Acute Psychosis as the Predominant Manifestation in a Patient with Systemic Lupus Erythematosus

Neuropsychiatric systemic lupus erythematosus (NPSLE) can occur at any time during the course of SLE, even during the remission phase of SLE [1]. A recent meta-analysis showed the prevalence of psychosis is 6.5% among patients with NPSLE [2]. Lupus psychosis is an infrequent symptom of NPSLE and has negative impacts on quality of life and health status. Psychosis as the only manifestation of NPSLE, independent of active SLE, is rare and causes a diagnostic and therapeutic dilemma.

Case Report

A 51-year-old female patient with a significant medical history was discharged against medical advice from the internal medical ward, despite receiving intravenous antibiotic treatment with ceftriaxone for a urinary tract infection. She experienced an acute onset of delusions toward the medical staff and auditory hallucinations about her family being tortured on the 2nd day of the hospitalization. There were no changes observed in her awareness or attention. Ceftriaxone was switched to oral cefuroxime on discharge. She had a history of SLE since the age of 19 years, initially presenting with symptoms of proteinuria and serositis. She had received a college education and worked as a manager at a travel agency for the decades. At the age of 47 years, she received a kidney transplantation due to lupus nephritis. Following the transplantation, there were no notable symptoms of SLE flare-up. In recent years, the patient's overall functioning was stable. She could do household tasks effectively and interacted well with others. She had been taking aspirin 100 mg, tacrolimus 4 mg, and prednisolone 5 mg daily for at least three years. Within two weeks of her discharge, the patient's infection was resolved, and her nephrologist discontinued cefuroxime. However, her psychosis began to worsen. She experienced profound auditory and tactile hallucinations, persecutory delusions, delusions of control, and monitoring. She was taken to a psychiatric clinic and subsequently referred to our hospital for further evaluation.

Upon admission, the patient presented herself with severe psychosis and agitation. Her vital signs were stable, and she remained conscious. The results of physical examinations did not reveal any remarkable abnormalities or signs of SLE flare-up. Serological data generally were within acceptable ranges (Table 1). Initially, psychotic disorder due to medical condition other than NPSLE was considered on a joint consultation with neurologist and rheumatologist, due to limited evidence of active SLE. To investigate the physical source of her psychosis, various tests were done. The findings of cerebrospinal fluid analysis revealed mildly elevated total blood protein levels (62 mg/dL) but no signs of pleocytosis or glucose consumption. An electroencephalogram showed mild diffuse cortical dysfunction. The pictures of brain magnetic resonance imaging (MRI) indicated cortical atrophy, subcortical and periventricular white matter changes, encephalomalacia in the right frontal lobe, and old infarcts over the bilateral frontal lobe. To rule out malignancy as a potential cause, we checked whole-body computed tomography scans and serum tumor markers, showing negative results. Blood levels of antiphospholipid antibodies were within normal limits, eliminating them as a contributing factor.

Table 1. Clinical presentation, laboratory findings, and symptoms rating scales comparison between before the corticosteroid therapy and after the therapy

	Before	After
BPRS	30	36[†]
Positive symptoms	Persecutory delusion	Minimal
	Delusion of telepathy	Nil
	Delusion of control	Nil
	Delusion of monitor	Minimal
	Jealous delusion	Nil
	Auditory hallucination	Minimal
	Tactile hallucination	Nil
Negative symptoms	Nil	Nil
MMSE	23/30	29/30
Active SLE symptoms	Arthritis as baseline	Same
SLE markers		
CRP	1.6 mg/L	Not tested
ESR	15 mm/h	Not tested
RF	< 20 IU/mL	
C3	92.7 mg/dL	Not tested
C4	44.2 mg/dL[§]	Not tested
Anti-DNA Ab	Negative	Not test
ANA × speckled	1: 40	Not tested
ANA × homogeneous	1: 40	Not tested
APS markers		
Cardiolipin Ab (IgG)	21 U/mL[§]	Not tested
Cardiolipin Ab (IgM)	0.1 U/mL	
β2glycoprotein IgG	1.4 U/mL	
β2glycoprotein IgM	0.1 U/mL	
FK-506 level (ng/mL)	6.9	7.0

[†]The BPRS score was recorded two weeks before discharge.
BPRS, brief psychiatric rating scale; MMSE, mini–mental state examination; SLE, systemic lupus erythematous; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; RF, rheumatoid factor; C3/4, complement 3/4; Anti-DNA Ab, anti-DNA antibody; ANA × speckled/homogeneous: anti-nuclear antibody speckled/homogenous pattern; APS, anti-phospholipid syndrome; FK-506, tarcolimus

In the beginning of this hospitalization, the patient received various antipsychotic medications, including risperidone and quetiapine, but showed variable effectiveness. Only olanzapine was found to be tolerable. It was titrated to a dosage of 25 mg/day and combined with a low dose of haloperidol (2.5 mg/day) to manage her symptoms. After a three-week psychiatric hospitalization and thorough examination, the diagnosis of NPSLE was established. As a result, she started to receive intravenous methylprednisolone pulse therapy, with a dose of 500 mg given daily for seven days. The treatment was then shifted to the oral form to continue managing her condition.

