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Lumbosacral radiculoplexus neuropathy: a "metabolic" neuropathy?

Aim: Lumbosacral radiculoplexus neuropathy (LRPN) is an immune-mediated neuropathy characterized by unilateral or asymmetrical motor and sensory involvement of the lower limbs. The aim of the study is to evaluate the influence of diabetes mellitus (DM), comorbidities and anthropomorphic variables on LRPN.

Methods: LRPN was identified among Olmsted County, Minnesota, residents during a 16-year period (2000–2015) using the facilities of the Rochester Epidemiology Project (Ng PS et al *Neurology. 2019 Mar 12;92(11):e1188-e1194*). Demographic and clinical data from 59 LRPN patients and 177 age/sex-matched controls were extracted, including body mass index, diabetes diagnosis and duration, microvascular complications, amputation, hypertension, dyslipidemia, heart failure, coronary artery disease, stroke, non-skin cancer, chronic kidney disease dementia, peripheral artery disease, and comorbid autoimmune disorders. The diagnosis of LRPN was based on clinical and electrophysiologic criteria:

1. History and neurologic examination characteristic of LRPN, i.e., an acute, subacute, or subacute to chronic onset of weakness, pain, prickling, or numbness in the lower limbs, with initial focal and unilateral distribution in the proximal (buttock, hip, or thigh) and/or distal (leg or foot) lower limb segments.
2. Electrophysiologic testing (nerve conduction and EMG) confirming an axonal process with lumbosacral involvement from at least 2 different root levels and from at least 2 different peripheral nerves; paraspinal denervation frequently present.

Results: Compared with controls, LRPN patients more frequently had DM, hypertension, obesity, dyslipidemia, stroke, dementia, and comorbid autoimmune disorder. On multivariate logistic regression analysis only DM (OR, 8.03; 95% CI, 3.86-16.7), comorbid autoimmune disorders (OR, 4.58; 95% CI, 1.45-14.7), stroke (OR, 4.13; 95% CI, 1.2-14.25), and BMI (OR, 1.07; 95% CI, 1.01-1.13) were risk factors for LRPN.
Conclusions: DM is the strongest risk factor for the development of LRPN. Altered metabolism and immune dysfunction seem to be the most influential risk factors. These results allow to better define the pathophysiology of LRPN.

Comment. The pathophysiology of LRPN is not yet fully clarified. The evidence of ischemic nerve damage and microvasculitis and upregulation of inflammatory mediators in the nerves of patients with LRPN has led to its definition as a variant of "non-systemic vasculitic neuropathy". This study demonstrates that mainly DM but also hypertension, stroke, obesity, dementia, dyslipidemia and autoimmune comorbidities were more frequent in patients with LRPN than in controls. Notably, in people with DM, the odds of developing LRPN increased eightfold, confirming recent findings by the same group (Ng PS eta al *Neurology. 2019 Mar 12;92(11):e1188-e1194*). These data identify a possible metabolic cause of the onset of LRPN. Dyslipidemia, obesity and DM can induce neuronal damage through various mechanisms: increased oxidative stress, systemic and local inflammation, accumulation of neurotoxic deoxysphingolipids. Rapid glycemic excursions and metabolic dysfunctions result in a lesion of peripheral nerves capable of triggering an inflammatory response against roots, plexus, and nerves, manifesting as LRPN. Finally, the association with autoimmune diseases confirms the pathophysiological hypothesis that LPRN is an immune-mediated neuropathy. Further studies are needed to confirm these findings.

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Reference. Pinto MV, Ng PS, Laughlin RS, Thapa P, Aragon Pinto C, Shelly S, Shouman K, Dyck PJ, Dyck PJB. Risk factors for lumbosacral radiculoplexus neuropathy. Muscle Nerve. 2021 Dec 30. doi: 10.1002/mus.27484. Epub ahead of print.
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