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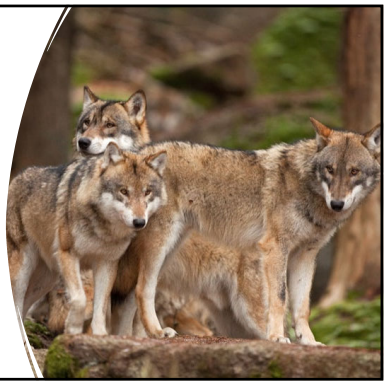
FUN FACT

LUPUS IS A LATIN WORD MEANING

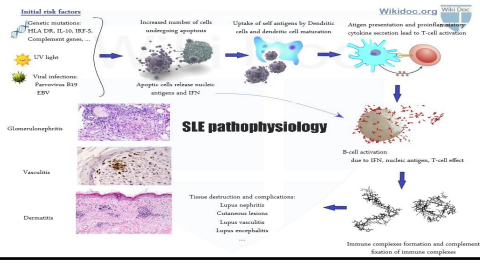
- TIGER
- SHEEP
- WOLF
- DOG

Lupus derives its name from the Latin word for wolf, and early descriptions of this disease used the term to describe the facial lesions that look like a wolf's bite.

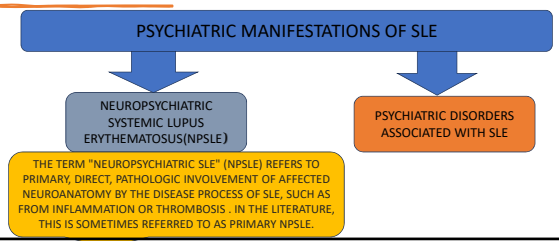


INTRODUCTION AND PATHOPHYSIOLOGY

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease with a wide range of clinical presentations resulting from its effect on multiple organ systems.



CLASSIFICATION OF PSYCHIATRIC MANIFESTATIONS



NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS (NPSLE) ACR CRITERIA 2001 REVISION

12 CENTRAL NERVOUS SYSTEM MANIFESTATIONS

Aseptic meningitis	Acute confusional state	Anxiety disorder	Cerebrovascular disease	Cognitive dysfunction
Demyelinating syndromes	Headaches	Movement disorder	Mood disorder	Myelopathy
Psychosis	Seizure			

NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS (NPSLE) ACR CRITERIA 2001 REVISION

7 PERIPHERAL NERVOUS SYSTEM MANIFESTATIONS

Mononeuropathy	Autonomic disorder	Cranial neuropathy	Myasthenia gravis
Plexopathy	Acute inflammatory demyelinating polyneuropathy	Polyneuropathy	

COGNITIVE DYSFUNCTION IN NPSLE (BRAIN FOG)

- Immune system dysregulation
- Breach in blood Brain barrier
- Neuroinflammation
- Disruption of neural circuits leading to cognitive dysfunction

TYPES OF COGNITIVE DYSFUNCTION IN NPSLE

Impairment in executive function

- Impairment in executive function is a hallmark of cognitive dysfunction in SLE.
- Impairment in executive functions includes difficulties with planning, organization, decision-making, and problem-solving.
- Patients may struggle with tasks that require multi-step processes or complex decision-making.

Memory Impairment

- Patients may experience difficulty with short-term memory, including forgetting recent conversations or tasks.
- Long-term memory can also be affected, leading to difficulty recalling past events.

Attention and Concentration Deficits

- Patients may struggle to focus on tasks, sustain attention, and filter out distractions.
- These deficits can impact academic, work, and social activities.

DIAGNOSIS OF COGNITIVE DYSFUNCTION

Neuropsychological testing involves battery of tests that evaluate various cognitive functions which helps identify specific cognitive deficits and their severity.

Brief screening tools can provide a quick assessment of cognitive function. Examples include the Montreal Cognitive Assessment (MoCA) and the Mini-Mental State Examination (MMSE).

