hATTR amyloidosis is diagnosed in a variety of ways; however, biopsies are commonly used to confirm the presence of TTR amyloid protein. Genetic testing may also be used to identify the specific TTR mutation and help confirm a diagnosis. Other diagnostic tests for hATTR amyloidosis may include nerve conduction studies, renal function tests, echocardiograms, cardiac magnetic resonance imaging (MRI), and scintigraphy with bone tracers.[17]

For more information on hATTR amyloidosis visit Alnylam.com or contact media@alnylam.com.

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