Recognizing and diagnosing hATTR amyloidosis

Multisystem involvement should raise suspicion of hATTR amyloidosis and prompt additional investigation.1,2

RED-FLAG SYMPTOMS AND/OR FAMILY HISTORY

<table>
<thead>
<tr>
<th>Sensory-motor neuropathy1,3,4</th>
<th>Autonomic neuropathy1,3,4</th>
<th>Cardiac manifestations4,5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain, tingling</td>
<td>GI symptoms</td>
<td>Fatigue</td>
</tr>
<tr>
<td>Altered sensation</td>
<td>Orthostatic hypotension</td>
<td>Dyspnea upon exertion</td>
</tr>
<tr>
<td>Bilateral carpal tunnel syndrome</td>
<td>Recurrent UTIs</td>
<td>Syncope</td>
</tr>
<tr>
<td>Weakness</td>
<td>Sexual dysfunction</td>
<td>Conduction abnormalities</td>
</tr>
<tr>
<td>Difficulty walking</td>
<td></td>
<td>Cardiac hypertrophy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diastolic dysfunction</td>
</tr>
</tbody>
</table>

Sensory-motor assessments
- Electromyography (EMG)
- Nerve conduction study (NCS)
- Quantitative sensory testing (QST)

Autonomic assessments
- Heart rate deep breathing
- Tilt table
- Sympathetic skin response (SSR)

Cardiac assessments
- Electrocardiography (ECG)
- Echocardiography (Echo)
- Speckle tracking echocardiography (STE)
- Cardiac magnetic resonance imaging (CMRI)

DIAGNOSTIC WORKUP3,6-9,a

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

To establish the presence of amyloid
- Nuclear scintigraphic imaginga (99mTc-PYP or 99mTc-DPD)
  - For patients with cardiac involvement
- Tissue biopsy (e.g., fat pad, heart, nerve)
  - Sensitivity of biopsy can vary by site; negative biopsy may not always rule out hATTR amyloidosis

To confirm a TTR variant
- Genetic testing

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

99mTc-DPD=technetium-99m-3,3-diphosphono-1,2-propanodicarboxylic acid; 99mTc-PYP=technetium-99m-pyrophosphate;
GI=gastrointestinal; hATTR=hereditary transthyretin-mediated; TTR=transthyretin; UTI=urinary tract infection.
Findings consistent with hATTR amyloidosis

**Neurologic findings**¹,³,⁶

- Axonal length-dependent sensory-motor neuropathy
- Small-fiber sensory neuropathy may progress to large-fiber sensory and motor neuropathy
- Bilateral carpal tunnel syndrome
- Abnormal hemodynamic response and reduced heart rate variability in autonomic testing (e.g., orthostatic hypotension)

**Cardiac findings**⁵,¹²,ᵇ

- 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 or pseudo-infarction pattern and/or atrioventricular block on ECG
- Subendocardial late gadolinium enhancement on CMRI

An algorithm for detecting transthyretin amyloidosis

<table>
<thead>
<tr>
<th>Serum and Urine Immunofixation and Serum Free Light Chain Assay</th>
<th>9⁹⁹mTc-PYP Scintigraphy Scan</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>YES</strong></td>
<td><strong>NO</strong></td>
</tr>
<tr>
<td>Tissue Biopsy</td>
<td><strong>NO</strong></td>
</tr>
<tr>
<td><strong>YES</strong></td>
<td></td>
</tr>
<tr>
<td>AL/ATTR Unlikely</td>
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<td>Genetic Testing</td>
<td>Scintigraphy with technetium-labeled bone tracers is a noninvasive method for detection of amyloid deposits in the heart.¹⁰,¹⁶,¹⁷</td>
</tr>
<tr>
<td>wtATTR</td>
<td>hATTR amyloidosis</td>
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Because progressive polyneuropathy occurs in hATTR amyloidosis, evaluation for signs and symptoms of sensory-motor and autonomic neuropathy should be conducted.³

**MONOCLONAL PROTEIN PRESENT?**

- Serum and Urine Immunofixation and Serum Free Light Chain Assay

**SCINTIGRAPHY SCAN**

- ⁹⁹mTc-PYP Scintigraphy Scan

**SCINTIGRAPHY SCAN**

- Grade 2/3 or H/CL ratio >1.5²

**Tissue Biopsy**

- Congo Red Positivity
- Tissue Typing

- AL/ATTR Unlikely
- AL or Other Amyloidosis

- AL/ATTR Unlikely
- Genetic Testing

- wtATTR
- hATTR amyloidosis