Case Report

Acute psychosis as the presenting manifestation of lupus

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Abstract

Neuropsychiatric manifestations like cognitive dysfunction, peripheral neuropathy, stroke headache, seizures in systemic lupus erythematosus (SLE) are quite common. However, psychosis as the sole presenting manifestation of SLE is rarely encountered clinically. If lupus is not kept as differential among patients with acute psychosis, delay in diagnosis and subsequent mismanagement are likely to happen. Here, we present a case of a young female presenting with acute psychosis as the predominant symptom and was further evaluated and diagnosed as a case of SLE. The patient was managed with immunosuppressive agents and carried an excellent outcome.

Keywords: Lupus, neuropsychiatric, psychosis, steroid

Introduction

Systemic Lupus Erythematosus (SLE) is an autoimmune disorder involving virtually any organ-system with a myriad of clinical manifestations. Neurological and psychiatric manifestations (both central and peripheral) such as cognitive dysfunction, psychosis, depression, headache, seizures, cerebrovascular diseases, demyelination, aseptic meningitis, cranial and peripheralneuropathies, myelitis [collectively known as neuropsychiatric SLE (NPSLE)] are present among two-thirds of the SLE patients.[1] Vasculopathy, antibody, immune complex, complement and cytokine-mediated neurotoxicity, disruption of the blood-brain barrier, loss of neuronal plasticity are probable pathophsiological mechanisms.[2] While literature shows NPSLE can present before or around the diagnosis of SLE in 28%–40% of cases,[1] acute psychiatric symptoms as the sole presenting feature is rarely encountered by internists, primary care physicians or psychiatrists and thus, may cause substantial diagnostic conundrum.[3-5] We report a case of a young female who presented with acute psychosis, subsequently diagnosed as SLE and managed successfully with immunomodulators. We also highlight the causes of acute organic psychosis, which might present to a primary care physician.

Case Presentation

A 22-year-old unmarried female graduate student presented in the emergency department with acute behavioral abnormality associated with staring, hearing voices, muttering, insomnia and aggressive behavior for 2 days. Her father gave a history of fatigue, low-grade fever and generalized skin rashes for last 1 month for which she was given some over-the-counter medication by a quack 4 days back and fever was remitted. On further probing, it was unfurled that the drug was tab prednisolone 10 mg which she had been taking once daily (OD). There was no history of headache, vomiting, seizure, altered consciousness. No recent stressful event, history of any psychiatric illness, addiction or intake of illicit drugs was present.

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On physical examination, she was conscious, alert, oriented, unkempt, restless, and irritable. She had increased motor activity, poverty of speech, perplexed affect, altered sleep cycle, delusion of persecution, visual and auditory hallucinations. She had mild pallor but was afebrile with normal hemodynamic parameters. There were no sign of focal neurological deficit and meningeal irritation. Multiple hypopigmented and hyperpigmented macular rashes were present, predominant on the upper limbs [Figure 1]. Examination of other systems didn't find any abnormality clinically.

The patient was initially managed with injection haloperidol 2 mg and injection promethazine 25 mg intramuscular two times a day (BD). Psychiatric consultation was taken and tab quetiapine 0.25 mg OD was added without any appreciable relief.

On laboratory examination, she had hemoglobin - 10.2 gm/dl (n = 12.5-16), platelet - 1.30 lakhs/dl (n = 1.4-4.5), C - reactive protein (CRP) - 106 mg/l ($n \leq 6$). Her liver function test, blood urea, serum creatinine, total and differential counts, serum electrolytes (sodium, potassium, and calcium), thyroid function test (including anti-thyroid peroxidase antibody), random blood sugar and urine examination were within normal. Serology of HIV and neurosyphilis were non-reactive. History of fever and rashes (although not typical lupus) prompted us to send anti-nuclear antibody (ANA) profile which was positive in 1:320 dilution along with anti-ds-DNA positive (+), anti P_0 (+++), anti U1snRNP (++).

Cerebrospinal fluid (CSF) analysis was suggestive of neuroinflammation [Leucocytes-30 cells/mm^3(n = 0-5cells/mm^3) with lymphocyte-90%, neutrophils-10%, red cell-02 cells/mm^3, protein 54.4mg/dl (n = 15-45), glucose-54mg/dl (n = 40-85)]. CSF was negative for Japanese Encephalitis, cytomegalovirus, herpes simplex virus- 1&2. Paired samples from serum and CSF were negative for antibodies associated with autoimmune encephalitis.

To rule out other organic and vascular causes, magnetic resonance (MR) imaging with MR angiography of the brain was done and revealed the normal study. Her chest X-ray, 2D-echocardiography, ultrasonography abdomen and electroencephalography were normal. Owing to her clinical presentation, differentials like functional psychosis, delirium, steroid psychosis, illicit drug abuse, metabolic encephalopathy (e.g., dyelectrolytemia, Wernicke's encephalopathy, and hepatocerebral degeneration), viral encephalitis, Wernicke's aphasia, CNS lupus, and autoimmune encephalitis were considered. Excluding other causes and in view of above clinical findings of anemia, thrombocytopenia, psychosis, skin manifestations, ANA +, Anti-ds-DNA +, Anti-SmAb +, Anti-Po +++, CSF suggesting lymphocytic pleocytosis with underlying SLE [fulfilling > 4/11 of the Systemic Lupus International Collaborating Clinics (SLICC) diagnostic criteria],[6] a diagnosis of CNS Lupus was made.

