Neuropsychiatric involvement in systemic lupus erythematosus: A case series

ABSTRACT

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Patients with systemic lupus erythematosus that suffers from one or more of several neuropsychiatric symptoms represent a subcategory termed “neuropsychiatric systemic lupus erythematosus” (NPSLE). Different environmental factors, such as infection, stress, and ischemia, mediated by inflammatory cytokines, may damage the blood–brain barrier, further contributing to neuropsychiatric symptoms. Antiribosomal-P antibodies are specifically related to psychosis in NPSLE. Three patients of systemic lupus erythematosus who developed features of psychosis are presented and the condition is briefly discussed.

Keywords: Antiribosomal-P antibodies, neuropsychiatric systemic lupus erythematosus, organic psychosis

CASE REPORTS

Case 1
A 20-year-old female, a known case of NPSLE, presented in catatonic state with mutism, waxy flexibility, negativism,

S ystemic lupus erythematosus (SLE) is an autoimmune inflammatory disorder that affects multiple body systems.[1] SLE patients who develop one or more of several neuropsychiatric symptoms form a distinct subcategory named neuropsychiatric SLE (NPSLE). More than half of SLE patients will suffer from NPSLE during the course of their disease.[2,3] Symptoms of NPSLE may range from mild diffuse ones to acute life-threatening events. The American College of Rheumatology (ACR) definition of NPSLE requires the satisfaction of each of four categorical criteria: the presence of delusions (and or) hallucinations without insight; the presence of functional impairment as a consequence; the absence of delirium; and the absence of any secondary cause (e.g., a concomitant neurological disorder) or condition primarily associated with psychosis (such as schizophrenia). The ACR classified NPSLE and identified 12 central nervous system forms and 7 peripheral nervous system forms.[4] Nearly 50% of NPSLE patients have a normal magnetic resonance imaging MRI,[5] but in the other patients, defects are found anywhere in the brain and especially in the subcortical white matter of the frontal and temporal lobe.[6] Three patients of SLE who developed neuropsychiatric symptoms are reported [Table 1].

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psychological pillow, and posturing and was on tablets lorazepam 1 mg, olanzapine 2.5 mg, and haloperidol 2.5 mg which were stopped. She was an agriculture student pursuing postgraduation. She started staying aloof in the past 1 month and would often sit alone and complain of being fearful along with multiple pains. Gradually, it increased to an extent that she stopped consuming food altogether as she was unable to open her mouth. She was also observed on multiple occasions that she was talking to herself or gesturing in the air and started fearing even her own parents. She would sit or lie in a single posture all days and eventually started passing urine in bed. That is when she was brought to the hospital and admitted under medicine. Lorazepam was uptitrated to 2 mg every 8 hourly and SOS and given intravenous (iv). Upon further interviews, her catatonia resolved, she was communicative but had reduced psychomotor activity. Lorazepam was then tapered and stopped. MRI shows small areas of restricted diffusion in pons on left and midbrain, likely to represent late acute infarcts. On mental status examination (MSE), her speech was spontaneous but considerably reduced in rate tone and volume, with distressed and anxious affect, delusions of persecution and reference and 3rd person auditory hallucinations with pervasive low mood and disturbed sleep and had stopped eating.

In view of these symptoms, tablet quetiapine was started at 25 mg and gradually increased to 75 mg along with chemotherapy (every fortnight regimen). Her sleep gradually improved and she was taught relaxation techniques to combat anxiety. Over a period of 1 month, her delusions resolved while the hallucinations though faint are still present. She is being given supportive psychotherapy and has currently improved and rejoined college.

**Case 2**
A 29 year old female, housewife, a known case of SLE since 2 years with a flare came agitated, irritable in emergency department with fearfulness, suspiciousness, muttering and smiling to self with a guarded affect and refusal to accept medicines. She had been gradually developing these symptoms for 2 months. MSE revealed a young female, lying in bed, having a scanning gaze, respectful toward examiner, rapport established with little difficulty; not maintaining eye-to-eye contact with normal psychomotor activity with a restricted, delusion of persecution and reference, third person auditory hallucination with a partial judgment. MRI showing gliosis in left temporal lobe with FLAIR hyperintensity within left amygdala which could be a post seizure transient abnormality or sclerosis. Chemotherapy was resumed and repeated psychiatric assessment was done for her and she improved on the same with regular cyclophosphamide with pulsed methylprednisolone with no psychotic features by the end of the month. Psychotherapy for mood features was done, and repeated evaluations have shown near-total improvement.

**Case 3**
A 30-year-old lady, married, was admitted with an SLE flare with fever rash and icterus. She also complained of low mood, decreased interest in routine activities, and easy fatigability. Her biofunctions were disturbed with decreased sleep and reduced appetite for 3 months. Gradually, she became withdrawn and was often seen muttering to self. She was then taken to a psychiatrist and was started on tablet haloperidol 5 mg HS. When she came...
to the emergency department, she was off medication for 10 days. On evaluation, she had delusion of persecution and reference with elementary hallucinations. She was restarted on tablet haloperidol which was gradually increased to 10 mg. She was also started on chemotherapy and her symptoms resolved within 20 days.

**DISCUSSION**

The most frequent NPSLE manifestations are seizures, generalized, or focal that may develop in 10%–20% of SLE patients and tend to occur early in its course.\(^7\) Clinical evidence of demyelination in NPSLE is reported in approximately 0.3% of cases. Chorea is the most common movement disorder in SLE, occurring in 2%–3% of patients. Parkinsonism, ataxia, and hemiballismus are rare.\(^8\) Chorea usually presents during the 1st years of SLE and is associated with antiphospholipid antibodies in 92% of cases.\(^3\)

Cognitive impairment is detected in 20%–80% of SLE patients.\(^9\) Depression is the most common mood disorder in NPLSE, and its lifetime prevalence may reach 65%.\(^10\) Depression in SLE is linked to several factors, the most important of which is the treatment with high doses of prednisone (20 mg or higher).\(^8\) Other factors include specific antibodies to ribosomal P, N-methyl-D-aspartate receptor, and other neuronal epitopes.\(^9\) Anxiety disorders are also common and affect up to 40% of patients.\(^8\) Organic psychosis occurs in 2%–11% of SLE patients; in 60% of these, it may be the presenting SLE symptom.\(^11\) SLE psychosis usually responds to immunosuppressive therapy. It is important to note also that the manifestations of NPSLE might overlap the neuropsychiatric manifestations of other autoimmune diseases. Autoantibodies are central for the diagnosis of SLE and medications for them were started after obtaining the reports of the same. In Case 1, antiribosomal P antibodies were positive and they could not be assessed in the other two cases due to financial constraint.

**CONCLUDING REMARKS**

Neuropsychiatric symptoms affect nearly half of the patients with SLE; however, the effect on disease severity, quality of life, and prognosis is tremendous. Symptoms of NSLE may range from mild diffuse ones to acute life-threatening events. Although the underlying mechanisms are still largely unruled, several pathogenic pathways are identified, such as antibody-mediated neurotoxicity, vasculopathy due to antiphospholipid antibodies and other mechanisms, and cytokine-induced neurotoxicity. For systemic cases, corticosteroids are the mainstay of treatment. For manifestations of severe central nervous involvement, iv pulsed cyclophosphamide has become an effective treatment, used both singly and in combination with other therapies (e.g. synchronous plasmapheresis). Combination pulsed cyclophosphamide with pulsed methylprednisolone is used for severe or refractory neuropsychiatric lupus, while haloperidol along with second-generation antipsychotics has been found to be effective in most cases.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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