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Abstracts

Articles appearing in the January 2021 issue

Chitinase 3–like 1 and Neurofilament Light Chain in CSF and CNS Atrophy in MS

Objective To investigate cross-sectional associations of CSF levels of neurofilament light chain (NfL) and of the newly emerging marker chitinase 3–like protein 1 (CHI3L1) with brain and spinal cord atrophies, which are established MRI markers of disease activity in MS, to study CHI3L1 and NfL in relapsing (RMS) and progressive MS (PMS) and to assess the expression of CHI3L1 in different cell types.

Methods In a single-center study, 131 patients with MS (42 RMS and 89 PMS) were assessed for NfL and CHI3L1 concentrations in CSF, MRI-based spinal cord and brain volumetry, MS subtype, age, disease duration, and disability. We included 42 matched healthy controls receiving MRI. CHI3L1 expression of human brain cell types was examined in 2 published single-cell RNA sequencing data sets.

Results CHI3L1 was associated with spinal cord volume (B = −1.07, 95% CI −2.04 to −0.11, $p = 0.029$), but not with brain volumes. NfL was associated with brain gray matter (B = −7.3, 95% CI −12.0 to −2.7, $p = 0.003$), but not with spinal cord volume. CHI3L1 was suitable to differentiate between progressive or relapsing MS ($p = 0.015$, OR 1.0103, CI for OR 1.002–1.0187), and its gene expression was found in MS-associated microglia and macrophages and in astrocytes of MS brains.

Conclusions NfL and CHI3L1 in the CSF were differentially related to brain and spinal cord atrophies. CSF CHI3L1 was associated with spinal cord volume loss and was less affected than NfL by disease duration and age, whereas CSF NfL was associated with brain gray matter atrophy. CSF NfL and CHI3L1 measurement provides complementary information regarding brain and spinal cord volumes.

Classification of Evidence This study provides Class II evidence that CSF CHI3L1 is associated with spinal cord volume loss and that CSF NfL is associated with gray matter atrophy.

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Mild Progressive Multifocal Leukoencephalopathy After Switching From Natalizumab to Ocrelizumab

Objective To describe the disease course of carryover progressive multifocal leukoencephalopathy (PML) after switching from natalizumab to ocrelizumab in 2 patients with relapsing-remitting MS.

Methods Two case reports with 1 year of follow-up and retrospective longitudinal measurements of serum neurofilament light (NfL) levels and B-cells.

Results PML was diagnosed 78 days (case 1) and 97 days (case 2) after discontinuation of natalizumab. Both patients developed mild immune reconstitution inflammatory syndrome (IRIS) despite B-cell depletion caused by ocrelizumab. NfL levels increased in both patients during PML-IRIS. PML-IRIS lesions stabilized after treatment with mefloquine and mirtazapine, followed by methylprednisolone, and both patients continued therapy with ocrelizumab when B-cells started to repopulate.

Conclusions The clinical course of carryover PML was mild in both patients, suggesting that B-cell depletion possibly did not aggravate PML-IRIS in these 2 patients.

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