Case Report

Psychosis in Patients with Systemic Lupus Erythematosus

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ABSTRACT

Neuropsychiatric manifestations in systemic lupus erythematosus (SLE) are common; however, psychosis *per se* is bit uncommon. They may be cognitive deficit, lupus headache, psychoses, seizures, peripheral neuropathy, and cerebrovascular events. Psychiatric symptoms in SLE can be functionally independent psychiatric disorders. It can be due to drugs (steroids) used for SLE or secondary to SLE because of its brain involvement, which is termed as neuropsychiatric systemic lupus erythematosus (NPSLE). No single clinical, laboratory, neuropsychological, and imaging test can be used to differentiate NPSLE from non-NPSLE patients with similar neuropsychiatric manifestations. Presently we are discussing about three cases of SLE with psychosis and which had different clinical presentation. The present reports also depict the approach to case differential diagnosis and management of the same.

Key words: *Neuropsychiatric systemic lupus erythematosus, organic psychosis, steroid psychosis, systemic lupus erythematosus*

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune, chronic inflammatory disorder affecting the connective tissue of multiple organ systems. It occurs on the background of disturbances of environmental, hormonal, and genetic factors. It is nine times more common in women.[1] Neuropsychiatric manifestations are present in two-thirds of the patients with SLE.[2] No single clinical, laboratory, neuropsychological, and imaging test can be used to differentiate neuropsychiatric systemic lupus erythematosus (NPSLE) from non-NPSLE patients with similar neuropsychiatric manifestations.[3] The most common neuropsychiatric manifestations in SLE are cognitive deficit (49.33%), lupus headache (23.11%; in 57.69% of these patients, tension-type), psychoses (12.00%), seizures (10.67%), and cerebrovascular events (9.78%).[3] Typical central nervous system (CNS) changes for NPSLE during magnetic resonance image examination are the multiple lacunar infarctions with temporal localization as well as a parenchymatous cerebral atrophy. Skin vasculitis, serositis, and pulmonary involvement are the most common extracerebral manifestations in patients with SLE and data for neuropsychiatric lesions (seizures, psychoses, and cerebrovascular events) being signs of general vascular pathology disease activity. The American College of Rheumatology established case definitions for 19 central and peripheral nervous system syndromes[4] listed in Table 1.

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CASE REPORTS

Case 1

A 20-year-old unmarried woman from middle socioeconomic status with urban bac kground presented

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Table 1: Neuropsychiatric manifestations of SLE

NPSLE associated with the central nervous system	NPSLE associated with the peripheral nervous system
Aseptic meningitis	Autonomic neuropathy
Cerebrovascular disease	Myasthenia gravis
Stroke	Peripheral neuropathy
Transient ischemic attack	Sensorineural hearing loss
Cerebral venous sinus thrombosis	Sudden onset
Cognitive disorders	Progressive
Delirium (acute confusional state)	Cranial neuropathy
Dementia	
Mild cognitive disorders	
Demyelinating syndrome	
Headaches	
Tension headaches	
Migraine headaches	
Movement disorders (chorea)	
Psychiatric disorders	
Psychosis	
Mood disorders	
Anxiety disorder	
Seizure disorders	
Transverse myelopathy	

SLE – Systemic lupus erythematosus; NPSLE – Neuropsychiatric systemic lupus erythematosus

to the Department of Psychiatry. She was a known case of SLE with predominant skin manifestations since 5 years, and she was treated by a dermatologist. The patient discontinued medication after 2 years on her own, as there was an improvement of symptoms after attaining the menarche. Again, for 3 months the patient noticed frequent hair fall, itching over the scalp, and intermittent low-grade fever. The patient also had continuous withdrawn/dull behavior, suspiciousness, referential ideas, hearing of voices, decreased self-care, and occasional crying episodes in the last 15 days. The dermatologist started 30 mg/day of prednisolone (tablet) after the onset of psychiatric symptoms. On physical examination, the patient was found to be pale. There was dark pigmentation all over her body and sparse and thin hair over her scalp, but there were no neurological deficits or signs of meningeal irritation. On mental status examination, the patient was found to be poorly kempt, restless, irritable, had poverty of speech, third person auditory hallucination, delusion of persecution, delusion of reference, and blunt affect but she was conscious and oriented. Baseline biochemical and hematological investigations were within normal limits; antinuclear antibody (ANA) test was positive (index ratio was 3.5 on ANA detect); and rheumatoid antibody test was negative. The patient was diagnosed to have organic delusional (schizophrenia-like) disorder (International classification of diseases (ICD)-F06.2)[5] secondary to SLE. Eventually the patient was started on 10mg/day of olanzepine (tablet). A significant improvement was observed in 2 weeks, and the patient was discharged. She remained free from psychiatric symptoms for the last 2 months.