Neuroimaging is indicated to evaluate for evidence of a structural cause, including one that may be separate from or comorbid with SLE, particularly if impairments are interfering with function or are progressive.

CSF examination is not typically performed to evaluate cognitive deficits, but it should be considered if the deficits develop acutely or are rapidly progressive or occur in the context of other concerning focal neurologic signs or symptoms.

MANGEMENT OF COGNITIVE DISORDERS IN NPSLE

A multidisciplinary approach involving rheumatologists, neurologists, and other specialists is crucial.

Cognitive rehabilitation programs and interventions can also improve cognitive abilities and coping skills.

Educate patients about the cognitive symptoms associated with NPSLE to facilitate early recognition and intervention.

Provide strategies for managing cognitive difficulties in daily life.

Encourage patients to seek support from family, friends, and support groups.

MOOD DISORDERS IN NPSLE

Mood disorders are neuropsychiatric manifestations characterized by disturbances in emotional state and mood regulation. In NPSLE, mood disorders such as depression and anxiety can be prevalent and significantly impact patient well-being. In one meta-analysis, the prevalence of major depression in SLE was 24 percent and anxiety 37 percent.

Depression is one of the most common neuropsychiatric manifestations in NPSLE.

Anxiety is another common mood disorder in NPSLE. It can coexist with depression or occur independently.

MOOD DISORDERS IN NPSLE

The relationship between NPSLE and mood disorders is bi-directional. Active SLE disease can worsen mood disorders, and mood disorders can exacerbate SLE symptoms.

Neuroinflammation and immune dysregulation underlie mood disorder like other NPSLE manifestations.

Anxiety and depression severity in NPSLE have some association with hemodynamic and functional connectivity changes of the brain frontolimbic neural circuit but not detectable by conventional brain MRI (cMRI)in most of the cases. Some studies suggest resting-state functional MRI (rs-fMRI) which is a noninvasive imaging technique using blood oxygenation level–dependent (BOLD) signal shows defect in perfusion and connectivity.

MANAGEMENT OF MOOD DISORDERS

Pharmacological Interventions:

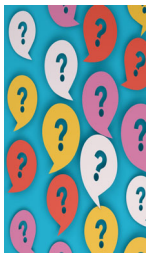
- Antidepressants, such as SSRIs, and anxiolytics, such as benzodiazepines, can be prescribed according to the standard indications in primary psychiatric disorders. Escitalopram, fluoxetine, and paroxetine are reportedly effective in cases of depression associated with lupus
- Medications should be carefully chosen, considering potential interactions with other NPSLE treatments.

Cognitive-behavioral therapy (CBT) and other forms of psychotherapy help patients develop coping strategies for mood symptoms.

Regular exercise has been shown to have positive effects on mood and overall well-being in NPSLE patients.

Mindfulness, relaxation exercises, and stress reduction techniques can help alleviate anxiety and depression.

ACUTE CONFUSIONAL STATE



Acute confusional state is uncommon psychiatric manifestations that had been reported in 4%~7% of lupus patients. It is a diffuse neurological dysfunction that is characterized by acute-onset and fluctuating level of consciousness, disorientation, diminished ability to focus attention, mood disturbances, and cognitive impairment. It is equivalent to delirium according to the Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (DSM-5).

The severity could vary widely from mild confusion and mildly disturbed attention to profound disorganization with agitation and hallucinations.

MANAGEMENT OF ACUTE CONFUSIONAL STATE

Acute confusional state in lupus patients should be differentiated with other causes, such as CNS infection, metabolic abnormalities, or adverse effect of corticosteroids. Altering the corticosteroid dosage was a prompt and beneficial manner to differentiate between acute confusional state due to lupus and corticosteroid-induced delirium.

Acute confusional state associated with lupus treatment includes corticosteroid with antipsychotics, such as low-dose haloperidol (under 3 mg per day) or atypical antipsychotics, including risperidone, olanzapine, and quetiapine.

