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CIDP and CASPR1: A Rare Form of CIDP with Severe Neuropathic Pain

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Abstract

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is the most common inflammatory neuropathy. Recently, autoantibodies against the Para nodal proteins are related to a kind of CIDP with a specific clinical and manifestations. The Contactin associated protein-1 (CASPR1) is a cell-adhesion protein tightly associated with Contactin in the Para nodal region and was identified as a possible antigen in inflammatory neuropathies. Patients with CIDP who presents autoantibodies against CASPR1 have a distinct disease course. Therefore, this study proposes that patients with CIDP should be tested to CASPR1.

Keywords: CIDP; CASPR1; Autoantibodies; Neuroinfammation

Commentary

Among infammatory neuropathies, chronic infammatory demyelinating polyradiculoneuropathy (CIDP) is the most common, with an estimated prevalence of about 0.8 to 8.9 per 100,000 adults, depending on the population studied [1,2]. It mainly afects young adults and the male population; however, it can appear at any age and in both sexes. Te disease has a heterogeneous presentation, usually insidious onset and impairs the patients' daily activities, may present a chronic progressive or remitting relapsing course. CIDP seems to afect more the Peripheral Nervous System [1]. Te pathophysiology described involves immune-mediated mechanisms and its main feature is symmetrical progressive paresis and impairment of sensory function in the limbs. Clinically, it manifests with paresthesia in the fngers, loss of strength and decreased refexes in the limbs. Tis pathophysiological mechanism makes the disease mostly responsive to immunosuppressive therapies [1,3].

CIDP is described as a disorder caused by multifocal demyelination of neurons. Te process involves an autoimmune reaction against diferent neuronal components, especially in the nodal and Para nodal regions. Recently, it had been observed that autoantibodies against the Para nodal proteins are related to a kind of CIDP with a specifc clinical and manifestations, which unlike the typical presentation and do not respond as well to immunosuppressive treatment [1,3,4].

CASPR1 is a trans membrane molecule that, associated with neurofascin-155 and contactin-1, forms an important complex in the structure of the Para nodal region and is responsible for mediating the binding between the myelin sheath and the axon [5]. Te CASPR1 has its coding gene located on chromosome 17q21.1 and was identifed as a possible antigen in infammatory neuropathies, being responsible for the production of anti-CASPR1 autoantibodies that cause the deposition of IgG immunoglobulin in the Para nodal region. Tese, in turn, when they bind to immune reactive neurons in the roots of the dorsal ganglion, trigger a painful clinical presentation. Such pathogenesis is an uncommon but important cause of infammatory neuropathies and has been little reported until now [4,6].

Patients with CIDP who presents autoantibodies against CASPR1 have a distinct disease course that involves onset at an older age, rapidly progressive course characterized by predominant motor weakness, proximal and distal, than sensitive and severe neuropathic pain [7] (Figure 1).

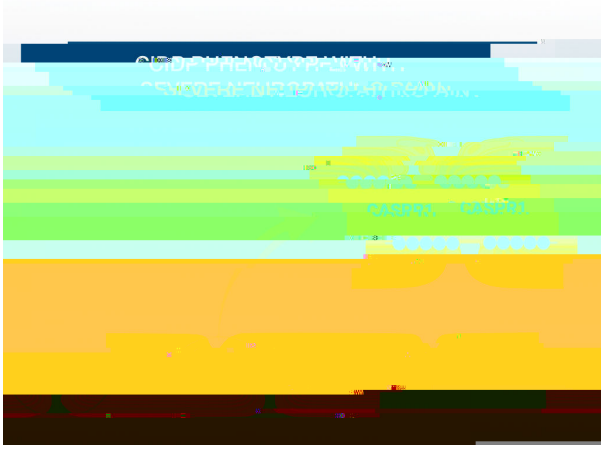

Figure 1: Contactin associated protein 1 (CASPR1) is a cell-adhesion protein located in the paranodal region and it is response to facilitating high-velocity nerve conduction and myelin homeostasis at the central and peripheral nervous system, what explain the severe neuropathic pain and the predominant motor weakness. CIDP: chronic infammatory demyelinating polyradiculoneuropathy.

In biopsy findings, severe and progressive lesions of the axons are found, as well as few thinly myelinated fibers and absence of onion bulbs, which indicates a different characteristic of the commonly found demyelination. In addition, the myelin sheath is little affected compared to the region Para nodal and Ranvier's nodes, which suffer a breakdown of their normal architectures [8].

Patients who develop antibodies against CASPR1 polyneuropathy present a different clinical course, with an important peripheral involvement [7] and are really important to know this type of CIDP, because the use of intravenous immunoglobulin is ineffective at these patients [3]. We suggest that patients with CIDP phenotype with severe neuropathic pain should be tested to CASPR1, as this clinic does not improve with conventional treatments. Thus, with the correct diagnosis and management of the disease, we save the great discomfort generated in patients, as well as the expenses with medicines that may not be used.

Conflicts of Interest

The authors declare that there are no conflicts of interest relevant to this work.

Ethical Approval and Consent to Participate

Not applicable

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