Case 2

A 17-year-old unmarried woman from rural background with lower socioeconomic status reported to the general medicine department. She had a history of 2 months of fever and joint pain and a history of 5 days of cough. She was diagnosed to have cutaneous lupus erythematosus for a year, and she was under 20 mg/day of prednisolone (tablet) in divided doses. The patient was admitted and evaluated. General physical examination revealed pallor, icterus, hyperpigmentation all over her body, including face, erythematosus skin lesions, diffuse hair loss, depigmented patches over the scalp, and erosions in the buccal mucosa. Chest radiograph was suggestive of miliary tuberculosis, and an electromyographic study was suggestive of mixed neurogenic and myogenic pathology. Most of the baseline biochemical and hematological investigations (except Hb% 8 g% and total bilirubin 4 mg/dl) were within normal limits. Immunological investigations showed positive anti-UI/Sm ribonucleoprotein antibody (RNPAb), anti-Sm Ab, anti-ds deoxyribonucleic acid (DNA) Ab, anti-histone Ab, anti-nucleosomal Ab, and anti-ribosomal Ab. The human immunodeficiency virus (HIV) test was nonreactive. After the review by the immunologist, the patient was diagnosed to have SLE with myositis with military tuberculosis. She was treated with 200 mg of ciprofloxacin bid (injection), 100 mg of amikacin iv tid (injection), 100 mg of hydrocortisone iv bid (injection), 1 g of ceftriaxone iv od (injection), and 400 mg/day of ethambutol (tablet). The patient was free from psychiatric complaints for initial 1.5 months. For 15 days, the patient presented with muttering, smiles to self, occasional crying spells, irrelevant speech, anger outbursts, and decreased sleep. There was no alteration in medication, changes in dosages, or onset of any fresh physical complaints in these 15 days. There was no history of either SLE or major psychiatric illness in family. There was no history of psychosis, depression, or mania, but she was premorbidly well adjusted. Mental status examination revealed poorly kempt, irrelevant speech, second person auditory hallucination, reduced range of mood, and absence of insight. The patient was diagnosed as organic delusional [schizophrenia-like] disorder (ICD-F06.2).[5] The patient was started on 10 mg/day of olanzepine (tablet) and increased to 20 mg/day. The patient showed 50% improvement in the first week, and she was discharged later.

Case 3

A 35-year-old woman was diagnosed with SLE since 2 years, and she was admitted in dermatology department for acute cutaneous exacerbation of SLE.

She was on 20 mg/day of predinisolone (tablet) and local skin applications for skin lesions. The immunological test revealed ANA positivity. Other baseline biochemical and hematological investigations were within normal limits. The patient was referred to psychiatric evaluation for the complaints of fearfulness and decreased sleep for 2 days. There were no significant family history, history of major psychiatric illness, and no similar or significant psychiatric illness. Mental status examination revealed that the patient had delusion of persecution, delusion of reference, irritability, and absence of insight. There was no diurnal variation or symptoms suggestive of delirium. There was no change in medication or doses prior to onset of psychiatric symptoms. The patient was diagnosed as organic delusional (schizophrenia-like) disorder (ICD-F06.2)[5] and started on 10 mg/day of olanzepine (tablet). The patient remitted from psychiatric symptoms in 1 week, and she was symptom-free even after follow-up of 2 months.

