



## **LONGITUDINAL EVALUATION OF AXONAL DYSFUNCTION, NEURONAL MARKERS AND PROINFLAMMATORY CYTOKINES IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS**

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### **BACKGROUND**

Involvement of the central nervous system is frequently observed in childhood-onset SLE patients (cSLE). Proton magnetic spectroscopy (1H-MRS) is an important non-invasive method of quantification of biological metabolites. The objective was to analyze during a period of  $13.5 \pm 9.4$  months, the presence of axonal dysfunction in cSLE and to determine clinical, laboratory and treatment features associated with its occurrence and to associate axonal dysfunction with sera Th1, Th2 and Th17 cytokines levels, neurofilament (NF-H) and S100 $\beta$ .

### **MATERIALS AND METHODS**

We included 123 consecutive cSLE patients from the Rheumatology outpatient unit and 76 healthy controls. All patients underwent two magnetic resonance imaging (MRI) exams. We performed multi voxel 1H-MRS using point resolved spectroscopy sequence over the superior-posterior region of the corpus callosum (3T Phillips® scanner) and signals from N-acetylaspartate (NAA), choline-based (Cho); creatine (Cr), glutamate (Glu), glutamine (Gln) and lactate (Lac). A complete clinical, laboratory and neurological evaluation was performed in all subjects. Neurological manifestations were analyzed according to the ACR classification criteria. Mood and anxiety disorders were determined through Beck Depression and Beck Anxiety Inventory. SLE patients were further assessed for clinical and laboratory SLE manifestations, disease activity [SLE Disease Activity Index (SLEDAI)], damage [Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI)] and current drug exposures. Th1 (IL-12, TNF- $\alpha$ , IFN- $\gamma$ ), Th2 (IL-6 and IL-10), Th17 (IL-17) cytokines, S100 $\beta$  and NF-H levels were measured by ELISA.

### **RESULTS**

NAA/Cr ratio ( $p=0.021$ ) and Lac/Cr ( $p=0.009$ ) levels were significantly decreased and Glu/Cr ( $0.004$ ) and Gln/Cr ( $p=0.042$ ) was increased in cSLE patients when compared to healthy controls. When compared cSLE in two times of MRI, 76.4% cSLE patients presented reduction of levels of NAA/Cr and 64.2% cSLE patients presented increased of levels of Cho/Cr. We observed that NAA/Cr was associated with symptoms of anxiety ( $p=0.04$ ), symptoms of depression ( $p=0.006$ ), anticardiolipin ( $p=0.042$ ) and correlated with S100 $\beta$  ( $r=-0.335, p=0.003$ ), NF-H ( $r=-0.241, p=0.035$ ) and TNF- $\alpha$  ( $r=-0.346, p=0.023$ ). Cho/Cr was associated with cognitive dysfunction ( $0.003$ ), use of antimalarial ( $0.05$ ), anti-SM ( $0.005$ ), symptoms of depression ( $0.006$ ), symptoms of anxiety ( $p=0.05$ ) and correlated with S100 $\beta$  ( $r=0.341, p=0.03$ ) and NF-H ( $r=-0.225, p=0.05$ ). Glu/Cr ratio was associated with presence of headache ( $p=0.05$ ), stroke ( $0.043$ ) and symptoms of depression ( $p=0.0007$ ).

### **CONCLUSION**

We observed significant axonal dysfunction in cSLE. Decreased NAA/Cr ratio was associated with symptoms of anxiety, depression, anticardiolipin, mood disturbance and correlated with S100 $\beta$ , NF-H and TNF- $\alpha$ . Increased Cho/Cr ratio was associated with neuropsychiatric manifestations, S100 $\beta$  and NF-H and Glu/Cr associated with headache, stroke and depression, suggesting brain injury.