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Many Fibromyalgia Patients Have Small-Fiber Polyneuropathy

Daniel M. Keller, PhD

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BOSTON — In a small study of patients labeled as having fibromyalgia, almost half actually had small-fiber polyneuropathy (SFPN), a potentially treatable condition.

Therefore, it is important that patients considered to have fibromyalgia be tested for SFPN, Anne Louise Oaklander, MD, PhD, associate in neurology at Massachusetts General Hospital and associate professor of neurology at Harvard Medical School in Boston, and colleagues reported here at the American Neurological Association (ANA) 137th Annual Meeting.

"Fibromyalgia is such a common and expensive health care problem and although most people are aware of its existence now, it has no associated pathology with it," she explained. "So it's not a diagnosis in the true sense of the word, and that leaves patients frustrated and unable to gain real traction towards a cure."

Dr. Oaklander noted that despite an emphasis on central mechanisms as the cause of fibromyalgia, these findings suggest that a specific — and

Toxic Neuropathy

sometimes treatable — type of peripheral neuropathy is a common cause of the condition.

"This is exciting for us because it's the beginning of objective data on what the actual cause of patients' symptoms may be," she said.

Widespread Chronic Pain

The condition is a syndrome with prominent widespread chronic pain. Thus, her laboratory tested the hypothesis that some patients with fibromyalgia may have SFPN, which "produces widespread chronic pain and very similar symptoms. The difference though is that small-fiber polyneuropathy is a true disease, meaning that there are objective tests for it, known causes, and the possibility of disease-modifying treatments and cure," Dr. Oaklander told *Medscape Medical News*.

The investigators recruited 25 patients 18 years of age or older from the community who met the best available clinical and research definition of fibromyalgia (mean age, 46.5 years), as well as 29 control participants (mean age, 44.8 years). The groups were well matched for demographic characteristics, including sex (76% to 79% women).

The researchers applied consensus-recommended diagnostic tests for SFPN, including standard diagnostic autonomic function testing, an early neuropathy scale, and PGP9.5 immunohistochemical staining of a 3-mm skin punch biopsy specimen from the distal portion of the leg. PGP9.5 is a pan-axonal marker.

The diagnostic test results and markers were analyzed in a blinded fashion. Intraepidermal nerve fiber (IENF) densities were normalized to control values expected for age and sex.

"The diagnostic criterion, universally accepted around the world, is that someone whose nerve fiber density in their biopsy is below the fifth centile of predicted value is considered to have definite small-fiber polyneuropathy," Dr. Oaklander said.

"The major finding of our study is that half of the cohort of fibromyalgia patients but none of an age-matched control group had evidence of nerve loss. And so to neurologists this meets the diagnostic criteria for small-fiber polyneuropathy."

For the various tests overall, 46% of the patients with fibromyalgia and 17% of controls ($P < .001$) met the rigorous criteria for SFPN.

More specifically, 40% of the patients with fibromyalgia met the SFPN diagnostic criteria upon IENF staining. Their IENF densities averaged 28% ± 6% of the predicted norm vs 47% ± 6% for controls ($P < .02$).

Interestingly, there was no overall difference between patients with fibromyalgia and controls on autonomic function testing. Among the fibromyalgia cohort, 17% met diagnostic criteria for SFPN on autonomic testing vs 15% of controls ($P = .67$).

Link to Diabetes

"The significance of this finding is that unlike with fibromyalgia there are known causes of small-fiber polyneuropathy, many of which are amenable to treatment," Dr. Oaklander pointed out. "The most common 1 in the U.S. is diabetes, even prediabetes. So we're now moving on to test this cohort of patients for potentially treatable causes, which offer them the possibility of improvement and perhaps even cure."

In all of her studies, she said that when she found small-fiber polyneuropathy, "a substantial proportion of patients turn out to have either diabetes or pre-diabetes. Most of them don't even know that. It's so common.

"We noticed that virtually all of the patients that we were able to give an ultimate diagnosis of small-fiber [polyneuropathy] in fact said, 'Oh, I've been told I have fibromyalgia for the last 10 years'."

Besides diabetes, causes of SFPN include malignancies, autoimmune conditions, toxins, and mutations, and possible symptoms overlap those of fibromyalgia. Some patients with SFPN may not have pain but may have sensory loss or autonomic symptoms, such as abnormal blood pressure or gastrointestinal disturbances. Dr. Oaklander added that people at the lower end of the normal range of test results for SFPN may eventually develop symptoms.

Her laboratory and some other academic and commercial ones are accredited to run the IENF density tests.

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