10 UNEXPECTED FINDING OF ANTICITRULLINATED PROTEIN ANTIBODIES IN CEREBROSPINAL FLUID OF RA PATIENTS WITH INTACT BLOOD BRAIN BARRIER

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Background The authors have recently shown upregulation of inflammatory mediators in cerebrospinal fluid (CSF) from patients with rheumatoid arthritis (RA), with correlations to fatigue mechanisms. The authors have now sought to investigate potential specific intrathecal immune activation focusing on the detection of anticitrullinated protein antibodies (ACPA), known to be highly specific and predictive for the development of RA.

Methods Thirteen female patients with ACPA-positive RA underwent lumbar puncture and collection of CSF and serum. CSF from 10 age-matched individuals with no inflammatory disease, and 26 age-matched patients with multiple sclerosis (MS) were included as controls. IgG ACPAs were measured using a commercial anti-CCP2 ELISA assay (Euro-Diagnostica, Malmö, Sweden). Serum samples were diluted 1:100 according to the protocol, while CSF samples were used undiluted. Analyses of CSF albumin and CSF/plasma albumin ratio were performed in clinical routine.

Results As expected, all RA patients were anticyclic citrullinated peptide (CCP) positive in serum (threshold for positivity: 25 U/ml) with levels ranging from 34 U/ml to more than 3200 U/ml. Interestingly, 7/13 RA patients were anti-CCP positive also in CSF, with levels ranging from 29 U/ml to 154 U/ml in undiluted samples. Anti-CCP levels in controls, on the other hand, were significantly lower; 2.19 $\pm$ 0.09 U/ml for non-inflammatory controls, and 2.54 $\pm$ 0.16 U/ml for MS patients (undiluted samples). In RA patients, there was a correlation between presence of anti-CCP antibodies in CSF and significantly higher serum anti-CCP levels (1453 $\pm$ 82 U/ml in RA with CCP positivity both serum/CSF versus 90 $\pm$ 46 U/ml, CCP negative in CSF; $p < 0.01$). No difference in CSF albumin or the CSF/plasma albumin ratio could be detected between these groups. All patients had normal CSF albumin and CSF/plasma albumin ratios, consistent with an intact blood brain barrier. No RA patient had any history of or symptoms of neurologic disease.

Conclusion Our data show, for the first time, the presence of ACPAs in CSF of RA patients. The association with high serum ACPA levels in these patients may suggest a leakage of antibodies, though data demonstrate intact blood brain barrier. Presence of autoantibodies like ACPA in the CSF may predispose for autoimmune reactions in the central nervous system, potentially affecting cerebral symptoms such as fatigue.