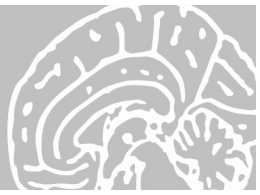
Combined central and peripheral demyelination (CCPD): Clinical features and immune mechanism



Ryo Yamasaki, MD, PhD[1], Hidenori Ogata, MD[2], and Jun-ichi Kira, MD, PhD[2]

[1]Department of Neurological Therapeutics, Neurological Institute, Graduate School of Medical Sciences, Kyushu University;
[2]Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University

Growing reports indicated that some multiple sclerosis (MS) patients have peripheral demyelinations and also some of the chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) patients have demyelinating lesions in the central nervous system (CNS). These combined central and peripheral demyelinations (CCPD) patients have unique characteristics in clinical signs, medical examinations and responses in treatment, but it is still controversial if these patients are distinct from MS or CIDP. We aimed to identify the target antigens for CCPD and to characterize clinical course of CCPD patients.

We screened target antigens by immunohistochemistry and immunoblotting using peripheral nerve tissues to identify target antigens recognized by serum antibodies from selected CCPD and CIDP cases. We then measured the level of antibody to the relevant antigen in 7 CCPD patients, 16 CIDP patients, 20 MS patients, 20 patients with Guillain-Barré syndrome (GBS), 21 patients with other neuropathies (ON), and 23 healthy controls (HC) by ELISA and cell-based assays using HEK293 cells. We have also reviewed the clinical data of CCPD patients.

At the initial screening, sera from two CCPD patients showed cross-like binding to sciatic nerve sections at fixed intervals, with nearly perfect co-localization with pan-neurofascin immunostaining at the node and paranode. ELISA with recombinant neurofascin revealed significantly higher mean optical density values in the CCPD group than in other disease groups and HC. Anti-neurofascin antibody positivity rates were 86% in CCPD patients, 10% in MS patients, 25% in CIDP patients, 15% in GBS patients, and 0% in ON patients and HC. The cell-based assay detected serum anti-neurofascin antibody in 5/7 CCPD patients; all others were negative. CSF samples from three CCPD patients examined were all positive. In anti-neurofascin antibody-positive CCPD patients, including those with a limited response to corticosteroids, intravenous immunoglobulin or plasma exchange alleviated the symptoms.

Anti-neurofascin antibody is frequently present in CCPD patients. Recognition of this antibody may be important, because antibody-positive CCPD patients respond well to intravenous immunoglobulin or plasma exchange.