Journal of the Neurological Sciences 360 (2016) 94–97

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Executive dysfunction, obsessive–compulsive symptoms, and attention deficit and hyperactivity disorder in Systemic Lupus Erythematosus: Evidence for basal ganglia dysfunction?☆

Ricardo Oliveira Horta Maciel [a], Gilda Aparecida Ferreira [b], Bárbara Akemy [a], Francisco Cardoso [a,*]

[a] Movement Disorders Clinic, Department of Neurology, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil
[b] Rheumatology Clinic, Department of Locomotor System, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

ARTICLE INFO

Article history:
Received 13 October 2015
Received in revised form 20 November 2015
Accepted 26 November 2015
Available online 27 November 2015

Keywords:
Haematological disorders
Neuropsychiatric Systemic Lupus Erythematosus
Movement disorder
Obsessive–compulsive disorder
Attention deficit disorder with hyperactivity
Cognitive symptoms

ABSTRACT

Introduction: Chorea is well described in a group of patients with Systemic Lupus Erythematosus (SLE). There is less information, however, on other movement disorders as well as non-motor neuropsychiatric features such as obsessive–compulsive symptoms (OCS), executive dysfunction and attention deficit and hyperactivity disorder (ADHD) in subjects with SLE.
Methods: Fifty-four subjects with SLE underwent a battery of neuropsychiatric tests that included the Mini Mental State Examination, the Montreal Cognitive Assessment, the Frontal Assessment Battery (FAB), the FAS verbal and the categorical (animals) semantic fluency tests, the Obsessive and Compulsive Inventory — Revised, the Yale-Brown Obsessive and Compulsive Scale and Beck's Anxiety and Depression Scales. ADHD was diagnosed according to DSM-IV criteria. SLE disease activity and cumulative damage were evaluated according to the modified SLE Disease Activity Index 2000 (mSLEDAI-2K) and the SLICC/ACR, respectively.
Results: Six (11.1%) and 33 (61.1%) patients had cognitive impairment according to the MMSE and MoCA, respectively. Eleven (20.4%) had abnormal FAB scores, and 5 (9.3%) had lower semantic fluency scores than expected. The overall frequency of cognitive dysfunction was 72.2% (39 patients) and of neuropsychiatric SLE was 77.8% (42 patients). Two patients (3.7%) had movement disorders. Fifteen (27.8%) had OCS and 17 (31.5%) met diagnostic criteria for ADHD. ADHD and OCS correlated with higher disease activity, $p = 0.003$ and 0.006, respectively. Higher cumulative damage correlated with lower FAB scores (p 0.026).
Conclusions: Executive dysfunction, ADHD, OCS, and movement disorders are common in SLE. Our finding suggests that there is frequent basal ganglia dysfunction in SLE.

1. Introduction

Cognitive impairment is common in patients with Systemic Lupus Erythematous (SLE). Depending on the population or the methods used for assessment, from 14 up to 80% of patients have some kind of cognitive dysfunction [1]. There is no predominant cognitive domain affected, and no unique pattern of dysfunction has been recognized as typical of SLE. Commonly, though, patients score lower than expected on tests of memory, visuospatial abilities, attention and executive function. The mechanism underlying cognitive impairment in SLE is not completely elucidated, but direct inflammatory damage to neuronal circuits and ischemic injury are thought to play a significant role in most cases. Indeed, frontal white matter lesions correlate with cognitive impairment in patients with SLE [2].

The 1999 ACR classification of Neuropsychiatric Lupus (NPSLE) recognizes three psychiatric syndromes related to SLE activity in the Central Nervous System (CNS): psychosis, mood and anxiety disorders [3]. Although less studied, other psychiatric features, such as obsessive–compulsive disorder (OCD) and attention deficit and hyperactive disorder (ADHD), have been described in patients with SLE [4,5]. Indeed, OCD and ADHD also frequently occur in other autoimmune diseases, such as Sydenham's chorea (SC) [6]. In the latter, ADHD and chorea are related to autoantibody-mediated basal ganglia dysfunction [7]. In addition, OCD is more frequent in patients with Rheumatic Fever than in controls, suggesting that anti-basal ganglia antibodies can cause OCD in the absence of chorea [8]. In SLE, chorea and other more infrequent movement disorders, such as parkinsonism, myoclonus and dystonia are often related to basal ganglia dysfunction [9]. We hypothesise that obsessive–compulsive symptoms (OCS) and ADHD are more frequent in patients with SLE than would be expected in a normal population and this

☆ Conflicts of interest: Francisco Cardoso has received consulting honoraria from Allergan and Roche. The other authors have no conflict of interest to declare.

* Corresponding author at: Av Pasteur 89/1107, CEP 30150-290 Belo Horizonte, MG, Brazil.
E-mail address: cardosofe@terra.com.br (F. Cardoso).

http://dx.doi.org/10.1016/j.jns.2015.11.052
0022-510X/

discrepancy could be due to a non-motor manifestation of basal ganglia dysfunction (with or without chorea) in neuropsychiatric SLE (NPSLE).

2. Methods

We evaluated 54 consecutive patients with SLE in an academic tertiary referral centre between June 2012 and November 2013. Inclusion criteria were as follows: 1) Diagnosis of SLE according to the ACR criteria [10], 2) age between 18 and 55 years, 3) minimum of 6 months follow-up and at least two office visits, 4) Informed consent for the participation in the study. We excluded patients who had other rheumatologic diseases (other than antiphospholipid syndrome) or other serious medical conditions that could impair completion of the study protocol (e.g., blindness) or confound data interpretation (e.g., previous severe psychiatric disease not related to SLE). The local Ethics Committee approved this study.

