Neurologic tools to recognize and diagnose hATTR amyloidosis

Family history and multisystem involvement, including neurologic manifestations, should raise clinical suspicion and prompt immediate investigation.1,2

Neurologic diagnostic workup.3,4 Several types of tests can help identify signs of hATTR amyloidosis. Diagnosis does not require all of these assessments.

- Sensory-motor assessments
  - EMG
  - NCS
  - QST
- Autonomic assessments
  - Heart rate deep breathing
  - Tilt table
  - SSR
  - QSART
- ESC measurement

Neurologic findings consistent with hATTR amyloidosis.2,4,5

- 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).
- A length-dependent pattern of sweat reduction.

Confirmatory assessments.1,6-8

- Tissue biopsy to determine presence of amyloid.
- Genetic testing to confirm a TTR variant.

Genetic testing is recommended in cases of suspected hATTR amyloidosis to aid in earlier diagnosis and prompt familial screening.6,9

This is not a complete list of all of the available diagnostic tools for hATTR amyloidosis. For more information on cardiac assessments, please see the reverse side.

*EMG and NCS may be normal in early stages of the disease.4

**Possible biopsy sites include labial salivary gland, subcutaneous fatty tissue of abdominal wall, skin, kidney, nerve, and gastrointestinal tract, including submucosa.1,8

The 2023 ACC Expert Consensus recommends serum and urine immunofixation electrophoresis and serum free light chain assay to exclude AL amyloidosis in the initial diagnostic workup.9

Sensitivity of biopsy can vary by site; negative biopsy may not always rule out ATTR amyloidosis.9

AL=amyloid light chain; ATTR=transthyretin-mediated; EMG=electromyography; ESC=electrochemical skin conductance; hATTR=hereditary ATTR; NCS=nerve conduction study; QSART=quantitative sudomotor axon reflex testing; QST=quantitative sensory testing; SSR=sympathetic skin response; TTR=transthyretin; wtATTR=wild-type ATTR.
Cardiac tools to recognize and diagnose hATTR amyloidosis

Family history and multisystem involvement, including cardiovascular manifestations, should raise clinical suspicion and prompt immediate investigation.1,2

Cardiac diagnostic workup10,11
Several types of tests can help identify the signs of hATTR amyloidosis. Diagnosis does not require all of these assessments.
- ECG
- ECHO
- CMRI

Cardiac findings consistent with hATTR amyloidosis9,11,12,a
- Left ventricular wall thickening, refractile myocardium (granular sparkling) on echocardiogram
- Reduced longitudinal strain more pronounced at the base than apex (apical sparing pattern)
- Low voltage or progressive reduction in QRS voltage over time or pseudo-infarction pattern and/or atroventricular block on ECG
- Subendocardial late gadolinium enhancement on CMRI

Confirmatory assessments1,8,9
- Nuclear scintigraphy (99mTc-PYP or 99mTc-DPD) or endomyocardial biopsy to determine presence of amyloid
- Genetic testing to confirm a TTR variant

Genetic testing is recommended in cases of suspected hATTR amyloidosis to aid in earlier diagnosis and prompt familial screening.8,9

This is not a complete list of all of the available diagnostic tools for hATTR amyloidosis. For more information on neurologic assessments, please see the reverse side.


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