DO YOU SEE THESE TYPES OF PATIENTS IN YOUR PRACTICE?

Hereditary transthyretin-mediated (hATTR) amyloidosis is a progressive, debilitating, often fatal disease that affects multiple organs and tissues, resulting in a highly varied symptom presentation.[1-6] Given the variability in clinical presentation, these patient profiles are not representative of all patients with hATTR amyloidosis.

Small-fiber neuropathy

Polyneuropathy and nephropathy

Autonomic neuropathy symptoms, HFpEF

Bilateral CTS, atrial fibrillation, intolerant to medication

Cathy, 55 years old

Patient profiles are composites created through a review of published literature and are not of actual patients.

Patient profile: Small-fiber neuropathy

Patient history and presentation

- History of bilateral CTS, release surgeries in both hands
- Progressive sensory neuropathy that began with neuropathic pain and paresthesia in feet 3 months ago and extended to lower legs
- Referred to gastroenterologist 2 years prior with alternating diarrhea and constipation, which has become more severe over the past month
- Recent onset of paresthesia in the hands
- Recent onset of early satiety and weight loss
- Neurologic exam reveals: Muscle weakness in the hands and feet, impaired balance
- Family history of sensory neuropathy

Results of clinical assessments

- Nerve conduction study: Reduced motor and sensory responses in lower extremities
- QSART: Reduced sweat volume in the distal legs and feet

Progressive sensory-motor and autonomic neuropathy may suggest hATTR amyloidosis.[1,5] **Now is the time to send this patient for genetic testing to confirm a TTR variant.**

To learn more about genetic testing or to order a test, visit **www.invitae.com/alnylam-act-ttr**.

CTS=carpal tunnel syndrome; QSART=quantitative sudomotor axon reflex test.

Mia, 48 years old

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Patient profile: Polyneuropathy and nephropathy

Patient history and presentation

- Presented to neurologist 3 months prior for evaluation of numbness and distal weakness; still seeking a diagnosis
- Returned for follow-up due to decline in ambulation over the past month; has started to use a cane when she leaves the house
- Under the care of a nephrologist for the last 12 months for management of mild renal insufficiency and recurrent urinary tract infections (4 during the past 6 months)
- Recurrent nausea and vomiting over the past 9 months
- History of hypertension
- Peripheral edema

Laboratory results

- Elevated serum creatinine
- Proteinuria

Results of clinical assessments

- Nerve conduction study: Reduced motor and sensory responses in lower extremities

Rapidly progressive sensory-motor neuropathy with multisystem involvement may suggest hATTR amyloidosis.[4-6] **Now is the time to send this patient for genetic testing to confirm the diagnosis.**

To learn more about genetic testing or to order a test, visit **www.invitae.com/alnylam-act-ttr**.

Sam, 60 years old

Patient profiles are composites created through a review of published literature and are not of actual patients.

Patient profile: Autonomic neuropathy symptoms, HFpEF

Patient history and presentation

- Sexual dysfunction over past year
- Alternating episodes of diarrhea and constipation
- Recent onset of numbness in both feet
- Reports recent bouts of dizziness when standing up
- History of hypertension; treated with beta blocker that was stopped because of persistent hypotension
- Dyspnea on exertion over past 6 months
- Referred by general practitioner to cardiologist for arrhythmia and lower extremity edema

Laboratory and imaging results

- Echo: LV ejection fraction 55%; LV wall thickness 15 mm at posterior wall
- Elevated NT-proBNP and troponin I
- ECG: Pseudoinfarction pattern
- CMRI: Diffuse subendocardial late gadolinium enhancement of both ventricles
- Heart rate deep breathing test: Absent heart rate variability

Sensory and autonomic neuropathy with HFpEF may suggest hATTR amyloidosis.[1,5,7] **Now is the time to send this patient for genetic testing to confirm a TTR variant.**

To learn more about genetic testing or to order a test, visit **www.invitae.com/alnylam-act-ttr**.

CMRI=cardiac magnetic resonance imaging; ECG=electrocardiogram; Echo=echocardiogram; HFpEF=heart failure with preserved ejection fraction; LV=left ventricle; NT-proBNP=N-terminal pro b-type natriuretic peptide.

Charles, 66 years old

Patient profiles are composites created through a review of published literature and are not of actual patients.

Patient profile: Bilateral CTS, atrial fibrillation, intolerant to medication

Patient history and presentation

- History of bilateral CTS
- Persistent atrial fibrillation was diagnosed 1 month prior, treated with calcium channel blocker and anticoagulants
- Returned for follow-up appointment with new-onset orthostatic hypotension, palpitations, tachycardia, fatigue; unable to work
- Family history of heart failure; father and aunt died at ages 62 and 64, respectively

Results of clinical assessments

- 2D Echo: LV ejection fraction 50%; thickened ventricular walls, speckled myocardium
- ECG: High-degree AV block; low QRS voltage
- Scintigraphy: Grade 3 myocardial uptake of ^{99m}Tc-PYP

Now is the time to rule out other types of amyloidosis. Monoclonal protein studies (serum and urine immunofixation electrophoresis, serum free light chain assay) can rule out AL amyloidosis, and genetic testing can be used to confirm a TTR variant.[7,8]

To learn more about genetic testing or to order a test, visit **www.invitae.com/alnylam-act-ttr**.

^{99m}Tc-PYP=technetium-^{99m}-pyrophosphate; AL=amyloid light chain; AV=atrioventricular; CTS=carpal tunnel syndrome; ECG=electrocardiogram; LV=left ventricle.

The Alnylam Act® program was created to provide access to genetic testing and counseling to patients as a way to help people make more informed decisions about their health.

AlnylamAct®

- While Alnylam provides financial support for this program, tests and services are performed by independent third parties
- Healthcare professionals must confirm that patients meet certain criteria to use the program
- Alnylam receives de-identified patient data from this program, but at no time does Alnylam receive patient-identifiable information. Alnylam uses healthcare professional contact information for research and commercial purposes
- Genetic testing is available in the US and certain other countries. Genetic counseling is available in the US
- Healthcare professionals or patients who use this program have no obligation to recommend, purchase, order, prescribe, promote, administer, use, or support any Alnylam product
- No patients, healthcare professionals, or payers, including government payers, are billed for this program

Alnylam Act is one option for genetic testing and counseling, offered at no charge for patients who may have hATTR amyloidosis.

Visit **www.invitae.com/alnylam-act-ttr** to learn more and to order a test.

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