Brain imaging patterns and blood brain barrier integrity in patients with SLE

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Background: Neuropsychiatric SLE (NPSLE) constitutes a major cause of morbidity in SLE. The pathogenesis of NPSLE has not been fully elucidated and diagnosis remains a challenge. Recent evidence suggests impaired blood brain barrier (BBB) integrity as a possible mechanism leading to neuropsychiatric damage in SLE, based on an animal model, and two MRI studies.

Aim: To assess brain imaging patterns in patients with SLE, NPSLE and healthy controls utilizing multi-parametric MRI methods relating to cerebral atrophy, tissue and BBB integrity. In addition, we aimed to assess correlations between imaging findings, clinical characteristics, and cognition.

Methods: Twenty-three patients with SLE (NPSLE n=11, non-NPSLE n=12), and 20 age and gender matched healthy subjects were recruited. The MRI protocol included high-resolution T1 sequence (MP2RAGE), diffusion tensor imaging (DTI), and dynamic contrast enhanced (DCE) imaging utilizing a 3-Tesla MRI scanner. Brain segmentation was performed to assess volumetric changes, tissue integrity and BBB permeability in various brain regions. Clinical parameters, cognition, and quality of life were assessed using validated questionnaires. Patients were divided into subgroups based on presence of NPSLE, SLE disease activity, disease duration, irreversible damage and presence of antiphospholipid antibodies. Comparisons were performed between the entire patient group and the control group, as well as between different subgroups, and correlations with clinical parameters and cognitive assessment were investigated.

Results: Abnormal findings on conventional MRI (cMRI) were seen in 74% of the SLE group and 82% of the NPSLE group. On volumetric analysis, bilateral cerebral atrophy was observed in the gray matter and nucleus accumbens, as well as the cerebellar cortex and white matter. These findings were not limited to NPSLE. Brain atrophy significantly correlated with disease duration. Significantly reduced tissue integrity (increased mean diffusivity) of the cerebellar cortex was seen in the NPSLE group compared to healthy controls. Significant correlations were detected between fractional anisotropy in the left and right ventral diencephalon and global cognitive scores. Five of the patients

with SLE (25%), 3 of whom were non-NPSLE, demonstrated BBB impairment in several cerebral gray and white matter regions, as expressed by high permeability values compared to healthy controls. Preliminary results in this cohort showed that these patients had significantly longer disease duration. **Conclusions:** In this study we have detected abnormal cMRI findings, brain atrophy and impaired BBB integrity among patients with SLE, which was not limited to patients with NPSLE. Our results suggest that impairment of the BBB occurs in patients with long disease duration. A breach in the BBB may allow access of pathogenic autoantibodies and cytokines, which may cause neuroinflammation, neuronal damage and cerebral atrophy. These results highlight the significance of disease duration on brain damage even in patients with SLE without overt NPSLE.