DO YOU SEE THESE TYPES OF PATIENTS IN YOUR PRACTICE?

Hereditary transthyretin-mediated (hATTR) amyloidosis is a debilitating, life-threatening disease that affects multiple organs, 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

HFpEF, autonomic symptoms

Atrial fibrillation, intolerant to medication, bilateral CTS

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, recent 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 neurologic 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 the diagnosis.**

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 neurologic 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.**

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Sam, 60 years old

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

Patient profile: HFpEF, autonomic symptoms

Patient history and presentation

- History of hypertension; treated with beta blocker that was stopped because of persistent hypotension
- Sexual dysfunction over past year
- Dyspnea on exertion over past 6 months
- Alternating episodes of diarrhea and constipation
- Recent onset of numbness in both feet
- Reports recent bouts of dizziness when standing up
- 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

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

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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: Atrial fibrillation, intolerant to medication, bilateral CTS

Patient history and presentation

- 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
- History of bilateral CTS
- Family history of heart failure; father and aunt died at ages 62 and 64, respectively

Results of cardiac 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 amyloidoses. 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 diagnosis of hATTR amyloidosis.[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.

AlnylamAct®

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

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

[a]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 receives contact information for healthcare professionals who use this program. Genetic testing is available in the U.S. and Canada. Genetic counseling is only available in the U.S. Healthcare professionals and patients who use this program have no obligation to recommend, purchase, order, prescribe, promote, administer, use or support any Alnylam product.

References: 1. Ando Y, Coelho T, Berk JL, et al. *Orphanet J Rare Dis*. 2013;8:31. **2.** Coutinho P, Martins da Silva A, Lopes Lima JL, et al. Excerpta Medica;1980:88-98. **3.** Vinik EJ, Vinik AI, Paulson JF, et al. *J Peripher Nerv Syst*. 2014;19:104-119. **4.** Adams D, Coelho T, Obici L, et al. *Neurology*. 2015;85(8):675-682. **5.** Conceição I, González-Duarte A, Obici L, et al. *J Peripher Nerv Syst*. 2016;21(1):5-9. **6.** Shin SC, Robinson-Papp J. *Mt Sinai J Med*. 2012;79(6):733-748. **7.** Dharmarajan K, Maurer MS. *J Am Geriatr Soc*. 2012;60(4):765-774. **8.** Gillmore JD, Maurer MS, Falk RH, et al. *Circulation*. 2016;133(24):2404-2412.

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