Neurofilaments and Glial Fibrillary Acidic Protein levels in relation to response to treatment in Multiple Sclerosis

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Background. Multiple sclerosis (MS) is a chronic neurodegenerative disease. The detection of neuronal damage and its quantification is critical. Neurofilament light chain (NfL) represents the most promising biomarker for MS disease activity, progression and prognosis. Glial fibrillary acidic protein (GFAP) represents another blood biomarker that can reliably be measured in serum samples and that is moderately correlated with NfL.

Methods. We measured NfL and GFAP levels in serum of patients and 71 healthy individuals using SIMOA technology. We selected: 26 patients undergoing a lower efficacy treatment (LET) (dimethyl-fumarate, DMF), and 57 patients undergoing a high efficacy treatment (HET) (ocrelizumab, OCRE). 9 patients undergoing LET and 29 undergoing HET were sampled both before and during treatment. Patients were classified as responder (R) or non-responder (NR) to current therapy using the NEDA-3 criteria.

Results. A correlation between both NfL and GFAP with age was confirmed in our cohort ($r = 0.692$, $p < 0.0001$; $r = 0.509$, $p < 0.0001$): their levels increased significantly in the seventh decade ($p<0.01$). For patients undergoing LET, GFAP was significantly increased at baseline in NR compared to R to DMF ($p<0.05$). The data also showed a significant NfL increase in patients before treatment compared to controls ($p<0.05$) and a decreasing trend in NfL and GFAP after treatment with DMF.For patients undergoing HET, we found a baseline trend of increased NfL levels in NR compared to R to OCRE. However, both NfL and GFAP were significantly higher in patients before treatment compared to controls (both $p<0.05$). Furthermore, data showed a decrease in NfL levels ($p=0.05$) but not in GFAP after treatment with Ocrelizumab.

Conclusions. There is a *significant increase of NfL and GFAP in MS patients before treatment* compared to controls which is not seen with both LET and HET. There is a *trend of decrease of NfL and GFAP* and of NfL only during LET and HET respectively. We found a *significant increase of GFAP in NR to LET, original data in the current literature*, and a trend of increase of NfL in NR to HET. Our results contribute to the understanding of NfL and GFAP as non-invasive tools to predict response to DMTs.

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