In refractory cases, cyclophosphamide, plasma exchange, and rituximab are reported to be effective.

SLE-RELATED NEUROINFLAMMATORY PROCESS, SO-CALLED "LUPUS PSYCHOSIS"

Psychosis could affect 2%~11% of lupus patients. 3 main features are:

Hallucinations: auditory hallucinations are common, but visual and tactile hallucinations can also occur.

Delusions: common are paranoid delusions or grandiose delusions.

Thought Disorders: disorganized thinking, incoherent speech, and difficulty maintaining a logical thought process can occur. Patients may have trouble expressing themselves coherently.

No specific abnormalities are usually noted on brain MRI in these patients; studies are often normal or show nonspecific white matter changes and/or atrophy .CSF examination may be normal or may show evidence of inflammation, such as a pleocytosis, elevated total protein content, elevated IgG index, and the presence of CSF oligoclonal bands, which are unmatched in a corresponding serum sample.

TREATMENT OF LUPUS PSYCHOSIS

In patients with severe symptoms and in whom suspicion for active SLE is high guidelines recommend initiating treatment with high-dose intravenous ("pulse") glucocorticoids along with an evaluation for non-SLE causes.

After non-SLE diagnoses have been excluded, immunosuppressive agents such as cyclophosphamide or mycophenolate can be added as steroid-sparing therapies. Intravenous immunoglobulin (IVIG) and Rituximab have also been used in refractory cases.

Antipsychotic drugs are also often prescribed concurrently to manage. The guidelines suggest that neuropsychiatric manifestations in SLE should be first evaluated and treated as in patients in without SLE, and then it should be co-related with the disease.

CASE HISTORY

A 28-year-old female presented to ER with acute behavioral abnormality associated with insomnia, hearing voices, and aggressive behavior for 3 days. Her mother gave a **history of fatigue , intermittent joint pains and generalized maculopapular rash for past 6 months**. All other 10-point review of system was negative. Past medical, family, surgical and social history was unremarkable. Pertinent positive findings on physical exam were that she was unkempt, restless, and had active auditory hallucinations. She had mild pallor but was afebrile with normal hemodynamic parameters. Examination of other systems didn't find any abnormality clinically. On laboratory examination, she had CBC CMP, UA, TSH WNL except **low hemoglobin of 10.2 gm/dl.** The patient was initially managed with haloperidol injection, later patient was admitted to psychiatry ward and started on Olanzapine 5 mg daily without any appreciable relief.

Highlighted points which should trigger medical consult and further testing?

FURTHER MANAGEMENT

Serology of HIV and neurosyphilis were non-reactive. History of fatigue joints pains and rashes prompted to send anti-nuclear antibody (ANA) profile which was positive in 1:320 dilution along with anti-ds-DNA positive . Cerebrospinal fluid (CSF) analysis was suggestive of lymphocytic pleocytosis and neuroinflammation. CSF was negative for Japanese Encephalitis, cytomegalovirus, herpes simplex virus- 1&2.CRP was elevated up to 106 .Her electroencephalography and MRI brain were normal. Excluding other causes and in view of above clinical findings of anemia, ,skin manifestations, psychosis ANA +, Anti-ds-DNA +, CSF suggesting lymphocytic pleocytosis with underlying SLE [fulfilling > 4/11 of the Systemic Lupus International Collaborating Clinics (SLICC) diagnostic criteria], a diagnosis of CNS Lupus was made.

Pulse therapy of methylprednisolone was started. Psychiatric symptoms started improving by third day During discharge, she was free from any neurocognitive or psychiatric deficits. She was prescribed oral prednisolone tapering dose , tab hydroxychloroquine 200 mg BD, and tab Olanzapine 5 mg OD with instruction of follow-up with Rheumatologist and psychiatrist in 1-2 weeks.

QUESTIONS

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