Functional impairments in white matter syndrome of neuropsychiatric systemic lupus erythematosus are similar to those observed in patients with multiple sclerosis

Alterações funcionais na síndrome de acometimento da substância branca do lúpus neuropsiquiátrico são semelhantes àquelas encontradas em pacientes com esclerose múltipla

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ABSTRACT

Objective: In order to compare white matter syndrome of neuropsychiatric systemic lupus erythematosus (NPSLE) and multiple sclerosis (MS), an assessment on demographic, medical history, and clinical data was proposed. **Methods**: Sixty-four patients with NPSLE and 178 with MS answered a questionnaire and were evaluated regarding functional system, expanded disability status scale (EDSS), Beck depression inventory (BDI), and Beck anxiety inventory (BAI). **Results**: The prevalence of autoimmune diseases and altered consciousness was similar in both groups, however it was higher than in the general population. Systemic signs and symptoms occurred from 2.9 to 61.9% of the MS cases, while neurological signs and symptoms occurred in 9.4 to 76.4% of the NPSLE ones. The motor, visual, and mental systems were the most affected in both diseases. The BDI in NPSLE had higher scores and the BAI in MS. **Conclusions**: The functional impairments in NPSLE were similar to those of MS, although greater impairment of the functional systems of cerebellar, sensitivity, and sphincters occurred in MS cases, and greater symptoms of depression, anxiety, and headache also occurred in it.

Key words: lupus erythematosus, systemic, multiple sclerosis, medical records, neurologic examination, depression, anxiety.

RESUMO

Objetivo: Com a finalidade de comparar a síndrome de acometimento da substância branca do lúpus neuropsiquiátrico (LESNP) e a esclerose múltipla (EM), foi proposta uma avaliação demográfica, da história médica e do exame clínico. **Métodos**: Sessenta e quatro pacientes com LESNP e 178 com EM responderam a um questionário para avaliar o sistema funcional, a expanded disability status scale (EDSS), o Beck depression inventory (BDI) e o Beck anxiety inventory (BAI). **Resultados**: A prevalência de doenças autoimunes e consciência alterada foi semelhante em ambos os grupos, mas foi superior comparada àquela da população geral. Sinais e sintomas sistêmicos ocorreram em 2,9 a 61,9% dos casos de EM, enquanto sinais e sintomas neurológicos foram encontrados de 9,4 a 76,4% na LESNP. Os sistemas motor, visual e mental foram os mais afetados nas duas doenças. O BDI foi superior em LESNP e o BAI na EM. **Conclusões**: As alterações funcionais em pacientes com LESNP foram similares às encontradas na EM, embora tenha ocorrido maior incapacidade dos sistemas funcionais cerebelar, de sensibilidade e dos esfíncteres na EM, sintomas depressivos, de ansiedade e cefaleia, também foram superiores.

Palavras-Chave: lúpus eritematoso sistêmico, esclerose múltipla, registros médicos, exame neurológico, depressão, ansiedade.

Neuropsychiatric systemic lupus erythematosus (NPSLE) is an entity involving the nervous system and the systemic lupus erythematosus (SLE). The American College of Rheumatology (ACR)[1] has subdivided this into 19 syndromes. The prevalence of NPSLE in the world literature ranges from 10 to 80%[2-9], and involvement of the central nervous system (CNS) occurs in 80 to 90% of all cases[10]. One of the least known and rarest syndromes is the white matter syndrome[11].

When CNS involvement is the first clinical presentation of SLE and magnetic resonance imaging (MRI) shows

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demyelinating lesions, there may be a dilemma regarding the differential diagnosis with multiple sclerosis (MS)[12]. While systemic manifestations are the typical manifestation of SLE, MS is characterized by involvement of the CNS. Nevertheless, some recent data have shown a group of MS patients who have systemic signs and symptoms[13-17], and this may lead to difficulty and delay in diagnosing MS within ten years[11,16,17].

The features common to these two diseases include the facts that they: are autoimmune, more prevalent in women, affect young adults more frequently, present a relapse-remitting clinical course and their immunopathological mechanisms overlap, due to participation of the class II molecular histocompatibility complex (MHC).

