Recognizing and diagnosing hATTR amyloidosis

Multisystem involvement should raise suspicion of hATTR amyloidosis and prompt additional investigation. A multidisciplinary approach is critical for diagnosis and management.

**RED-FLAG SYMPTOMS AND/OR FAMILY HISTORY**

- **Sensory-motor neuropathy**
  - Pain, tingling
  - Altered sensation
  - Bilateral carpal tunnel syndrome
  - Weakness
  - Difficulty walking

- **Autonomic neuropathy**
  - GI symptoms
  - Orthostatic hypotension
  - Recurrent UTIs
  - Sexual dysfunction

- **Cardiac manifestations**
  - Fatigue
  - Dyspnea upon exertion
  - Syncope
  - Conduction abnormalities
  - Cardiac hypertrophy
  - Diastolic dysfunction

**DIAGNOSTIC WORKUP**

Several types of tests can help identify the signs of hATTR amyloidosis. Diagnosis does not require all of these assessments.

- **Neurologic assessments**
  - Electromyography (EMG)
  - Nerve conduction study (NCS)
  - Quantitative sudomotor axon reflex test (QSART)
  - Sympathetic skin response (SSR)
  - Tilt table
  - Heart rate deep breathing
  - Valsalva maneuver

- **Cardiac assessments**
  - Electrocardiography (ECG)
  - Echocardiography
  - Cardiac magnetic resonance imaging (CMRI)

**CONFIRMATORY TESTING**

- Genetic Testing
- Tissue biopsy + Congo red
- Scintigraphy (for patients with cardiac involvement)

*See back side for findings associated with hATTR amyloidosis and a scintigraphy algorithm for diagnosis.

*Sensitivity of biopsy can vary by site; negative biopsy may not always rule out hATTR amyloidosis.

GI=gastrointestinal; hATTR=hereditary transthyretin-mediated; UTI=urinary tract infection.
Findings consistent with hATTR amyloidosis

**Neurologic findings**¹,⁴,⁸
- Axonal length-dependent sensory-motor neuropathy
- Small-fiber sensory neuropathy may progress to large-fiber sensory and motor neuropathy
- Reduced sweat gland function, which may follow a length-dependent pattern
- Abnormal hemodynamic response and reduced heart rate variability in autonomic testing

**Cardiac findings**³,⁶
- Left ventricular wall thickening, refractile myocardium (granular sparkling) on echocardiogram
- Reduced longitudinal strain that may be more pronounced at the base than the apex
- Low voltage or progressive reduction in QRS voltage over time
- Pseudo-infarction pattern and/or atrioventricular block
- Subendocardial late gadolinium enhancement on CMRI

Use of scintigraphy to detect amyloid deposition in the heart

**Scintigraphy with technetium-labeled bone tracers is a noninvasive method for detection of amyloid deposits in the heart**⁹

If signs and symptoms of cardiac amyloidosis are identified, monoclonal protein studies (which may include serum and urine protein electrophoresis and immunofixation) should be conducted to rule out AL amyloidosis.⁹,ᵇ

![99mTc-PYP Scintigraphy Scan Diagram](image)

**References:**

Because progressive polyneuropathy also occurs in hATTR amyloidosis, evaluation for signs and symptoms of sensory-motor and autonomic neuropathy should be conducted.⁴