Clinical manifestations of neuropsychiatric systemic lupus erythematosus in Polish patients: a single centre study from West-Pomeranian Region of Poland

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Clinical Manifestations of Neuropsychiatric Systemic Lupus Erythematosus in Polish Patients. A single centre study from West-Pomeranian Region of Poland.

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Short title: Clinical Manifestations of NPSLE in Polish Patients.

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Introduction: Systemic lupus erythematosus (SLE) is an autoimmune disease, causing systemic inflammation and organ failure through loss of tolerance to autoantigens and the formation and accumulation of immune complexes in tissues and organs. The prevalence of SLE is different among different regions of the world [1]. Neuropsychiatric systemic lupus erythematosus (NPSLE) is a currently poorly understood manifestation of SLE. NPSLE is associated with high mortality [2]. It may occur regardless of SLE activity and without serological activity [3]. There are large discrepancies in the available literature regarding the prevalence of NPSLE – ranging from 14% to over 80% in adults [4]. Almost 20 years ago, the American College of Rheumatology defined 19 neurological syndromes covering both the central and peripheral nervous system on the basis of which the neuropsychiatric form of SLE is diagnosed to this day. The central nervous system syndromes include aseptic meningitis, cerebrovascular disease, demyelinating syndrome, headache, movement disorder, myelopathy, seizures, acute confusional state, anxiety disorder, cognitive dysfunction, mood disorder, and psychosis. The peripheral nervous system syndromes include cranial neuropathy, acute inflammatory demyelinating polyradiculoneuropathy, autonomic disorder, single/multiplex mononeuropathy, myasthenia gravis, plexopathy, and polyneuropathy [5]. However, neurological syndromes may overlap in the same patient or completely new syndromes may appear which are not included in the ACR classification [6]. Despite numerous studies in this field, the actual prevalence of NPSLE in the world population, as well as the reported prevalence of specific NPSLE-defining symptoms, are still unclear. Given this and the lack of data on the prevalence of neuropsychiatric symptoms in the Polish population, the aim of this publication was to investigate the configuration of neuropsychiatric symptoms in patients with NPSLE.
Patients and Methods:
The study involved 154 adult patients diagnosed with NPSLE, hospitalized at the Department of Rheumatology, Pomeranian Medical University in Szczecin. The control group consisted of 133 additional post-traumatic patients with multiple traumas but without evidence of central nervous system injury, hospitalized at the Emergency Department of the Public Hospital no. 1 in Szczecin who had neither SLE nor NPSLE. Data concerning neuropsychiatric symptoms were collected from all patients. Data were collected using a binary system, 0 – no symptom, 1 – present symptom. The study was approved by the bioethics committee of the Pomeranian Medical University in Szczecin (KB-0012/120/04/19).

Statistics:
In order to compare characteristics of NPSLE patients with non-NSPLE patients, Fisher Exact Test (qualitative data) and Mann-Whitney Test (quantitative data) were applied. In addition, univariable and multivariable logistic regression models were calculated for assessing the odds ratio of selected risk factors of NPSLE incidence among NPSLE patients and non-NSPLE patients (p<0.05 was considered to indicate statistical significance). All calculations were performed in R statistical environment (R Version 3.4.4 2018-03-15).

Results:
Analysis of neuropsychiatric symptoms in patients with NPSLE and patients without NPSLE.
Based on univariable and multivariable logistic regression models, it was observed that in the group of NPSLE patients compared to non-NPSLE patients, more people experienced headache (OR=16.15, p<0.001; OR=11.53, p<0.001), cognitive impairment (OR=7.59, p<0.001; OR=3.06, p=0.01), depression (OR=10.87, p<0.01; OR=3.43, p<0.01), cerebrovascular event (OR=7.18, p<0.01; OR=9.75, p<0.01) and seizures (OR=6.84, p<0.01; OR=12.57, p<0.01) (Table 1).
Discussion:  
Our analysis shows that the risk of NPSLE is particularly high in individuals with: headache (OR=16.15, p<0.001; OR=11.53, p<0.001), cognitive impairment (OR=7.59, p<0.001; OR=3.06, p=0.01), depression (OR=10.87, p<0.01; OR=3.43, p<0.01), cerebrovascular event (OR=7.18, p<0.01; OR=9.75, p<0.01) and seizures (OR=6.84, p<0.01; OR=12.57, p<0.01).

