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ORIGINAL ARTICLE

Subclinical memory dysfunction in Malaysian systemic lupus erythematosus patients: Association with clinical characteristics and disease activity – A pilot study

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KEYWORDS

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Abstract *Aim of the work:* This work aimed to determine the frequency of subclinical memory dysfunction in a group of Malaysian systemic lupus erythematosus (SLE) patients and to study its relation to clinical characteristics, laboratory investigations and disease activity.

Patients and methods: Fifteen SLE patients attending the Universiti Kebangsaan Malaysia Medical Centre (UKMMC) and not known to have neuropsychiatric lupus were recruited. These patients were assessed using the Wechsler Memory Scale. Disease activity was assessed using the SLE disease activity index 2000 (SLEDAI-2K).

Results: The median age of the patients was 28 years (25–37 years) and they were 14 females and one male. Their median disease duration was 9.3 years (4.8–10 years). Their median SLEDAI-2K was 4 (0–6). Memory dysfunction was identified in 7/15 (46.7%) SLE patients and was significantly associated with lower serum thyroxine levels (median 12.27; 11.8–13.3 μg/dl) ($p = 0.027$) compared to those without memory impairment (15.48; 14.39–16.56 μg/dl). Auditory memory impairment was associated with the education level as the auditory memory index was significantly lower in patients with secondary education ($n = 7$, median 88; 86.5–91.5) compared to those who received tertiary education ($n = 8$, median 103; 97.5–119.5) ($p = 0.025$) while visual memory was influenced by disease duration ($p = 0.016$). There was no association between overall memory dysfunction and disease duration, number of relapses, clinical manifestations and SLEDAI-2K scores.

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Conclusion: There is a high frequency of subclinical memory dysfunction among SLE patients. A remarkable association is present with lower thyroxine. Auditory memory impairment is related to the level of education and visual memory to disease duration.

1. Introduction

Systemic lupus erythematosus (SLE) is a systemic chronic autoimmune disease that can affect all organs. The pathogenesis remains elusive and the etiology is multifactorial [1]. Several factors as cytokine overproduction [2,3], oxidative stress [4], matrix metalloproteinase [5] and apoptosis [6] play a considerable role in the development of SLE. The kidney is commonly involved signifying the value of regular screening for early and appropriate management [7]. Comorbidities as dyslipidemia and metabolic syndrome [8,9] could lead to functional disability, impaired quality of life and significantly affect disease activity and damage.

Neurological manifestations are common among SLE patients and these are highly diverse and often have major prognostic consequences. One of the most prevalent neuropsychiatric SLE (NPSLE) manifestations is cognitive dysfunction [10] reported to be as high as 81% [11], while compilation from multiple databases showed that it ranged between 21% and 67% [12]. The most common cognitive impairment in SLE patients is memory dysfunction [10,13]. Memory dysfunction in SLE patients was found to be associated with multiple risk factors including antiphospholipid antibodies, consistent corticosteroid use, diabetes, higher depression score and lower education level [11]. A contribution of higher disease activity to the development of memory impairment has been reported [12].

Memory functioning generally refers to the ability to retain learned information over time and is one of several primary domains of cognitive ability typically evaluated in the context of a comprehensive neuropsychological assessment [14,15]. It is important to note that memory is typically viewed as a group of related abilities based on the duration of time that information is retained (short vs. Long term) and the content that is stored [15–17]. Furthermore, memory is also composed of multiple processes which include encoding, storage and retrieving which are typically linear in progression. Any defect in any of these steps will impair memory functioning and each of these must be assessed in order to provide a comprehensive understanding of a patient's memory functioning [15,18].

The Wechsler Memory Scale (WMS) is a battery of subtests frequently administered in a neuropsychological assessment [19] and is designed to evaluate multiple aspects of learning and memory. Since the first edition that was published in 1945 [20], it has been repeatedly revised and updated to the current 4th edition (WMS-IV). Administration of this new edition in its entirety generates primary index scores for immediate and delayed memory as well as secondary indexes of visual working memory, auditory memory and visual memory [21]. In the 4th edition, only three out of seven subtests were retained from the previous version whereas the remaining four tests are new. There are no data as regards this vital aspect in our local SLE population. The aim of this study was to determine frequency of subclinical memory dysfunction in a group of Malaysian SLE patients and to study its relation to clinical characteristics, laboratory investigations and disease activity.

2. Patients and methods

This was a cross-sectional study which recruited SLE patients from both the Rheumatology and Nephrology/SLE clinics at the Universiti Kebangsaan Malaysia Medical Centre (UKMMC) (Grant: FF-260-2012) and not known to have history of neuropsychiatric lupus. The SLE patients fulfilled the American College of Rheumatology revised classification criteria [10] and were >18 years old. An SLE disease activity index-2000 (SLEDAI-2K) was calculated for the studied patients [22]. All patients were administered the Wechsler Memory Scale-4th edition UK version (WMS-IV^{UK}) questionnaire [23] by the researcher. This study was approved by the UKMMC Medical Research and Ethics Committee (MREC) with the research code, FF-260-2012 and all the included patients gave an informed consent.

The Wechsler Memory Scale-4th edition (WMS-IV) is an individually administered battery of tests designed to assess memory functioning in individuals aged 16–90 [23]. It is developed and published by Pearson Education Inc. It is organized into five main memory index scores: auditory, visual, visual working, immediate and delayed memory indices. These index scores are scaled on a metric mean of 100 ± 15. An index score of less than 90 in any main category is considered to be below normal, and defined as memory impairment.

2.1. Statistical analysis

Demographic data of participants were recorded and charted accordingly. Data were analyzed using SPSS version 20.0. All numerical data were subjected to normality testing using Kruskal–Wallis Analysis. Data were analyzed using non-parametric tests and expressed as median with interquartile range (IQR). For categorical data, chi-square with Yate's correction was used and for non-categorical data, Mann–Whitney U and Kruskal–Wallis tests were used. A p-value of $\leqslant 0.05$ was considered significant.

3. Results

Fifteen SLE patients with a median age of 28 years (25–37 years), 14 females and 1 male with disease duration of 9.3 years (4.8–10 years) were included. The sociodemographic data, level of education and comorbidities of the patients are presented in Table 1.

There was no association between overall memory dysfunction and duration of SLE, number of relapses, number of major systems involvement and SLEDAI-2K scores as shown in Table 2. However, visual memory was influenced by disease