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Letters to the Editors Related to Published Articles

The Relationship Between Restless Legs Syndrome and Neuropathy

We commend Gemignani and colleagues for important observations[1] on the prevalence of Restless Legs Syndrome (RLS) in 104 patients with symptoms of exclusive small fiber neuropathy, peripheral neuropathy, or mononeuropathy multiplex. The co-occurrence of neuropathy and RLS has been studied from two standpoints in the past, without reaching a consensus: the frequency of neuropathy in RLS patients, and the frequency of RLS in neuropathy patients. The estimated frequency of one condition when the other is present has varied between 5%[2] and 45%,[3] due in part to the use of restrictive definitions, inclusion of only certain subtypes of neuropathy, excessively stringent electrodiagnostic criteria, or examination of a sample of RLS patients, who tend to be younger than the average neuropathy population, and perhaps less likely to have neuropathy. If the frequency of RLS in neuropathy patients is, at the very least, higher than the estimated population prevalence of 10%,[4] the identification and treatment of RLS may represent an often overlooked opportunity to improve the quality of life in patients with peripheral neuropathy.

The data presented by Gemignani et al. suggest that the prevalence of RLS is about 3 times higher in the setting of peripheral neuropathy than in the general population. The authors excluded patients whose RLS was the only manifestation of neuropathy when the onset occurred before age 50 or if there was no associated disease to explain the peripheral neuropathy. The age limit is somewhat arbitrary; the authors themselves have previously reported increased prevalence of RLS in younger patients with hereditary motor and sensory neuropathy.[5] The population of patients with Type 2 diabetes (and consequently, neuropathy) in the United States is growing younger, and two previous studies have reported a higher prevalence of RLS than that reported in the general population among these patients, up to 24%[6] and 27%.[7] Excluding idiopathic peripheral neuropathy patients with RLS may also result in underestimating the prevalence of both conditions. The authors also excluded those with a family history of RLS, despite a previous study showing that up to 13% of patients with both peripheral neuropathy and RLS will have a positive family history.[8] Therefore, we suspect that Gemignani et al. would not have found substantially lower frequencies of RLS had they studied all peripheral neuropathy patients without restriction.

As the authors noted, they could not have used the recently revised criteria for RLS[9] at the time they conducted their study. The most significant change from the original criteria[10] involves substitution of the concept of relief with movement for "motor restlessness," a term that often caused confusion. However, given that the authors conducted a formal clinical interview to assess whether patients met the necessary criteria, we do not believe much information was lost using the older criteria for RLS.

Overall, we concur with the authors' conclusion that the prevalence of RLS is increased in patients with peripheral neuropathy, and this raises interesting questions about pathophysiology. The study unfortunately restricted laboratory investigation to values of hemoglobin and mean corpuscular volume, to assess for anemia. Iron is an essential co-factor for tyrosine hydroxylase, the rate-limiting enzyme involved in the synthesis of dopamine, and currently, RLS is viewed as a consequence of central dopaminergic dysfunction. Given repeated observations that when RLS and neuropathy coexist, the neuropathy tends to involve axon loss rather than myelin, further research is needed to study the role of ferritin deficiency and its potential impact on axon health.

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