The present study was designed bearing in mind the diagnostic difficulties in clinical practice, regarding two diseases that overlap and may have similar comorbidities. The aim in the present study was to compare a population of patients with NPSLE with another of MS ones, who were seen at the university hospital of the Federal University of Goiás Medical School. This study was carried out by assessing the personal and family medical histories, the neurological examination, the possible comorbidities, and the existence of appropriate markers that might help in the differential diagnosis of these two diseases.

METHODS

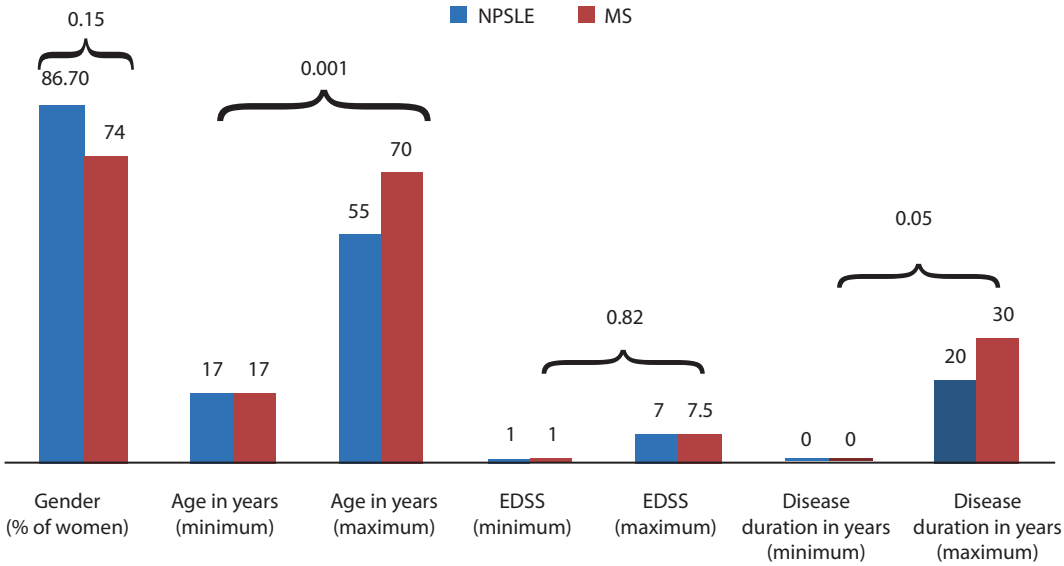
This study included 178 patients with MS and 64 with NPSLE who were attended at the Departments of Neurology and Rheumatology of the university hospital of the Federal University of Goiás Medical School, in Goiânia, Goiás, Brazil. The diagnosis of SLE was established in accordance with the ACR classification criteria[1], while the MS diagnosis was established in accordance with the 2005 version of the McDonald criteria[18]. The present study was approved by the institution's Research Ethics Committee. The evaluations were carried out by means of a questionnaire that asked for personal and family history data, another one on general and neurological symptoms, a neurological examination assessing functional systems, the expanded disability status scale (EDSS), and the Beck anxiety and depression inventories (BAI and BDI) to evaluate symptoms of depression and anxiety[19,20]. Regarding statistical analysis, the Mann-Whitney test was used for numerical variables, while the χ^2 and Fisher's exact tests were used for categorical variables. The statistical software used was SPSS, version 17.0, and results were taken to be statistically significance if $p \leq 0.05$.

RESULTS

The results are presented in Figure and in Tables 1 to 5. Figure shows the distribution of the patients according to disease type, with regard to gender, age, EDSS, and disease duration. Table 1 lists the personal and family history data. Table 2 presents the systemic and neurological signs and symptoms. Data on the states of depression and anxiety can be seen in Tables 3 and 5, and Table 4 shows the functional system assessment.

The demographic variables of this study appointed that the current age and disease duration were both greater for MS patients.

The systemic manifestations showed differences in relation to the following variables: skin, lungs, heart, kidney, hematological tests, hypersensitivity to sun exposure, joint pain, and inflammation. All of these were



NPSLE: neuropsychiatric lupus; MS: multiple sclerosis; EDSS: expanded disability status scale.

