Cognitive Dysfunction, Depression and Anti N-Methyl-D-Aspartate Receptor Antibodies and Anti- Ribosomal P In Systemic Lupus Erythematosus Patients In Argentina

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Abstract Text

Background/Purpose: Cognitive dysfunction (CD) and depression (D) are common manifestations of neuropsychiatric systemic lupus erythematosus (SLE) and they have been linked to antibodies (abs) like ribosomal P (anti-P), phospholipids and to the NR2 subunit of human N-Methyl-D-Aspartate receptor (anti NR2-NMDAR). The aim of the study was to describe the frequency of neurocognitive dysfunction and depression in patients with SLE and to assess their association with anti-NR2, anti-P and anticardiolipins (aCL) abs.

Methods: Patients who fulfilled the ACR classification SLE criteria were recruited in this cross-sectional study. Demographic and clinical information was obtained during the interview. Anti NR2-NMDAR isotype IgG was determined by commercial ELISA (Cis Biotech, Inc), cut off value=2ng/ml, anti-DNA ds, aCL IgG/IgM by ELISA, anti-P by Lineal Immunoassay. Psychiatric evaluation, DSM IV, Hamilton (anxiety) and Depression Beck scales were applied. The ACR tests were applied to evaluate CD. Cognition was assessed in 4 domains: (1) attention, (2) memory, (3) executive skills and (4) language. Individual tests were: Trail Making Test Part A (1) and Part B (2), Digit symbol (2), Clock Drawing Test (2), SPAN (2), Rey-Osterrieth Complex figure test (3), Rey Auditory Verbal learning test (3), immediate and delayed logical memory(3), semantic Fluency (4). Z-scores (representing standard deviations [SD] from the tests standardization sample mean) were generated for each test. Overall mean z-scores were then determined for each subject in each of the four domains, method used by Diamond (A&R 2006).CD was defined as a mean z score worse than -1.0 in at least one domain. Statistical analyses: data are presented as mean ±SD and percentages. Fisher exact test for categorical variables. Alpha=0.05.

Results: 50 SLE patients, mean age 46±13 yrs, female 96%, white 76%, *mestizos*20%, disease duration 18±12 yrs, SLEDAI ≤ 4 66%, SLICC ≤ 1 68%. Antibodies to NR2 52% (7/26 strong positive), anti-P 12%, aCL IgG 18%, aCL IgM 20%.Global CD 82%,depression 56% and anxiety 56%. Analyzing by groups (table 1) no significant differences with age (p=0,30) or disease duration(p=0,76) were observed

	Without CD and D n= 3 (6%)	**Only CD n=19 (38%)**	**With CD and D n=22 (44%)**	**Only D n=6 (12%)**	**p value**
NR2-NMDA (n=7)	0	3	1	3	0,056
anti-P (n=6)	0	1	3	2	0,26

a-CL Ig G (n=9)	0	2	7	0	0,21
a-CL Ig M(n=10)	0	3	7	0	0,30

Conclusion: We found cognitive dysfunction and depression in our patients with SLE. Although the differences among the groups were not statistically significant, there was higher frequency of anti NR2 in depression and higher frequency of aCL and anti-P in cognitive dysfunction. These antibodies did not appear in patients without depression or cognitive impairment. No association was found between CD and NR2 abs, perhaps due to abs levels that may fluctuate over time or to methodological differences in abs assay detection. These findings would requiere a great number of patients to assess the possible association between these antibodies and these manifestations of neuropsychatric SLE.