After six weeks of hospitalization, the patient was discharged with minimal residual psychosis so that she could ignore the contents of hallucinations and delusion, and at the subsequent outpatient clinic visit, the antipsychotics were simplified to olanzapine 5 mg/day. Her cognitive function mostly was recovered (Table 1).

Comment

Similar reports by Chang et al. [3] and Kumar et al. [4], describing patients exhibiting NPSLE during a remission phase of SLE with mood and psychotic symptoms, our patient also showed delusions and hallucinations without any support from laboratory evidence (Table 1) or physical signs of SLE flare-up. Several neuroimaging tools to evaluate NPSLE were reviewed by Govoni et al. [5], including conventional brain MRI. Common findings on patients with NPSLE are small punctate focal lesions in subcortical white matter (15%–60%), followed by cortical atrophy, periventricular white matter changes, ventricular dilatation, and major infarcts, which are all compatible with our patient. In an international cohort study, the majority of patients with lupus psychosis have been described to experience their first episode either in the year before or within three years following the diagnosis of SLE [6]. Such a prolonged interval between SLE diagnosis and the first episode of psychosis is rare. However, a 40-year single-center retrospective study showed that patients develop lupus psychosis over a mean ± standard deviation of 17.56 ± 11.0 years of follow-up [7]. The time interval for the onset of lupus psychosis varies remarkably among different patients, leading to diagnostic challenges. Psychosis symptoms in patients with NPSLE include paranoid and grandiose delusions, as well as auditory and visual hallucinations [6].

Patient's psychosis continues to progress even after the discontinuation of antibiotics. Some case reports and a recent systemic review have shown cases of tacrolimus-induced psychosis [8]. Considering its relatively low incidence and the absence of other neurotoxic sequelae, we were less inclined to favor this differential diagnosis in our patient. Furthermore, her level of consciousness and alertness remained stable without suggesting the presence of delirium.

In a Taiwanese study, Chen et al. reported that a certain proportion of individuals with schizophrenia also have autoimmune diseases [9]. Therefore, when assessing lupus psychosis, we suggest to consider schizophrenia as a potential differential diagnosis. In our patient, the diagnosis of schizophrenia was ruled out due to the absence of a significant family history, negative symptoms, and an acute onset. After a comprehensive review of the patient's history and examination, the diagnosis of NPSLE was later established.

The management of NPSLE is dependent on the predominant mechanism of its development, including inflammation and vascular injury. In cases involving autoimmune-mediated inflammatory injuries, most studies in NPSLE have used immunosuppressive therapy in combination with high-dose corticosteroids. However, some evidence has indicated a better response to single cyclophosphamide than to single methylprednisolone [1]. The rôle of psychotropic drugs in the treatment of NPSLE is symptomatic treatment [10]. Thus, identifying the cause of NPSLE in a patient who is in the remission phase of SLE is crucial to manage it. (The institutional review board at National Cheng Kung University Hospital approved the publication of this case report [IRB protocol number = A-EC-111-027 and date of approval = September 20, 2022]. The patient also signed written informed consent for this publication).

Declaration of Patient Consent

The authors certify that they have obtained appropriate patient consent forms. In the form, the patient has given her consent for the images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal the identity, but anonymity cannot be guaranteed.

Data Availability Statement

The data used to support the findings of this study are available from the corresponding author upon request.

Financial Support and Sponsorship

The authors received no financial support for the research, authorship, and/or publication of this article.

Conflicts of Interest

The authors declared no potential conflicts of interest in writing this article.

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Received: Sep. 21, 2023 revised: Oct. 24, 2023 accepted: Oct. 25, 2023
date published: Dec. 22, 2023

Access this article online

Quick Response Code:

Website: https://journals.lww.com/TPSY

DOI: 10.4103/TPSY.TPSY_34_23

How to cite this article: Lin CT, Lin TY, Lu TH. Acute psychosis as the predominant manifestation in a patient with systemic lupus erythematosus. Taiwan J Psychiatry 2023;37:205-7.