Neuroinflammation and neuroaxonal damage in multiple sclerosis: a cross-sectional cerebrospinal fluid-based proteome study

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INTRODUCTION AND AIM

Neuroaxonal damage is strongly related to disease progression in multiple sclerosis (MS) [1]. In MS, axonal loss is considered the detrimental consequence of central nervous system (CNS) inflammation [2]. While several treatments are effective in reducing the inflammatory activity of the disease, no therapy is available to directly counteract axonal damage [3]. The study of cerebrospinal fluid (CSF) inflammatory markers closely related to axonal damage can help to identify novel immunological pathways responsible for a more severe neuronal injury.

The aim of this study was to explore the correlations between a panel of CSF inflammation-related proteins (IRPs) and a well-established marker of neuro-axonal damage, namely CSF neurofilament light (NfL).

PATIENTS AND METHODS

The levels of NfL and of 92 IRPs were determined in the CSF of patients with radiologically isolated syndrome (RIS, n=6), clinically isolated syndrome (CIS, n=32), relapsing remitting MS (RRMS, n=51), progressive MS (PMS, n=8) and in the CSF of patients with other neurological diseases as control group (OND, n=36). NfL was assessed through a newly developed in-house ELISA while the 92 IRPs were determined with a proximity extension assay (PEA) using the Proseek Multiplex Inflammation I kit (Quark Bioscience, Uppsala, Sweden) (Figure 1) (Figure 2).

RESULTS - IRPs

• Out of the 92 IRPs, 41 were excluded from the analysis because of a call rate < 75% (75% of all the patients had values below the lower limit of detection).
• 44 IRPs were not significantly different between patients and controls.
• 8 proteins (listed according to p-values from p<0.0001 to p=0.049: CDS, IL12B, TNFβ, MIPIa, TNFαF14, TNFαF9, CXCL11) were significantly increased in the CSF of MS patients (Figure 4) (Figure 5).

RESULTS – NfL

• CSF NfL levels were significantly higher in RIS, CIS, RRMS and PMS patients as compared to controls (p<0.001) (Figure 3).
• No significant differences in CSF NfL values were found between RIS, CIS, RRMS and PMS patients.

CONCLUSIONS

• In MS patients several IRPs are increased as compared to controls.
• Several IRPs positively correlate with the degree of neuroaxonal damage.
• The IRPs we have found to be increased in MS and to correlate with neuroaxonal damage reflect different immunological pathways including B cell activity and lymphoid neogenesis.

References