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Peripheral neuropathy linked to obstructive sleep apnea?

OSA may not be the first thing that comes to mind when examining a patient with peripheral neuropathy, but treating the sleep disorder can produce surprising benefits.

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CASE ▶ A 57-year-old white woman presented with symptoms of bilateral "stocking-like numbness" and the sensation of "wearing socks for a few weeks" but denied any injury, previous chemotherapy, or diabetes. Her medical history was positive for untreated obstructive sleep apnea (OSA), obesity (body mass index, 36 kg/m^2), osteoarthritis in various joints, impaired fasting glucose with normal glycosylated hemoglobin (HbA1c), hypertension, gastroesophageal reflux disease, hypothyroidism, hypercholesterolemia, and osteoporosis.

Our initial examination revealed decreased sensation to light palpation and pin prick over the distal portion of her lower extremities in a stocking-like fashion. Proprioception was decreased at the distal joint of the big toe. Her deep tendon reflex pattern was symmetric with 2+ at the knees, ankles, and toes. The rest of her lower extremity exam was within normal limits and there were no obvious vascular abnormalities.

Given the suspicion of peripheral neuropathy, the patient underwent laboratory tests and a nerve conduction study. Vitamin B_{12}, vitamin B_1, methylmalonic acid (MMA), thyroid function, thyroid peroxidase (TPO), serum protein electrophoresis (SPEP), rapid plasma reagin (RPR), sedimentation rate, vitamin D, complete blood count, and chemistry profile 24 were all negative. The antinuclear antibody test revealed a homogenous 1:80 titer with a negative nuclear deoxyribonucleic acid. Her fasting glucose had been elevated between 107 to 117 mg/dL in the last 5 years but HbA1c was normal (5.8%). The patient had not been diagnosed with diabetes and her latest glucose values had been stable.

However, electromyography and a nerve conduction study were abnormal, with electrophysiological evidence of mild axonal polyneuropathy. During the month prior to her presentation, she had developed burning pain in addition to the numbness/stocking sensation. Pregabalin, gabapentin, duloxetine, celecoxib, hydrocodone, methadone, and other medications were ineffective. Eventually the foot pain became so severe—she described it as "walking on tacks"—that she was unable to walk.

Our team decided to do a nerve block to relieve the pain. Initially she underwent right and later left peroneal and posterior tibial nerve blocks, which gave her immediate relief that lasted about 2 months.

Relief from the pain, but what about the OSA symptoms?

In the meantime, our patient developed increasing OSA symptoms, including snoring, nonrestorative sleep, daytime somnolence, and fatigue. (To learn more about OSA, see "Obstructive sleep apnea: A diagnostic and treatment guide" on page 565.)

Her history of mild-to-moderate OSA dated back 2 years, and included an apnea-hypopnea index (AHI) of 20 events per hour

and 133 episodes of oxygen desaturation with a low O_2 desaturation of 83%. The patient had never been treated, however, because she felt that she couldn't tolerate the continuous positive airway pressure (CPAP) mask.

The patient finally agreed to a CPAP titration study. Her AHI improved from 20 to <2 events per hour; the oxygen desaturation dropped from 133 to 104 episodes; and the lowest O_2 desaturation went from 83% to 85%.

When we initially started CPAP, our patient did not tolerate it very well. However, after consulting with our sleep clinic, she was placed on bilevel positive airway pressure, which she did tolerate. Surprisingly, she also noticed immediate improvement of the neuropathic foot pain; after a few weeks it resolved completely.

Still no foot pain…We continue to follow the patient's progress and, after 3 years, she remains free of foot pain. Her initial numbness remains, however. She has not developed diabetes, with similar fasting sugar levels and an HbA1c of 5.4%. She is not taking any medication for neuropathic pain, but remains on methadone for unrelated severe intractable osteoarthritic pain of the lumbar spine, bilateral knee joints, and left hip.

After starting CPAP, the patient noticed immediate improvement of the neuropathic foot pain; after a few weeks, it resolved completely.

The link between sleep apnea and neuropathy

Our case report suggests that clinicians should consider OSA as a cause of neuropathic pain. A recent review of the literature supports the relationship between the 2 conditions.

The prevalence of neuropathy in the general population is 2.4%, rising to 8% with advancing age.[1] Many different types of peripheral neuropathy have been described; they have different symptoms and characteristics, depending on the specific part of the nervous system that is affected.[2]

The literature reveals a strong association between OSA and peripheral neuropathy and sight-threatening retinopathy.[3] One study found that nearly 60% of patients with diabetes and OSA also have peripheral neuropathy.[4] Another report found that OSA is an independent risk factor for axonal damage of peripheral nerves.[5] Furthermore, a case-control study revealed that the impaired neural function is at least partly reversible with treatment for sleep apnea.[4] Finally, Tahrani et al[6] have found that "neuropathy prevalence was higher in patients with OSA than those without" (60% vs 27%; $P<.001$), which supports our case finding.

The specific mechanism linking OSA and neuropathy remains elusive, but the evidence suggests that peripheral nervous tissue is affected by chronic endoneural hypoxia in this patient population.[7] In patients with OSA, 2 types of nerve dysfunction are apparent: ischemia-related axonal degeneration and resistance to ischemic nerve failure.[8]

An approach worth considering. While nerve blocks did provide some relief for our patient, they are not a long-term solution. To our knowledge, this case report is the first one published in the United States describing resolution of neuropathic pain by treatment of OSA. This approach is certainly worth considering in patients who have not responded to more traditional therapy. **JFP**

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