CASE REPORT

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Neuropsychiatric Systemic Lupus Erythematosus (NPSLE)

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Introduction

Systemic lupus erythematosus (SLE) is a complex autoimmune disease with variable clinical features[1]. Involvement of the nervous system has been recognised ever since the disease was first reported, and may involve both the central and peripheral nervous systems[2]. Neuropsychiatric symptoms affect up to 90% of patients with SLE, with cognitive impairment, headache and mood disorder being the most commonly recognised syndromes[2].

However, findings of neuropsychiatric symptoms in male patients subsequently diagnosed to have SLE is uncommon. Here, we report a case who presented with seizures and behavioural problems and was diagnosed to have SLE. The patient responded to cyclophosphamide and corticosteroid treatment adequately.

Case report

A 29-year-old male presented to emergency department in our hospital with complaints of fever for 10 days, two seizure episodes since evening, followed by altered sensorium.

In the emergency room, the patient was in altered sensorium. He had a 3rd episode of seizure (GTCS) in the emergency room and was managed with appropriate anti-epileptic medication. There was no history of nausea, vomiting, headache, diarrhoea, shortness of breath, chest pain, head trauma or ear discharge.

Patient had history of prolonged fever about 8 months ago and was found to have bilateral pleural effusion which was drained with bilateral inter-costal drainage tube but the exact cause was not ascertained and patient was managed with antibiotics at a tertiary care hospital in New Delhi. His fever reappeared again after 2 months. He had abdominal distention at that time and exploratory laparotomy was done in view of SAIO which was inconclusive (CB-NAAT was also negative). He was managed on antibiotics and discharged from that hospital. He also had inguinal lymphadenopathy in the 2 months, for which biopsy was done but was inconclusive. Serum ANA was also negative at that time.

There was a history of significant weight loss. There was no history of tuberculosis, hypertension or diabetes. He did not have a history of joint pains, oral ulcers, alopecia, or Raynaud's phenomenon.

His vitals were: Pulse rate - 86/min, blood pressure - 116/68 mmHg, respiratory rate - 16/min, SpO2 of 99% at room air and temperature of 103.8° F. General physical examination showed pallor and presence of erythematous rash on bilateral cheeks. On the day of admission, mini-mental state examination (MMSE) was 16/30. There was no sensory involvement in any limb. Cerebellar and meningeal signs were absent. The abdominal examination revealed a midline scar of 11 cm. The respiratory and cardiovascular systems examination was unremarkable.

According to American College of Rheumatology/European League Against Rheumatism classification criteria for SLE, the patient had a score of 25/51[3]. A diagnosis of neuropsychiatric SLE (NPSLE) was thus made.

Table: Laboratory investigations.

Haemoglobin	6.3 g/dl
White cell count	1,280/mm^3
Neutrophils	68%
Lymphocytes	22%
Platelet Count	1,18,000/mm^3
Albumin	2.5 g/dl
Globulin	3.9 g/dl
Alanine aminotransferase	750 U/L
Aspartate aminotransferase	320 U/L
Alkaline phosphatase	239 U/L
Bilirubin (total)	0.41 mg/dl
Creatinine	0.8 mg/dl
Urea	36 mg/dl
Uric acid	6.6 mg/dl
S. electrolytes (Na, K Cl, Ca, Mg, P)	WNL
Thyroid profile	WNL
RBS at presentation	116 mg/dl

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Peripheral blood film	Pancytopenia with microcytic hypochromic anaemia
Bone marrow aspiration	Pancytopenia with myeloid hyperplasia
Bone marrow biopsy	Mild increase in myeloid and megakacytic precursors. Mild decrease in erythroid precursors.
HIV 1,2 , Hepatitis B surface antigen Anti-hepatitis C virus	All non-reactive
Urine Routine and microscopy	Within normal limits
Blood culture and senstivity	No growth after 72 hrs
ESR	85 mm/hr
CRP	Negative
Rapid malaria antigen test	Negative
Dengue IgM, IgG and NS1Ag	All negative
ECG	Sinus tachycardia
COVID-19 RT-PCR (Nasopharyngeal Swab)	Negative
Rectic, count	0.5%
PT/INR	15.9 sec/1.21
USG whole abdomen	Minimal ascites
Mantoux test	Negative
Chest X-ray, HRCT chest, NCCT Head, MRI brain, 2-D Echo	WNL
S. ANA by EIA (positive > 1.2, Equivocal 1 - 1.2, negative < 1)	Positive 4.13
Anti-dsDNA by EIA (positive > 1.1, Equivocal 0.9 - 1.1, negative < 0.9)	Positive 6.1
Urine creatinine/albumin ratio (normal < 30 mg/g)	602.48 mg/g
C3, C4	WNL
APLA IgM, APLA IgG	Negative

The patient was manged with intravenous methylprednisolone 1,000 mg OD for 3 consecutive days. Subsequently we started oral methylprednisolone, in tapering doses, and Cyclophosphamide pulse of 1 gm IV with Mesna 600 mg, hydroxychloroquine, anti-psychotics, anti-epileptics, haematinics, proton pump inhibitor, calcium and vitamin D. His neuropsychiatric symptoms subsided, fever settled over next 3 days and MMSE improved significantly from 16/30 to 24/30 at discharge.

