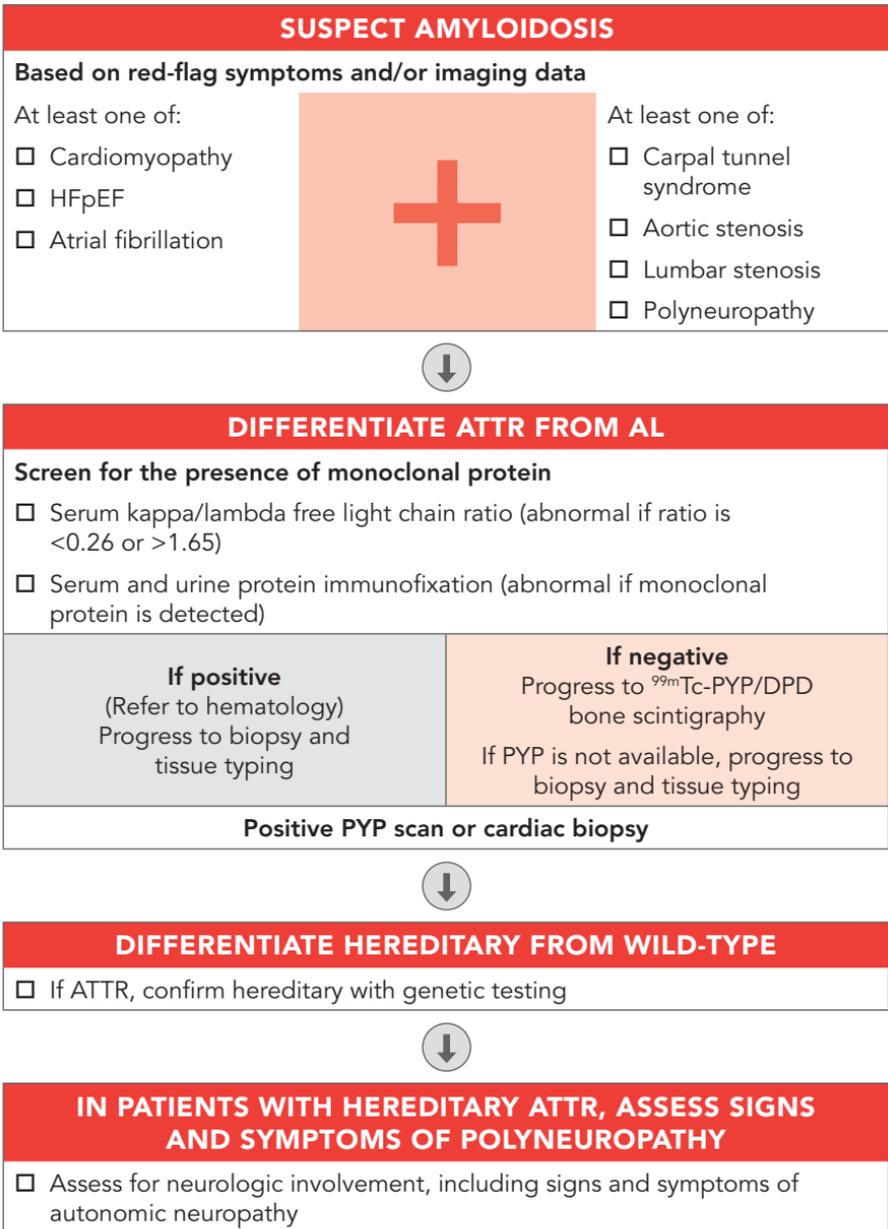


DIAGNOSING HEREDITARY AMYLOID TRANSTHYRETIN (ATTR) AMYLOIDOSIS WITH CARDIOMYOPATHY AND POLYNEUROPATHY

- Hereditary ATTR amyloidosis is an underrecognized cause of cardiomyopathy and polyneuropathy¹
- Recognizing hereditary ATTR amyloidosis can be challenging because of the multisystem nature of the disease. Many patients experience a mixed phenotype, exhibiting both neuropathic and cardiac manifestations. Although specific genotypes have been traditionally associated with predominant cardiac features, most mutations result in clinical heterogeneity that include signs and symptoms of polyneuropathy^{1,2}

DIAGNOSTIC ALGORITHM FOR HEREDITARY ATTR AMYLOIDOSIS*3-7



AL, amyloid light chain; ATTR, amyloid transthyretin; HFpEF, heart failure with preserved ejection fraction; ^{99m}Tc, technetium-99m; PYP, pyrophosphate; DPD, 3,3-diphosphono-1,2 propanodicarboxylic acid.