DISCUSSION

All the three cases noted above fulfilled the criteria for NPSLE. From the same institution, a series of four cases of SLE were reported in 1982, of which two had depressive episodes and one had acute psychosis during the exacerbation of SLE.[6] In the present series, all of them had acute psychosis (organic delusional (schizophrenia-like) disorder or organic psychosis according to ICD-10). According to ICD-10,[5] diagnostic features of organic psychosis are as follows:

1. Evidence of cerebral disease, damage, or dysfunction or of a systemic physical disease, known to be associated with one of the listed syndromes;
2. A temporal relationship (weeks or a few months) between the development of the underlying disease and the onset of the mental syndrome;
3. Recovery from the mental disorder following removal or improvement of the underlying presumed cause; and
4. Absence of evidence to suggest an alternative cause of the mental syndrome (such as a strong family history or precipitating stress).

Recently in 2008, Monov and Monova had developed an approach for making the diagnosis of NPSLE.[3] Common differential diagnosis that has to be considered are functional psychosis, delirium, steroid psychosis, and other drug-induced psychosis. As there were no apparent significant stressors apart from exacerbation of SLE and absence of family history of psychosis, functional acute psychosis is ruled out. On detailed assessment of above cases, it was found that they did not have symptoms of delirium (ICD-10),[5] such as impairment of consciousness and attention, global disturbance of cognition, and disturbance of sleep-wake cycle. Lastly, none of the drugs used (apart from steroids) to treat above cases are known to exacerbate or cause psychosis. Steroids may cause psychosis, but psychiatric side effects with corticosteroids appear to be dose dependent. The Boston Collaborative Drug Surveillance Program (N=676)[7] examined psychiatric symptoms in patients free of psychiatric disease prior to steroid treatment. Diagnosis during steroid exposure includes mania, depression, and psychosis. Severe psychiatric illness was uncommon (1.3%) with doses less than 40 mg/day of prednisolone but increased to 18.4% at doses above 80 mg/day of prednisolone. This strongly suggests that psychiatric symptoms are dose dependent. Two of the above three cases were on less than 40 mg/day of prednisolone and one was on 200 mg/day of hydrocortisone (injection), which is equivalent to 50 mg of prednisolone (5 mg of prednisolone is equivalent to 20 mg of hydrocortisone).[8] The most commonly reported corticosteroid-induced psychiatric disturbances are affective, including mania, depression, or mixed states. Most often, patients receiving short-term corticosteroid therapy present with euphoria or hypomania whereas long-term therapy tends to engender depressive symptoms.[9] Most of the psychiatric symptoms secondary to steroids occur in first 1–2 weeks.[10,11] In the above case series, all patients were on steroids for more than 2 weeks with nonaffective symptoms. Thus, the psychiatric symptoms in the above cases described are unlikely to be due to steroids.

In any case of suspected organic psychiatric illness, psychotropics have to be started at lower dose and gradually built up because they are prone for more CNS side effects, such as extrapyramidal side effects (EPS). In the above cases, the patients were started on olanzepine 2.5 mg initially and gradually built up to 10–20 mg/day. None of the above patients had any acute side effects of olanzepine. We chose olanzepine because it has good efficacy and tolerability and is less likely to have EPS.[12]

The pattern of psychotic spectrum disorders in SLE is not systemically studied, but most common form appears to be acute psychosis, which was true in the above case series. Prognosis is good for acute psychosis; even present cases had good prognosis on short-term follow-up. Findings of NPSLE on magnetic resonance imaging (MRI) of the brain are frequently unremarkable, and abnormalities are nonspecific.[13] A study by Steens *et al*.[14] using magnetization transfer imaging, a quantitative MRI technique, concluded that in SLE patients with a history of neuropsychiatric symptoms, the gray matter is particularly affected. So gray matter abnormalities might be the underlying pathology behind occurrence of psychosis.[15]

CONCLUSIONS

SLE is a chronic autoimmune disorder with occasional CNS manifestations. In a few situations, this disorder presents with psychiatric complaints but the psychotic features are infrequent. Psychosis in patients with SLE has to be differentiated from functional psychosis, delirium, steroid psychosis, and other drug-induced psychosis. Most of these patients are prone to CNS side effects because of already underlying CNS damage and so antipsychotics with least EPS, such as quetiapine or olanzepine, can be used.

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