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Abstracts

Articles appearing in the May 2019 issue

Profiling individual clinical responses by high-frequency serum neurofilament assessment in MS

Objective To evaluate individual neurofilament light chain (NfL) variation over the time of disease course and the potential of NfL measurement to predict treatment response in patients with MS.

Methods We investigated 15 patients with MS after immune reconstitution treatment with alemtuzumab (ATZ). Monthly serum NfL (sNFL) measurements were correlated with Expanded Disability Status Scale, MRI, and relapse activity over an observational period of up to 102 months.

Results Before ATZ, sNfL was significantly increased in correlation with previous relapse/MRI activity. After ATZ, sNfL decreased quickly within the first 6 months. In patients classified as NEDA-3, sNfL declined and persisted at an individual low steady-state level of <8 pg/mL. During follow-up, 34 sNfL peaks with a >20 fold increase could be detected, which were associated with clinical or MRI disease activity. Even patient-reported relapse-suspicious symptoms, which have not been confirmed because relapses were accompanied by sNfL, increase, proposing sNfL assessment as a marker for relapse activity. sNfL started to increase earliest 5 months before, peaked at clinical onset, and recovered within 4–5 months. sNfL presented at higher levels in active patients requiring ATZ retreatment compared with responder patients. During 2 documented pregnancies, sNfL was at a low level, whereas a postpartum transient sNfL increase was seen without any signs of activity.

Conclusions This study applied a long-term high-frequency sNfL assessment in an ATZ-treated cohort, allowing a holistic profiling on the individual level and highlighted that sNfL can eminently complement the individual clinical and MRI monitoring in clinical practice.

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PD1 pathway in immune-mediated myopathies: Pathogenesis of dysfunctional T cells revisited

Objective To investigate the relevance of dysfunctional T cells in immune-mediated myopathies. We analyzed T-cell exhaustion and senescence, in the context of programmed cell death protein 1 (PD1)-related immunity in skeletal muscle biopsies from patients with immune-mediated necrotizing myopathy (IMNM), sporadic inclusion body myositis (sIBM), and myositis induced by immune checkpoint inhibitors (irMyositis).

Methods Skeletal muscle biopsies from 12 patients with IMNM, 7 patients with sIBM, and 8 patients with irMyositis were analyzed by immunostaining and immunofluorescence as well as by quantitative PCR. Eight biopsies from nondisease participants served as controls.

Results $CD3^+CD8^+$ T cells in biopsies from IMNM, sIBM, and irMyositis were largely PD1-positive, while $CD68^+$ macrophages were sparsely positive to the ligand of programmed cell death protein 1 (PD-L1). The sarcolemma of myofibers was $PD\text{-}L2^+$ and was colocalized with major histocompatibility complex Class I. $CD68^+$ macrophages were colocalized with PD-L2. Senescent T cells were strongly enriched in skeletal muscle of sIBM, revealing a distinct immunologic signature. Biopsies from patients with irMyositis showed mild signs of senescence and exhaustion.

Conclusion Persistent exposure to antigens in IMNMs and sIBM may lead to T-cell exhaustion, a process controlled by the PD1 receptor and its cognate ligands PD-L1/PD-L2. To our knowledge, these data are the first evidence of presence of dysfunctional T cells and relevance of the PD1 pathway in IMNM, sIBM, and irMyositis. These findings may guide the way to a novel understanding of the immune pathogenesis of immune-mediated myopathies.

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A. Zekeridou and V.A. Lennon. 2015;2:e110. doi.org/10.1212/NXI.0000000000000110

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C. Finke, J. Heine, F. Pache, et al. 2016;3:e229. doi.org/10.1212/NXI.0000000000000229

Reduction of $CD8^+$ T lymphocytes in multiple sclerosis patients treated with dimethyl fumarate

C.M. Spencer, E.C. Crabtree-Hartman, K. Lehmann-Horn, B.A.C. Cree, S.S. Zamvil. 2015;2:e76. doi.org/10.1212/NXI.0000000000000076

Treatment of spontaneous EAE by laquinimod reduces Tfh, B cell aggregates, and disease progression

M. Varrin-Doyer, K.L. Pekarek, C.M. Spencer, et al. 2016;3:e272. doi.org/10.1212/NXI.0000000000000272

Microglial activation, white matter tract damage, and disability in MS

E. Rissanen, J. Tuisku, T. Vahlberg, et al. 2019;3:e443. doi.org/10.1212/NXI.0000000000000443

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Neurology 2019;93;787
DOI 10.1212/WNL.0000000000008392