

Inflammation and degeneration in neuropsychiatric SLE

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Abstract

CNS involvement has been reported to occur in 14-75% of patients with SLE, and it is associated with increased mortality. Acquisition of valuable treatment remedies increases the need for early recognition of CNS manifestations in SLE and evaluation of responses to the medication. To assess the presence of inflammation and degeneration in NPSLE, Cerebrospinal fluid (CSF) from lupus patients was examined.

It was shown that patients with NPSLE displayed elevated CSF levels of IL-6 and IL-8 compared to SLE patients without CNS engagement. Follow-up of five patients being successfully treated for NPSLE revealed profound decrease of intrathecal IL-6 levels.

Both IL-6 and IL-8 are known to upregulate MMP-9 that plays an important role in disruption of the integrity of the BBB and the influx of inflammatory mononuclear cells into the CNS. CSF levels of MMP-9 were significantly increased in patients with NPSLE as compared to SLE patients without CNS engagement as well as compared to healthy controls. Subgroup analysis revealed significant correlation between increased CSF-MMP-9 levels and MRI verified brain pathology.

Intrathecal neurofilament and GFAP are markers for neuronal and astroglial brain damage. CSF levels of both molecules were significantly increased in patients with NPSLE as compared to SLE patients without CNS engagement as well as compared to healthy control. Importantly, intrathecal levels of NFL correlated significantly with CSF levels of IL-6, indicating that IL-6 mediated neuronal destruction might occur during CNS lupus. After successful cyclophosphamide treatment, levels of both proteins significantly decreased.

Intrathecal amyloidogenic proteins displayed significantly decreased levels regarding APP and A β 42 in all SLE patients as compared to healthy controls. In contrast, CSF-tau levels were significantly increased in SLE patients showing MRI verified brain damage.

In conclusion it was shown that intrathecal release of inflammatory cytokines leads to synthesis and release of MMP-9, ending up with insult of brain parenchyma resulting in release of neuronal and astrocytic degradation products and ending up in MRI verifiable lesions and clinical states of brain deficiency.

Key words: NPSLE, CSF, IL-6, IL-8, MMP-9, NFL, GFAP, Tau, APP, β -amyloid, IFN- γ

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