*The above algorithm represents a pathway for diagnosis of polyneuropathy within ATTR cardiac amyloidosis, as outlined in the following publications.³⁻⁷

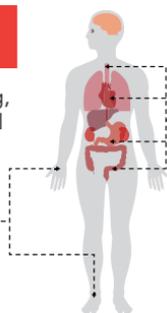
BECAUSE HEREDITARY ATTR AMYLOIDOSIS CAN HAVE MULTISYSTEM MANIFESTATIONS, IT IS IMPORTANT FOR CARDIOLOGISTS TO EVALUATE THEIR PATIENTS FOR MANIFESTATIONS OF POLYNEUROPATHY

POLYNEUROPATHY OF HEREDITARY ATTR AMYLOIDOSIS CAN AFFECT VARIOUS ORGANS, PROGRESSES RAPIDLY, AND LEADS TO SIGNIFICANT MORBIDITY

- Polyneuropathy contributes to the cardiovascular impact of the disease
 - Autonomic symptoms can affect the heart, leading to arrhythmias, and can play a critical role in poor outcomes^{8,9}
 - Orthostatic hypotension from autonomic dysfunction is a common cause of syncope in patients with cardiac amyloidosis⁹
- Polyneuropathy can drastically reduce patients' quality of life
 - Quality of life declines rapidly, particularly early in the disease; over a matter of years, a patient can decline from walking without assistance to being wheelchair-bound^{10,11}

Peripheral Sensorimotor Neuropathy¹²⁻¹⁴

- Numbness, tingling, swelling, burning, and other abnormal feelings in hands and feet
- Neuropathic pain
- Walking disability
- Loss of balance



Autonomic Neuropathy¹²⁻¹⁴

- Constipation and diarrhea that often alternate
- Nausea and vomiting
- Orthostatic hypotension
- Urinary incontinence retention
- Sweating abnormalities
- Sexual dysfunction

CONSIDER ASKING THE FOLLOWING QUESTIONS TO IDENTIFY SIGNS OF POLYNEUROPATHY IF YOU SUSPECT HEREDITARY ATTR AMYLOIDOSIS:

- Has anyone in your family ever been diagnosed with hereditary ATTR amyloidosis or any progressive form of neuropathy (eg, diabetic neuropathy, chronic inflammatory demyelinating polyneuropathy [CIDP], or idiopathic neuropathy)?
- Are you experiencing signs of peripheral neuropathy:
 - In your upper extremities such as tingling, loss of sensation, or neuropathic pain in your hands or arms?
 - In your lower extremities such as tingling, loss of sensation, neuropathic pain or motor weakness in your feet or legs, or difficulty walking?
- Are you experiencing any signs of autonomic dysfunction such as dizziness upon standing (orthostatic hypotension), severe diarrhea or constipation, unintentional weight loss or sexual dysfunction?

No-cost, confidential genetic testing and counseling is available through the hATTR Compass program to patients suspected of having or clinically diagnosed with hATTR amyloidosis with polyneuropathy.

Learn more at:
www.hATTRCompass.com



REFERENCES

1. Benson MD, Uemichi T. *Amyloid*. 1996;3:44-56; 2. Coelho T et al. *Curr Med Res Opin*. 2013;29:63-76; 3. Gertz MA. *Blood Cancer J*. 2018 May;8(5):44;8:44;1-8; 4. Gillmore JD et al. *Circulation*. 2016;24:2404-2412; 5. Nativi-Nicolau J, Maurer MS. *Curr Opin Cardiol*. 2018 Sep;33(5):571-579; 6. Maurer MS et al. *Circ Heart Fail*. 2019 Sep;12(9):e006075; 7. Dorbala S et al. *J Nucl Cardiol*. 2019 Aug 29. doi: 10.1007/s12350-019-01760-6. 8. Kapoor M. *J Neuromuscul Dis*. 2019;6(2):189-199; 9. Gonzalez-Duarte A. *Clin Auton Res*. 2019;29(Suppl 1):1-9. 10. Coelho T. *Muscle Nerve*. 2017;55(3):323-332; 11. Adams D. *J Neurol*. 2020. doi:10.1007/s00415-019-09688-0. 12. Ando Y et al. *Orphanet J Rare Dis*. 2013;8:31; 13. Conceição I et al. *J Peripher Nerv Syst*. 2016;21(1):5-9; 14. Gertz MA et al. *J Am Coll Cardiol*. 2015;66(21):2451-2466.