Figure. Demographic distribution according to disease type (neuropsychiatric lupus or multiple sclerosis), in relation to age, expanded disability status scale, and disease duration, among patients in Goiânia and in the surrounding areas.

higher in patients with NPSLE, but they did not have all the systemic symptoms and signs (range from 34.5 to 68.3%). The most important manifestations were: joint pain (arthralgia), hematological disorders, joint inflammation (arthritis), and hypersensitivity to sun exposure. Systemic symptoms and signs were present in 2.9 to 61.9% of the MS patients, and the most important of these were: joint pain (arthralgia), hypersensitivity to sun exposure, and joint inflammation (arthritis).

Regarding variables related to neurological signs and symptoms, there were significant differences in visual disorders, sensitivity disorders, abnormalities of coordination, walking and movements, and speech and swallowing dysfunction. All of these were greater in patients with MS.

There was no significant difference regarding personal and family history, except for symptoms of depression, anxiety, psychosis and other psychiatric diseases, which were all greater in patients with MS.

Table 1. Distribution of data related to personal and familiar history according to disease type (neuropsychiatric lupus or multiple sclerosis) for age, expanded disability status scale and disease duration, among patients in Goiânia and in the surrounding areas.

Data	NPSLE (n=47)	%	MS (n=110)	%	p-value
Personal					
Psoriasis	02	4.5	01	0.9	0.09
Diabetes	02	4.5	07	6.3	0.29
Neurological disease	00	0.0	05	5.5	0.15
Hematological disease	03	6.8	07	6.4	0.32
Familiar					
Relative with psoriasis	03	6.4	10	9.1	0.29
Relative with diabetes	17	38.6	48	43.6	0.23
Relative with lupus	06	13.6	10	9.1	0.32
Relative with arthritis	07	15.9	32	29.1	0.20
Relative with neurological diseases	09	20.5	45	40.9	0.14
Relative with hematological diseases	05	11.4	12	10.9	0.32

NPSLE: neuropsychiatric lupus; MS: multiple sclerosis.

Table 2. Systemic and neurological signs and symptoms in patients with neuropsychiatric lupus and multiple sclerosis in the sample from Goiânia and surrounding areas.

Signs and symptoms	NPSLE (n=55)	%	MS (n=105)	%	p-value
Skin disorders	23	41.9	11	10.5	0.00
Hypersensitivity to sun	31	56.4	35	33.3	0.00
Mucosal disease (mouth sores)	19	34.5	25	23.8	0.15
Joint pain (arthralgia)	45	81.9	65	61.9	0.01
Joint inflammation (arthritis)	31	56.4	26	24.8	0.00
Lung disorders	15	27.3	03	2.9	0.00
Heart disorders	13	23.6	06	5.7	0.00
Hematological disorders	27	68.3	21	17.1	0.00
Renal disorders	25	49.1	18	20.0	0.00
Headache	26	38.2	60	73.3	0.23
Consciousness disorders	21	47.3	77	57.1	0.27
Visual disorders	23	41.8	85	81.0	0.00
Sensitivity disorders	27	49.1	85	81.0	0.00
Strength disorders	42	76.4	78	74.3	0.50
Coordination disorders	21	38.2	52	49.5	0.00
Balance disorders (vertigo)	21	38.2	21	20.0	0.17
Urinary incontinence	17	30.9	44	41.9	0.12
Urinary retention	17	30.9	68	64.8	0.17
Walking disorders	24	43.6	60	57.1	0.01
Movement disorders	16	29.1	40	38.1	0.00
Speech disorders	10	18.2	42	40.0	0.01
Swallowing disorders	09	16.4	16	15.2	0.00
Olfactory disorders	05	9.4	15	14.3	0.31
Taste disorders	06	11.3	60	57.1	0.60

NPSLE: neuropsychiatric lupus; MS: multiple sclerosis.

Table 3. Depression and anxiety symptoms and other psychiatric disorders in patients with neuropsychiatric lupus and multiple sclerosis and in their relatives, in the sample from Goiânia and surrounding areas.

Depression, anxiety symptoms, and other psychiatric disorders	NPSLE (n=56)	%	MS (n=108)	%	p-value
Personal depressive symptoms	16	30.4	66	61.1	0.00
Personal anxiety symptoms	39	84.8	88	81.5	0.62
Other personal psychiatric conditions	27	34.5	25	23.8	0.15
Personal psychosis	01	2.2	14	12.9	0.04
Depression symptoms in the family	10	21.7	54	50.0	0.00
Anxiety symptoms in the family	19	41.3	62	57.4	0.07
Other psychiatric conditions in the family	07	15.2	45	41.7	0.00
Psychosis in the family	00	0.00	09	8.3	0.04

NPSLE: neuropsychiatric lupus; MS: multiple sclerosis.