We recorded patients' demographics and reviewed charts to determine age of onset of the disease, initial clinical manifestations, current and previous corticosteroids and immunosuppressive treatments, past neuropsychological manifestations of SLE, positivity for antiphospholipid antibodies and presence of secondary Antiphospholipid Syndrome (APS). Patients underwent a battery of cognitive tests, which included the Mini-mental State Examination (MMSE) [11], the Montreal Cognitive Assessment (MoCA) [12], the Frontal Assessment Battery (FAB) [13], the FAS verbal fluency test and the category (animals) semantic fluency test [14]. Cut-off scores were defined according to previously published data in the Brazilian population [15–18]. The presence and severity of obsessive and compulsive symptoms were assessed with the Revised Obsessive and Compulsive Inventory (OCI-R) [19] and the Yale-Brown Obsessive and Compulsive Scale (YBOCS) [20]. A score equal to or greater than 21 was used as a cut-off for clinically significant OCS [19]. The presence of ADHD symptoms was evaluated according to the DSM-IV criteria with the exception of the criterion presence of symptoms before seven years of age. Patients also completed Beck's Depressive [21] and Anxiety Inventories [22]. A score equal or greater than 21 and 16 were, respectively, considered as clinically meaningful.

We recorded disease activity and damage according to the Modified Systemic Lupus Erythematosus Disease Activity Index 2000 (mSLEDAI-2K) [23] and the Systemic Lupus International Collaborative Clinics/American College of Rheumatology Damage Index (SLICC) [24]. One neurologist (RHM) performed clinical history and examination in all patients and recorded the presence of neuropsychological manifestations of the disease according to the 1999 ACR criteria. Confirmatory tests were ordered when deemed necessary for diagnosis support.

2.1. Statistical analysis

Analysis of data was done using SPSS 20.0 (Statistical Package for Social Sciences, IBM Corporation Software Group, USA), and significance was defined as p value <0.05.

3. Results

Fifty four patients were included in this study. Of the 54 patients studied, 17 (31.5%) were classified as white and 37 (67.5%) as non-white. Female to male ratio was 8:1. Mean age at assessment was 36.5 ± 10.4 years, and mean disease duration was 11.1 ± 7.3 years. Median years of education were 10.0 (6.0–11.0) years. Median mSLEDAI-2K was 2.5 (0–9.25) and median SLICC was 1.0 (0–2). The majority of patients were using corticosteroids or immunosuppressants (83.3% and 59.2%, respectively) and median corticosteroid dosage per day was 10.0 (5.0–15.0) mg. Five patients (9.3%) had secondary antiphospholipid syndrome according to the 2006 Sydney criteria [25]. Clinical characteristics are summarized on Table 1.

Table 1
Clinical data of 54 SLE patients.

	No. of patients	%
Gender		
Male	6	11.1
Female	48	88.9
Race		
White	17	31.5
Non-white	37	68.5
Years of education		
1–3 years	2	3.7
4–7 years	13	24.1
8–11 years	30	55.6
12 or more years	9	16.7
APS		
Absent	49	90.3
Present	5	9.3
Anticardiolipin positivity	14	25.9
Lupus anticoagulant positivity	8	14.8
Medications		
Corticosteroids	45	83.3
Antimalarials	29	53.7
Immunosuppressants	32	59.2
Antidepressants/anxiolytics	23	42.6
Anticonvulsants	5	9.2
Clinical manifestations at time of study		
Malar rash	4	7.4
Oral ulcers	11	20.4
Vasculitis	1	1.9
Arthritis	6	11.1
Psychosis	1	1.9
Nephritis	9	16.7
Leukopenia	1	1.9
Thrombopenia	1	1.9

Cognitive impairment was detected in 6 (11.1%) patients according to the MMSE, but this figure rose to 33 (61.1%) when the MoCA was used. Executive dysfunction was frequent in patients, with 11 (20.4%) individuals scoring below normal on the FAB. FAB scores were negatively correlated to SLICC scores ($r = -0.302$, $p = 0.026$). Five patients (9.3%) also scored lower than expected according to education on the semantic fluency test. Mean scores on the FAS verbal fluency were 27.9 ± 9.5. The overall frequency of cognitive dysfunction in our sample, considering the presence of abnormal scores in any of the MEEM, MoCA, FAB, or verbal fluency scores, was 72.2% (39 patients).

Obsessive–compulsive symptoms were frequent in our sample with 15 (27.8%) patients having abnormal scores on the OCI-R. Five patients (9.3%) had moderate or severe symptoms, as detected by the YBOCS. There was a strong positive correlation between OCI-R and YBOCS scores ($r = 0.653$, $p < 0.000$). A diagnosis of ADHD was made in 17 patients (31.5%) according to DSM-IV criteria. Of those, 12 (70.5%) were classified in the predominant inattentive subtype, 3 (17.6%) were in the predominant hyperactive subtype and the remaining 2 (11.7%) were in the combined inattentive-hyperactive subtype. Executive dysfunction was more common ($p = 0.039$) and mSLEDAI-2K scores were higher in patients with ADHD than in patients without the latter — median score of 8 [2–14] vs. 2.00 (0–4), $p = 0.003$. The presence of clinically meaningful depressive and anxiety symptoms was found in, respectively, 16 (29.6%) and 25 (46.3%) patients. Patients with more severe obsessive–compulsive symptoms were more anxious ($r = 0.544$ $p < 0.000$). Mean and standard deviations of scores in each neuropsychiatric test are shown in Table 2.

We found a positive correlation between daily corticoid dosage and Beck's Depressive Inventory score ($r = 0.375$, $p = 0.006$). Cognitive dysfunction also appeared to be more common in patients currently using corticosteroids, although statistical significance was not reached ($p = 0.056$). There was a negative correlation between FAB scores and