Recognizing and diagnosing hATTR amyloidosis

Multisystem involvement should raise suspicion of hATTR amyloidosis and prompt additional investigation.[1,2] A multidisciplinary approach is critical for diagnosis and management.[2,3]

RED-FLAG SYMPTOMS AND/OR FAMILY HISTORY[1]

Sensory-motor neuropathy[1,4,5]

- Pain, tingling
- Altered sensation
- Bilateral carpal tunnel syndrome
- Weakness
- Difficulty walking

Autonomic neuropathy[1,4,5]

- GI symptoms
- Orthostatic hypotension
- Recurrent UTIs
- Sexual dysfunction

Cardiac manifestations[5,6]

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

DIAGNOSTIC WORKUP[4,7,a]

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

Sensory-motor assessments

- Electromyography (EMG)
- Nerve conduction study (NCS)

Autonomic assessments

- Heart rate deep breathing
- Tilt table

Cardiac assessments

- Electrocardiography (ECG)
- Echocardiography (Echo)
- Cardiac magnetic resonance imaging (CMRI)

CONFIRMATORY TESTING[2,4,5,8]

Genetic testing

Tissue biopsy + Congo red[b]

Scintigraphy (for patients with cardiac involvement)[a]

[a]See page 2 for findings associated with hATTR amyloidosis and a scintigraphy algorithm for diagnosis.
[b]Sensitivity of biopsy can vary by site; negative biopsy may not always rule out hATTR amyloidosis.[2]

GI=gastrointestinal; hATTR=hereditary transthyretin-mediated; UTI=urinary tract infection.

Findings consistent with hATTR amyloidosis

Neurologic findings[1,4,7]

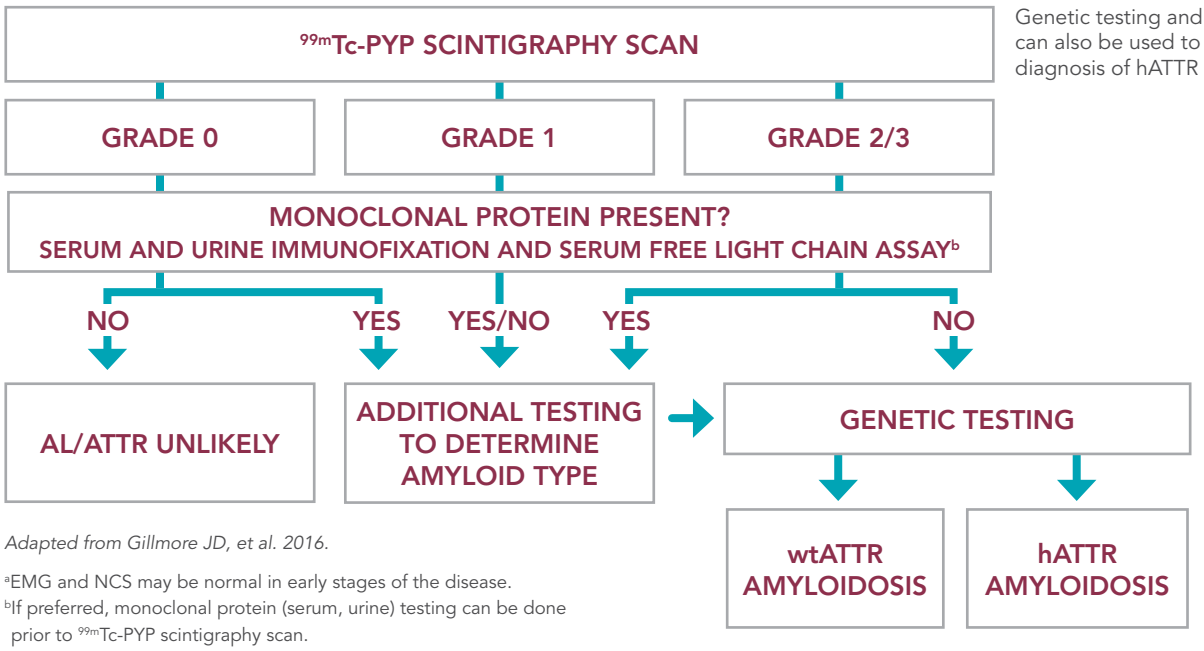
- Axonal length-dependent sensory-motor neuropathy[a]
- Small-fiber sensory neuropathy may progress to large-fiber sensory and motor neuropathy[a]
- Bilateral carpal tunnel syndrome
- Abnormal hemodynamic response and reduced heart rate variability in autonomic testing (e.g., orthostatic hypotension)

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 or pseudo-infarction pattern and/or atrioventricular block on ECG
- 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.[8,9]



Genetic testing and tissue biopsy can also be used to confirm a diagnosis of hATTR amyloidosis.

Adapted from Gillmore JD, et al. 2016.

[a]EMG and NCS may be normal in early stages of the disease.
[b]If preferred, monoclonal protein (serum, urine) testing can be done prior to ^{99m}Tc-PYP scintigraphy scan.

^{99m}Tc-PYP=technetium-^{99m}-pyrophosphate; AL=amyloid light chain; ATTR=transthyretin-mediated; hATTR=hereditary ATTR; wtATTR=wild-type ATTR.

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

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