Table 4. Neurological examination according to functional system in patients with neuropsychiatric lupus and multiple sclerosis, in the sample from Goiânia and surrounding areas.

Score on the functional scale (mean)	NPSLE (n=61)	SD	MS (n=118)	SD	p-value
Pyramidal functions	1.93	1.39	2.23	1.18	0.14
Sensorial functions	0.99	1.04	1.46	1.11	0.01
Cerebellum functions	0.53	0.68	0.97	1.03	0.00
Brainstem functions	1.02	1.16	0.98	1.15	0.86
Intestinal or bladder functions	0.46	1.31	1.14	1.31	0.00
Visual functions	1.42	1.56	1.54	1.52	0.63
Mental functions	1.32	1.75	1.52	0.89	0.19

NPSLE: neuropsychiatric lupus; MS: multiple sclerosis; SD: standard deviation.

Table 5. Depression and anxiety symptoms assessed using Beck depression and anxiety inventories in patients with neuropsychiatric lupus and multiple sclerosis, in the sample from Goiânia and surrounding areas.

Depression and anxiety symptoms	NPSLE (n=56)	%	MS (n=108)	%	p-value
BDI 21					
Minimum	07	17.5	18	35.3	0.001
Mild	06	15.0	17	33.3	
Moderate	11	27.5	14	27.5	
Severe	16	40.0	02	3.9	
BDI 13	18	45.0	25	48.0	0.81
BAI					
Minimum	14	36.8	06	12.0	0.02
Mild	08	21.1	19	38.0	
Moderate	16	42.1	25	50.0	

NPSLE: neuropsychiatric lupus; MS: multiple sclerosis; BDI: Beck depression inventory; BAI: Beck anxiety inventory.

DISCUSSION

The results from the demographic investigation confirmed the known findings for both diseases, which were more prevalent in young adults and females. The higher average age of MS patients reflected the longer disease duration of MS in relation to NPSLE, in this population.

Neurological involvement may be assessed using functional factors and EDSS scores, however these methods did not show any differences between both diseases. The main deficits were motor (pyramidal), visual and mental, although lack of strength was an important complaint among these patients. Sphincter abnormalities could not be properly assessed in all patients, since 49.1% of the NPSLE patients presented kidney disease.

The presence of complaints and general signs in MS patients opens up a discussion regarding the possible existence of a special group of individuals who might have different genetic components.

The clinical manifestations regarding neurological involvement in cerebellar sensitivity and sphincter functions were greater in MS patients.

There were no differences in the prevalence of other autoimmune diseases between MS and NPSLE, although the one of autoimmune diseases among the patients' relatives was higher than in the general population. Headaches and

consciousness disorders also presented higher prevalence than those previously reported[21-28].

Depression, anxiety and psychotic symptoms, as well as other psychiatric conditions, were important for both diseases, but they were seen more in MS patients. This finding may reflect specific neuronal lesions. Interestingly, the BDI 21 results showed that depressive symptoms were more frequent and severe in SLE patients, but when the BDI 13[29] was used, this shorter form did not identify differences between the diseases.

The questions in BDI 13 are related to emotional symptoms: sadness, feelings of failure, hopelessness, anhedonia, guilt, feelings of punishment, unhappiness, self-accusation, suicidal ideation, crying easily, irritability, lack of interest in people, and indecision. The complementary questions, on the other hand, reflect body symptoms: change in body image, difficulties at work, insomnia, fatigue, lack of appetite, weight loss, somatic worries, and lack of libido. It is therefore understandable that patients with SLE, who have more severe body symptoms, will have a higher score when such symptoms are taken into consideration[30].

In conclusion, neuropsychiatric manifestations were important in SLE, and functional system impairments were similar to those of MS cases, although there were differences in terms of greater severity of functional impairment in cerebellar sensory and sphincter systems in MS patients. The prevalence of autoimmune diseases was higher than would be expected for the general population, while the one of depression and anxiety symptoms such as headache was statistically higher in MS cases. The latter finding can theoretically be correlated with pathophysiological process and location of MS lesions, and this may be a subject for future investigations.

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