Clinical Features and Outcomes of Neuropsychiatric Systemic Lupus Erythematosus

PARISA DELKASH
RHEUMATOLOGIST
SBMU
Neurologic Disorder

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- Seizures
- Psychosis
- Mononeuritis multiplex
- Myelitis
- Peripheral or cranial neuropathy
- Acute confusional state
  in the absence of other causes
**EULAR/ACR**

- **Delirium (2 points)**
  - Characterized by:
    1) Change in consciousness or level of arousal with reduced ability to focus
    2) Symptom development over hours to < 2 day
    3) Symptom fluctuation throughout the day
    4) Either:
      - (4a) acute/subacute change in cognition (e.g., memory deficit or disorientation), or
      - (4b) change in behavior, mood, or affect (e.g., restlessness, reversal of sleep/wake cycle)

- **Seizure (5 points)**
  - Primary generalized seizure or partial/focal seizure

- **Psychosis (3 points)**
  - Characterised by 1) delusions and/or hallucinations without insight and 2) absence of delirium
Female 180 (92.8)

Age (years) 29.8 ± 10.8

SLE duration (years), mean ± SD 3.09 ± 4.40

NP duration (years), mean ± SD 2.78 ± 4.16

>1 NP subtype 71 (36.6) Subtypes of NPSLE
Central nervous system involvement 184 (94.8)
- Seizure 71 (36.6)
- Acute confusional state 49 (25.3)
- Cerebrovascular disease 30 (15.5)
- Headache 27 (13.9)
- Psychosis 22 (11.3)
- Cognitive impairment 19 (9.8)
- Mood disorder 17 (8.8)
- Demyelination 6 (3.1)
- Dyskinesia 1 (0.5)
- Myelitis 5 (2.6)
- Aseptic meningitis 4 (2.1)
- Anxiety disorder 3 (1.5)
- Peripheral nervous system involvement 21 (10.8)
- Cranial neuropathy 8 (15.5)
- AIDP 3 (1.5)
- Single/multiplex mononeuropathy 5 (3.6)
- Polyneuropathy 5 (4.1)
- Increased CSF pressure 73 (37.6)
- Increased CSF protein 78 (40.2)
NPSLE ranges from 12.2% to 94.7% for SLE patients.

This wide range is probably due to the high variability of NP presentations and differences in study designs.

36.6% had more than one NP subtype.

The diversity and heterogeneity of NP presentations suggest that multiple pathogenetic mechanisms are involved in NPSLE.
Nervous system involvement is common in SLE and is a major cause of morbidity and mortality.

Seizure is predictive of poor prognoses for SLE.

NPSLE leads to a decline in the quality of life and can be life threatening.

In this study, NP syndromes usually occurred within 3 years after onset of SLE.

NPSLE commonly occurs in young and middle-aged patients, and it often occurs during the early stage of SLE.
most common manifestations were *seizure* (36.6%)
Acute *confusional* state (25.3%)
cerebral *vascular* disease (15.5%)
*headache*, and *psychosis*
Pathways involved in NPSLE development, including antibodies, cell-related inflammation, cytokine-related inflammation, and complement activity.

Pathogenesis of seizure in SLE is not clear; may be multifactorial. Systemic inflammation, focal microvascular brain injuries, infarction, direct auto-antibody effects on neuronal networks, and/or APS may all have a role.
presence of active disease and the presence of circulating autoantibodies are major risk factors for NP events.

Risk factors for seizures in SLE include disease activity, female sex, race, aPL level, and younger age positive anti-β2GP1.

NP manifestations and antiphospholipid antibody positivity is believed to be associated with cerebrovascular events.
Compared with the non-NPSLE group, NPSLE patients were significantly more likely to have typical lupus symptoms.

- Higher Disease Activity Index
- Positive rate of anti-ribosomal P protein antibodies
- NPSLE significantly decreased survival rates of SLE patients.
- Patients with elevated serum creatinine, hypocomplementemia and SLEDAI - 2K scores $\geq 15$ had shorter survival periods.
NPSLE patients had a significantly higher likelihood of also having malar rash, oral ulcer, alopecia, arthritis, serositis, renal disorder, fever.

Leukopenia, thrombocytopenia- and hypocomplementemia significantly more frequently occurred in NPSLE patients.

Thrombocytopenia was significantly and strikingly correlated with NP involvement in SLE patients.

SLEDAI score of NPSLE patients with seizure was significantly higher.

Anti-RibP is more specifically associated with specific NPSLE manifestations, CNS involvement, depression, and psychosis.
ESR and CRP levels of NPSLE group were significantly higher.

Positive rate of anti-β2GP1 antibodies for seizure patients was higher.

But the positive rates of the anti-Sm antibodies and anti-SSB antibodies in the NPSLE group were significantly lower.
Other anti-bodies, such as autoantibodies to NMDA receptor subunit NR2 (anti-NR2) and anti-glucose-regulated protein 78 (anti-GRP78) have been associated with the development of diffuse NPSLE.

Presence of anti-NMDA in CSF but not in serum is associated significantly with overwhelming CNS abnormalities, suggesting the importance of direct access of autoantibodies to brain dysfunction.

It may be advantageous to have more sensitive antigens to allow for earlier detection and treatment.
Several cytokines have been preliminarily proven to be related to NPSLE, including type I IFN receptor inhibition, macrophage colony-stimulating factor 1 receptor (CSF1R), and Bruton tyrosine kinase (BTK) inhibitor.
MRI is still the most commonly used imaging technique for the detection and evaluation of NPSLE in clinical practice. MRI analysis; 61.0% had abnormal results. Small vessel disease was the most common abnormal finding, followed by inflammatory-like lesions and large vessel disease.
studies showed that the prevalence of inflammatory lesions ranged from 0% to 38.1%

more than 30% of NPSLE patients had normal cranial MRI results. Nearly half of the abnormal MRI results showed WMH (white matter hyperintensities), mainly involving the frontal lobe and parietooccipital lobe.

inflammatory lesions may be related to cerebral vasculitis in SLE patients, which can be diffuse or have focal distribution, and the large and small arteries can be involved.
white matter hyperintensities (78.0%) mainly focal and most often involved the frontal lobe

- lumen infarction (6.0%)
- subcutaneous infarction (14.0%)
- microhemorrhage on MRI (12%)
- brain atrophy (38.0%)
patients with inflammatory lesions and LVD had shorter survival periods and independent prognostic factors of death.

A correlation between inflammatory lesions and clinical features was not found in this study, but the survival rate of patients with inflammatory lesions on MRI was significantly reduced.

abnormal cranial MRI results are poor prognostic factors for patients with diffuse NPSLE
Lumbar puncture and CSF examinations
- elevated CSF pressure (37.6%)
- elevated CSF protein levels (40.2%)
High disease activity and positive rate of anti-ribosomal P protein antibodies may be risk factors for NPSLE.

NPSLE decreases survival rates of SLE patients.

Renal insufficiency and high disease activity are predictive of poor prognoses for NPSLE patients.

Abnormal cranial MRI results are poor prognostic
The main causes of death were infection (37.5%), SLE-related causes 31.25%:
  - pulmonary hypertension
  - nervous system involvement
  - sudden cardiac death
  - unknown cause (31.25%)