On follow-up at 1st, 2nd and 3rd month, the patient was asymptomatic. He was given his 2nd,3rd and 4th doses of Cyclophosphamide. His haemoglobin improved to 10.9 gm/dl, TLC count of 9,700/mm^3, platelet count of 1,72,000/mm^3 with normal LFT, RFT and no albuminuria. He is still on regular follow-up.

Discussion

According to numerous studies, NPSLE was found to develop before or during the diagnosis of SLE in nearly 28% to 40% of adult SLE patients, and NPSLE developed in nearly 63% patients within one year after the diagnosis of SLE[4]. However, it may be seen as late as 15 years after the initial diagnosis of SLE[5].

SLE tends to be more severe in men and in paediatric patients[6]. Here, we report an uncommon case of male SLE with neuropsychiatric features which responded to cyclophosphamide and corticosteroid treatment along with anti-psychotics and anti-epileptics. The cognitive functions improvement was remarkable during follow-up and his anti-psychotics were reduced, accordingly.

Cognitive dysfunction can occur in the early stages of disease process but is rare[7]. While cognitive function can deteriorate throughout the disease course, it often fluctuates or improves over time[8]. The profile of cognitive deficits seen in SLE is varied but the most frequently affected domains are attention, memory, visuospatial processing, language, problem solving, speed of information processing and executive function[9].

Serum ANA is now taken as the compulsory entry criterion for diagnosing SLE with new ACR/EVLAR 2019 criteria[3].

MRI is the preferred imaging modality in patients with suspected NPSLE[6]. The most commonly noted abnormalities are small, hyperintense, T2-weighted, focal white matter lesions located in the periventricular and subcortical white matter of the frontoparietal regions of brain[6]. Nevertheless, these findings are nonspecific and can be observed in other disease processes, such as atherosclerotic vascular disease and multiple sclerosis (MS)[6]. Other common MRI findings include cortical atrophy, ventricular dilation, cerebral oedema, diffuse white matter abnormalities, gray matter abnormalities, infarction, leukoencephalopathy, and haemorrhage[6]. However, MRI in the present case was reported as normal. A study of 74 patients with new-onset neuropsychiatric lupus found normal MRI results in 42% of patients[10].

In severe cases, in addition to glucocorticoids and hydroxychloroquine, cyclophosphamide or rituximab (if refractory) should be added[6]. In thrombotic aetiology, with anti-phospholipid antibody (aPL), anti-coagulants are given while aPL negative patients are given anti-platelets[6]. In primary NPSLE, adjuvant therapy like anti-depressants, anti-psychotics, anti-convulsants, anxiolytics can be added[6]. In secondary NPSLE, treatment of underlying pathology is main-stream[6].

The present case could be classified as a case of SLE rather late in the course; it appears that it began as a case of undifferentiated connective tissue disease which later evolved as SLE. During early course of the disease serum

Entry criterion

Antinuclear antibodies (ANA) at a titer of ≥1:80 on HEp-2 cells or an equivalent positive test (ever)

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If absent, do not classify as SLE
If present, apply additive criteria

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Additive criteria

Do not count a criterion if there is a more likely explanation than SLE.
Occurrence of a criterion on at least one occasion is sufficient.
SLE classification requires at least one clinical criterion and ≥10 points.
Criteria need not occur simultaneously.
Within each domain, only the highest weighted criterion is counted toward the total score§.

Clinical domains and criteria	Weight
Constitutional	
Fever	2
Hematologic	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	4
Neuropsychiatric	
Delirium	2
Psychosis	3
Seizure	5
Mucocutaneous	
Non-scarring alopecia	2
Oral ulcers	2
Subacute cutaneous OR discoid lupus	4
Acute cutaneous lupus	6
Serosal	
Pleural or pericardial effusion	5
Acute pericarditis	6
Musculoskeletal	
Joint involvement	6
Renal	
Proteinuria >0.5g/24h	4
Renal biopsy Class II or V lupus nephritis	8
Renal biopsy Class III or IV lupus nephritis	10

Immunology domains and criteria	Weight
Antiphospholipid antibodies	
Anti-cardiolipin antibodies OR	
Anti-β2GP1 antibodies OR	
Lupus anticoagulant	2
Complement proteins	
Low C3 OR low C4	3
Low C3 AND low C4	4
SLE-specific antibodies	
Anti-dsDNA antibody* OR	
Anti-Smith antibody	6

Total score: 25/51

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Classify as Systemic Lupus Erythematosus with a score of 10 or more if entry criterion fulfilled.

ANA was reported as negative.

Abbreviations

NPSLE, Neuropsychiatric Systemic Lupus Erythematosus; SLE, systemic lupus erythematosus; ANA, antinuclear antibody; MMSE, Mini-Mental State Examination; TLC, total leucocyte count; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; UACR, Urine Albumin-to-Creatinine Ratio.

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