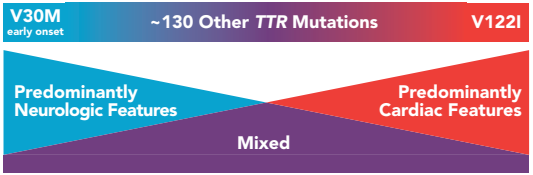
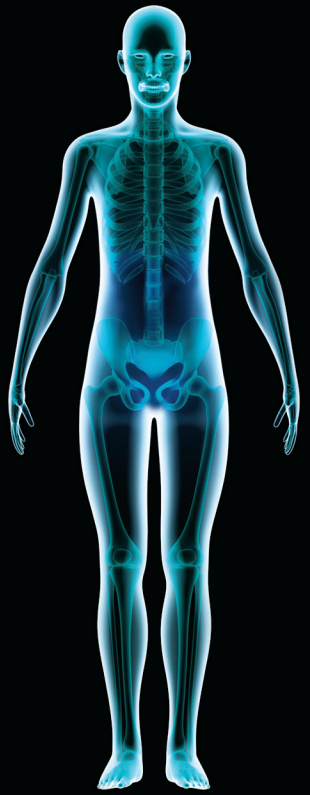
Hereditary ATTR amyloidosis is a systemic disease

that presents with a wide range of symptoms

hATTR amyloidosis lies on a spectrum of neurologic and cardiac symptoms, depending on the *TTR* mutation[3,4]



- While primarily associated with neuropathy, 29% of patients with the V30M (early onset) mutation experience cardiac symptoms[2]
- V122I mutation presents primarily with cardiomyopathy, but 30%–60% of these patients experience neuropathy[5,6]
- **Coordination with neurologists or cardiologists is often warranted in many patients with hATTR amyloidosis**



Hereditary ATTR amyloidosis is a rare, progressive, and fatal disease manifested by buildup of transthyretin amyloid causing[1,2]:

PERIPHERAL SENSORIMOTOR NEUROPATHY
- Numbness and tingling in the hands and feet
- Neuropathic pain
- Walking disability

AUTONOMIC NEUROPATHY
- Orthostatic hypotension
- Sexual dysfunction
- Incontinence

BILATERAL CARPAL TUNNEL SYNDROME

GI SYMPTOMS
- Uncontrolled diarrhea
- Alternating diarrhea/constipation

NEPHROPATHY
- Proteinuria
- Mild azotemia

OCULAR MANIFESTATIONS
- Vitreous opacities

CARDIOVASCULAR MANIFESTATIONS
- Heart failure
- Conduction blocks
- Arrhythmias

When a patient presents with a cluster of 2, 3, or more red-flag symptoms, suspect hATTR amyloidosis

AL, amyloid light-chain; ATTR, amyloid transthyretin; GI, gastrointestinal; hATTR, hereditary amyloid transthyretin; MGUS, monoclonal gammopathy of undetermined significance; ^{99m}Tc-PYP, technetium-99m pyrophosphate; TTR, transthyretin

In hATTR amyloidosis,
hope starts with diagnosis

HISTOPATHOLOGY AND TYPING

- Congo red staining is gold standard for detecting amyloid deposits[7]
- Common biopsy sites: fat tissue, rectum, sural nerve, and labial salivary gland[8]
- Amyloid fibril typing with immunohistochemistry and/or mass spectrometry is necessary to differentiate ATTR amyloidosis and other amyloid forms, including AL amyloidosis[9]

NUCLEAR SCINTIGRAPHY

- Nuclear scintigraphy with ^{99m}Tc-PYP can help assess for amyloid in the heart even in patients with hATTR with polyneuropathy[10]
- Must be combined with testing for serum monoclonal protein to rule out other types of amyloidosis[10]

GENETIC TESTING

- Genetic testing can support/exclude an hATTR amyloidosis diagnosis[11]
- Presence of a heritable *TTR* mutation has important implications for a patient's family

45%–57% of patients with hATTR amyloidosis are misdiagnosed[12,13]

- Misdiagnoses can include: idiopathic polyneuropathy, carpal tunnel syndrome, congestive heart failure, AL amyloidosis, and more

It is possible that those with presumed AL amyloidosis actually have hATTR amyloidosis[14]

- Protein typing to determine the precursor protein is important for choosing the right treatment
- 49% of hATTR (single study involving V122I mutation) patients can present with monoclonal gammopathy of undetermined significance (MGUS),[15] which can make differentiating AL and ATTR amyloidosis difficult

AL and ATTR amyloidosis have different natural histories and therapies[11,16]

- AL amyloidosis treatments include chemotherapy and stem cell transplantation, which can be harmful to patients with ATTR amyloidosis[11,14]

To learn more about hereditary ATTR amyloidosis, visit
www.hATTRGuide.com
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