Hereditary ATTR amyloidosis: a life-threatening, multisystem disease\textsuperscript{1-4}

Hereditary ATTR (hATTR) amyloidosis is an inherited, rapidly progressive, life-threatening disease.\textsuperscript{2,3,5} It is caused by a mutation in the transthyretin (TTR) gene that results in misfolded TTR proteins accumulating as amyloid fibrils in multiple sites including the nerves, heart, and gastrointestinal tract.\textsuperscript{2,6,7} Patients with hATTR amyloidosis can present with symptoms across a spectrum that includes\textsuperscript{1,3,4}:

- Peripheral sensory-motor neuropathy
- Autonomic dysfunction
- Cardiomyopathy

**Constellation of possible signs and symptoms of hATTR amyloidosis**

**CNS manifestations**
- Progressive dementia
- Headache
- Ataxia
- Seizures
- Spastic paresis
- Stroke-like episodes

**Ocular manifestations**
- Vitreous opacification
- Glaucoma
- Abnormal conjunctival vessels
- Papillary abnormalities

**Cardiovascular manifestations**
- Conduction block
- Cardiomyopathy
- Arrhythmia

**Nephropathy**
- Proteinuria
- Renal failure

**Autonomic neuropathy**
- Orthostatic hypotension
- Recurrent urinary tract infections (due to urinary retention)
- Sexual dysfunction
- Sweating abnormalities

**CNS manifestations**
- Nausea & vomiting
- Early satiety
- Diarrhea
- Severe constipation
- Alternating episodes of diarrhea & constipation
- Unintentional weight loss

**GI manifestations**
- Neuropathic pain
- Altered sensation (ie, change in sensitivity to pain and temperature)
- Numbness and tingling
- Muscle weakness
- Impaired balance
- Difficulty walking

Symptom presentation can be highly varied even among individuals in the same family. However, certain symptom clusters should raise suspicion of a single underlying condition.\textsuperscript{1,8}


See the reverse side to learn how to recognize the red-flag symptoms of hATTR amyloidosis.
Recognize the red flags.
Suspect hereditary ATTR amyloidosis.

Patients with hATTR amyloidosis require an early and accurate diagnosis due to the rapid natural progression of the disease\(^1,9,10\)

The clinical manifestation of hATTR amyloidosis can vary widely, and recognizing the signs can be crucial to an early diagnosis.\(^1\)

**Clinical findings that may indicate hATTR amyloidosis**

### Historical and physical findings
- Heart failure with a normal or preserved ejection fraction in the absence of hypertension, particularly in men
- Hypotension in a person with previous hypertension
- Evidence of right-sided heart failure: loss of appetite, hepatomegaly, ascites, and lower extremity edema
- Intolerance of commonly used cardiovascular medications: digoxin, calcium channel blockers, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, and beta blockers
- Bilateral carpal tunnel syndrome

### Imaging findings

**ECG**
- Low QRS voltage ± thick interventricular septum (low voltage to mass ratio)
- Pseudo-infarction pattern
- Progressive reduction in QRS voltage over time

**Echo**
- Thick interventricular septum
- Refractile myocardium (granular sparkling)
- Low tissue Doppler velocities, strain, or strain rate

**CMRI**
- Thick interventricular septum
- Subendocardial late gadolinium enhancement

**Scintigraphy Scan**
- Cardiac uptake of \(^{99m}\text{Tc-DPD}\) or \(^{99m}\text{Tc-PYP}\)

*In addition, consider hATTR amyloidosis in a patient who has a family history of ANY of these symptoms.*

ECG=electrocardiogram; CMRI=cardiac magnetic resonance imaging; \(^{99m}\text{Tc-DPD}=\text{technetium-}^{99m}\text{-3,3-diphosphono-1,2-propanodicarboxylic acid}; \(^{99m}\text{Tc-PYP}=\text{technetium-}^{99m}\text{-pyrophosphate}.

Adapted from Dharmarajan K, Maurer M. *J Am Geriatr Soc.* 2012;60(4):765-774.

To learn more about hATTR amyloidosis and genetic screening made available at no charge through Alnylam Act™, visit [www.hATTRamyloidosis.com](http://www.hATTRamyloidosis.com).

**References:**