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[1]

Sensory-motor neuropathy[1,3,4]

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

Autonomic neuropathy[1,3,4]

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

Cardiac manifestations[4,5]

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

DIAGNOSTIC WORKUP[3,6-9,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)
- 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)

ESTABLISH A DIAGNOSIS[2,3,9-11]

To establish the presence of amyloid

- Nuclear scintigraphic imaging[a] (^{99m}Tc-PYP or ^{99m}Tc-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

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

^{99m}Tc-DPD=technetium-^{99m}-3,3-diphosphono-1,2-propanodicarboxylic acid; ^{99m}Tc-PYP=technetium-^{99m}-pyrophosphate; GI=gastrointestinal; hATTR=hereditary transthyretin-mediated; TTR=transthyretin; UTI=urinary tract infection.

Findings consistent with hATTR amyloidosis

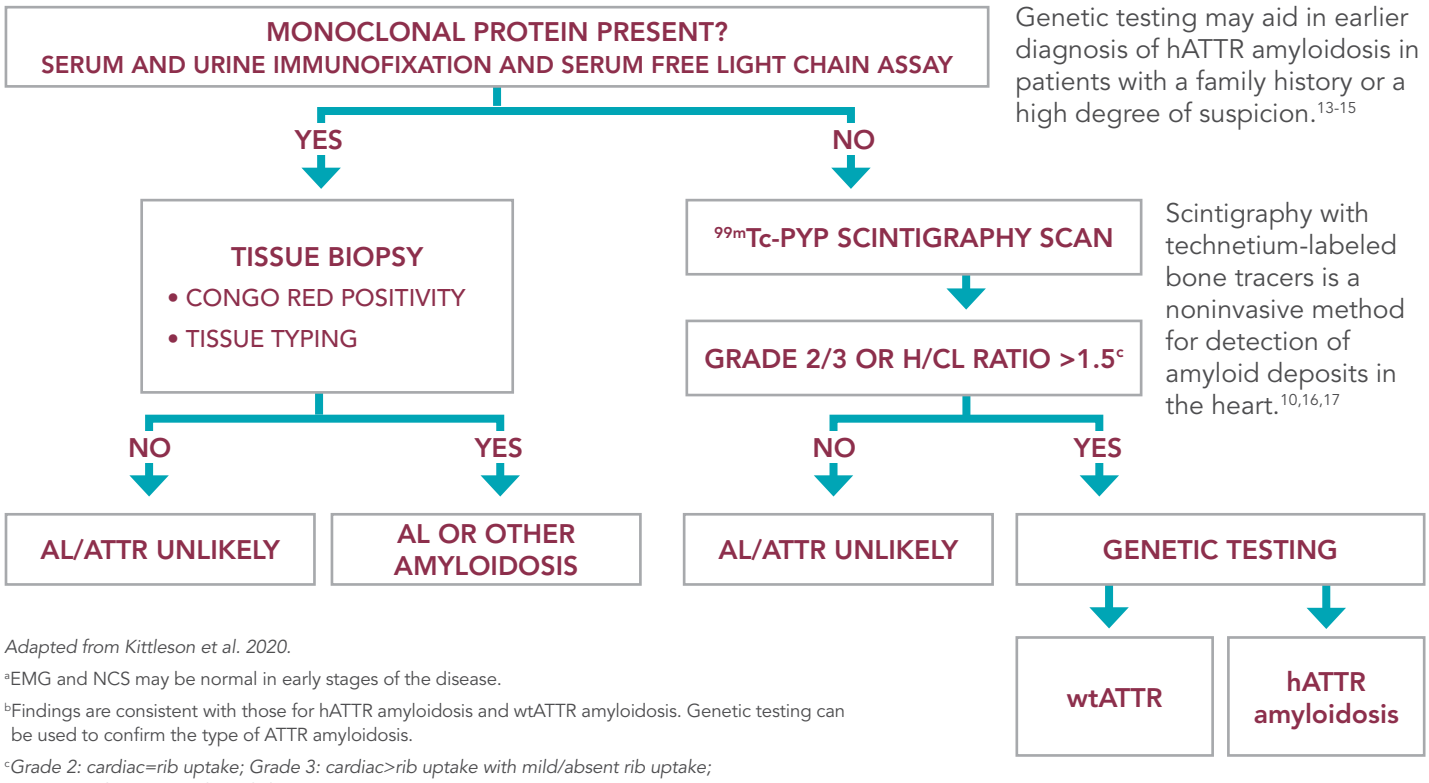
Neurologic findings[1,3,6]

- Axonal length-dependent sensory-motor neuropathy[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[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



Genetic testing may aid in earlier diagnosis of hATTR amyloidosis in patients with a family history or a high degree of suspicion.[13-15]

Scintigraphy with technetium-labeled bone tracers is a noninvasive method for detection of amyloid deposits in the heart.[10,16,17]

Adapted from Kittleson et al. 2020.

[a]EMG and NCS may be normal in early stages of the disease.

[b]Findings are consistent with those for hATTR amyloidosis and wtATTR amyloidosis. Genetic testing can be used to confirm the type of ATTR amyloidosis.

[c]*Grade 2: cardiac=rib uptake; Grade 3: cardiac>rib uptake with mild/absent rib uptake; H/CL ratio: heart/contralateral chest ratio*

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

Because progressive polyneuropathy occurs in hATTR amyloidosis, evaluation for signs and symptoms of sensory-motor and autonomic neuropathy should be conducted.[3]

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