Headache is an extremely common condition in the general population. It is also one of the most frequently reported complaints by patients with SLE. However, several studies have not confirmed that the incidence of headache in SLE patients is higher than in the general population. In our analysis, headache was the most common neurological manifestation reported by patients with NPSLE which is also confirmed by other studies [7,8].

The prevalence of cerebrovascular events in NPSLE patients in our study was higher than in previous studies [9,10]. This may be due to our binary data collection system, which did not take into account the division of cerebrovascular events into ischemic, hemorrhagic, and venous arterial incidents (some studies allow for just one category of these incidents).

Cognitive assessment of SLE patients may vary over time. Changes in cognitive function may be temporary and not clearly related to SLE activity. Assessment of cognitive function in individuals with SLE requires careful clinical judgement, in which consideration should also be given to other factors and disorders, such as depression, that may be triggering or exacerbating these disorders. In our study, the prevalence of cognitive impairment in NPSLE patients was similar to the results of other studies [11,12].

Patients with SLE may also suffer from seizures. These are usually generalised, although sometimes focal seizures may also be present. In our analysis, 13.6% of patients with NSPLE had epilepsy, which is in the range of the reported prevalence of epilepsy in SLE patients in other studies [9,10].
Depression is a common disease in the general population. However, it is more frequently observed in chronic disease patients. Approximately 15% of SLE patients exhibit depressive disorders. This is confirmed by our study in which depression was the second most prevalent NPSLE symptom after headaches.

Our study was subject to certain limitations, which must be taken into account. This was a single center retrospective study, with a limited number of NPSLE patients. We selected only the most common NPSLE symptoms. Further prospective studies with a larger sample size are needed.

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REFERENCES:


Table 1. Analysis of risk factors of Neuropsychiatric lupus.
Status = 1 – diseased (NPSLE); Status = 0 – healthy (no NPSLE)

<table>
<thead>
<tr>
<th>Factors</th>
<th>Status</th>
<th>Univariable Logistic Regression Models</th>
<th>Multivariable Logistic Regression Model *</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NPSLE (n = 154)</td>
<td>No NPSLE (n = 133)</td>
<td>OR</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td>0.98</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>10 (6.5%)</td>
<td>8 (6%)</td>
<td>1.09</td>
</tr>
<tr>
<td>F</td>
<td>144 (93.5%)</td>
<td>125 (94%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>134 (87%)</td>
<td>39 (29%)</td>
<td>16.15</td>
</tr>
<tr>
<td>no</td>
<td>20 (13%)</td>
<td>94 (71%)</td>
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</tr>
<tr>
<td>Cognitive impairment</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>yes</td>
<td>86 (56%)</td>
<td>19 (14%)</td>
<td>7.59</td>
</tr>
<tr>
<td>no</td>
<td>68 (44%)</td>
<td>114 (86%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Depression</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>97 (63%)</td>
<td>18 (13.5%)</td>
<td>10.87</td>
</tr>
<tr>
<td>no</td>
<td>57 (37%)</td>
<td>115 (86.5%)</td>
<td>1.0</td>
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<tr>
<td>Cerebrovascular event</td>
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<td>yes</td>
<td>39 (25%)</td>
<td>6 (4.5%)</td>
<td>7.18</td>
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<tr>
<td>no</td>
<td>115 (75%)</td>
<td>127 (95.5%)</td>
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<tr>
<td>Seizures</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>21 (13.6%)</td>
<td>3 (2.3%)</td>
<td>6.84</td>
</tr>
<tr>
<td>no</td>
<td>133 (86.4%)</td>
<td>130 (97.7%)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

* Full adjusted model; Independent variables: Age(Quantitative); Sex(F/M); Headache(yes/no);
Cognitive impairment(yes/no); Depression(yes/no); Cerebrovascular event(yes/no);
Seizures(yes/no).