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Diagnosing ATTRv-PN: What's in Your Toolbox?

Announcer:
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Dr. Khella:
This is CME on ReachMD, and I'm Dr. Sami Khella.

Let's look at strategies that are currently being used to diagnose ATTR-variant polyneuropathy. Let me start with the red flag symptoms in a patient who has a neuropathy. The first red flag is that this is a progressive neuropathy, especially if a patient has proximal and distal weakness and a prior history of carpal tunnel syndrome, I think you really have to be careful that this may be amyloidosis when there is also comorbid heart failure and a prior history of carpal tunnel syndrome. So those would be the red flag symptoms that I would consider to be associated with amyloidosis.

Again, to reiterate a progressive sensory motor neuropathy with a prior history of carpal tunnel syndrome and heart failure should make you think of ATTR. In addition, as I said, this is a systemic illness, so these patients often have an autonomic neuropathy in addition to a polyneuropathy, where they have diarrhea, constipation, orthostatic hypotension with lightheadedness and possibly even syncope. There may be weight loss just from inanition, as well as early erectile dysfunction in a younger man because the neuropathy, while typically it presents in people in their 50s, 60s, or 70s, it can also present in patients earlier on, younger patients in their 30s or 40s. Not a common thing, but this is certainly common in the V30M patients. So the neuropathy can be progressive, can be associated with other systemic illnesses, as I mentioned, GI [gastrointestinal] and cardiac.

Once a patient is suspected of having amyloidosis, you need 2 things before a diagnosis is made. You need genetic confirmation, and that is done through a TTR gene analysis. And if the confirmation comes back with a pathogenic variant, you're not done yet. You still need to show that there is evidence of amyloid deposition in some tissue. Now if a patient has a sensory motor neuropathy, or even just a sensory neuropathy, and has the pathogenic gene, which in the United States, by the way, is the V122I; that's the most common variant. The T60 is the second most common variant, and that's the Irish mutation, so-called because it occurs in that population. And, of course, worldwide is the V30M.

And once you have a pathogenic variant, you need to make sure that you, of course, do genetic testing and counseling on the family members, as well as demonstrating that the patient has amyloid deposition, that that patient has the disease and not just the carrier state. By doing a nerve biopsy or skin biopsy, salivary gland, or a biopsy of the GI tract, you can demonstrate Congo red-positive stain. If you've demonstrated those 2 things, a genetic test and evidence of amyloid in the tissue, you have confirmation of disease activity. You can also, instead of a biopsy, do pyrophosphate scanning, which will show evidence of a cardiomyopathy due to amyloidosis. And it's highly specific and highly sensitive, but you have to be sure that you check the serum protein electrophoresis and immunofixation before doing the test to exclude the possibility that the patient has a light-chain-related cardiomyopathy from a malignant plasma cell clone. So the clinical score that you can use in the office to determine the degree of disability that the patient has, is the Neuropathy Impairment Score, which really is the quantified neurologic examination. You can also use the INCAT [Inflammatory Neuropathy Cause

and Treatment] score, or you can use the I-RODS [Inflammatory Rasch-Built Overall Disability Scale]. All of those have been validated for amyloid polyneuropathy and are quite useful.

So if I'm going to provide you with a takeaway from what I've just said, I'll summarize by saying that amyloid polyneuropathy is part of a systemic illness. So these patients have a dysautonomia, they have a cardiomyopathy, they have a prior history of carpal tunnel syndrome, they may have diarrhea, constipation, lightheadedness, inanition or cachexia as a feature of the disease, and that if you are very careful to monitor the progression, this is a progressive disease. It's a progressive illness.

So I hope that you have found this lecture to be as informative as it was short, and I thank you for listening.

Announcer:
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