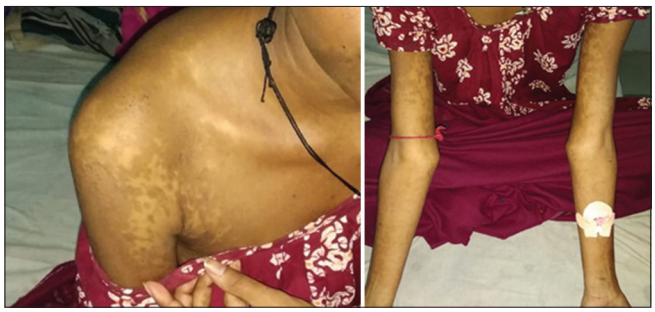

Figure 1: Maculopapular rashes in bilateral forearms, which served as a clinical clue towards psychosis secondary to a probable connective tissue disease

Pulse therapy of methylprednisolone for (1 gm methylprednisolone dissolved in 250 ml normal saline intravenously for 3-4 hours OD for consecutive 5 days) was started. Psychiatric symptoms started improving by third day and post-pulse therapy CSF showed marked reversal of neuroinflammation [leucocytes-3 cells/dl (all lymphocytes), protein - 35.1 mg/dl, glucose - 67 mg/dl]. During discharge, she was free from any neurocognitive or psychiatric deficits. She was prescribed oral prednisolone (30 mg/day), tab hydroxychloroquine 200 mg BD, and tab quetiapine 25 mg OD with instruction of weekly follow-up. Oral steroid was tapered off and replaced with mycophenolatemofetil (MMF) 500 mg BD within 3 weeks. Quetiapine was gradually tapered off and stopped within 2 weeks.

After 3 weeks of discharge, the patient again presented with similar kind of psychiatric complaints in the emergency. She was given pulse therapy of methylprednisolone like before and psychotic symptoms abated within 2 days. This time intravenous monthly cyclophosphamide pulse therapy was planned (750 mg/m^2 body mass index for 6 months). After 1-year completion of the cyclophosphamide therapy, she had been devoid of any recurrence of neuropsychiatric symptoms and did not require antipsychotics in the intervening period. At present, she is on hydroxychloroquine 200 mg OD and MMF 500 mg OD.

Discussion

This case presented to the emergency department with acute onset psychosis as the predominant complaint. While admitting the patient and providing symptomatic treatment with antipsychotics is imperative, searching for clues for any organicity is highly recommended.[7] In our case, the history of fever and presence of skin lesions prompted us to search for co-existing connective tissue disorders. The presence of anemia, thrombocytopenia and increased CRP further strengthened the suspicion and ultimately characteristic ANA profile clinched the diagnosis. Thus, these early subtle biochemical features should be taken seriously as most of the times these are the only biochemical clues without any florid features of end-organ damage classical of SLE. Table 1 lists the disorders presenting with secondary psychosis which might be encountered in Medicine or Neurology ward.[7,8]

Among the psychiatric manifestations of SLE, cognitive dysfunctions appear to be the most common manifestation.[9] In

Table 1: Secondary causes acute psychosis

Etiology	Disease
Vascular	Wernicke's aphasia, Subdural hematoma
Infection	Syphilis, HIV, HSV I and II, Sepsis
Vitamin deficiency	B_1, B_3, B_{12}
Heavy metal deposition	Copper, Manganese, Calcium, Iron
Autoimmune	Paraneoplastic/autoimmune encephalitis (particularly *N*-methyl D-aspartate +), Hashimoto encephalopathy, Connective tissue disorders (like SLE), CNS vasculitis
Drugs	Steroid, isoniazide, chloroquine, levodopa
Endocrine	Thyrotoxicosis, Myxedema madness, Pheochromocytoma, Cushing's syndrome
Substance abuse	Alcohol, cannabis, ecstasy
Seizures	Temporal lobe epilepsy
Dementia	Behavioral variant of frontotemporal dementia, Demetnia with Lewy bodies, Alzheimer's disease
Inborn errors of metabolism	Lysosomal storage disorders, Acute intermittent porphyria
Dyselectrolytemia	Hyponatremia, Hypernatremia, Hypercalcemia
Others	Metachromatic leukodystrophy, Huntington's chorea, Brain tumor, ICU psychosis

different cohorts, psychosis has been reported among 0%–11% NPSLE cases.[10,11] Study in Indian patients showed psychosis was the predominant symptom.[12] Psychosis in SLE can occur either due to neuro-lupus or drugs used to treat it (e.g., glucocorticoid and chloroquine) or flare-up of premorbid psychiatric condition due to disease burden.[11,13] In the present case, steroid-induced psychosis was a close differential. Steroid may cause psychosis, usually with a higher dose of prednisolone (>40 mg/day), is dose dependent. Psychosis usually starts within 1-2 weeks of initiation of steroids and improves on with holding the drugs. Mania, depression or mixed states are more commonly associated with steroid-induced psychiatric disturbances. Euphoria or hypomania is more common among patients on short-term steroid therapy, whereas depressive symptoms are more common in patients on long-term therapy. SLE patients are also more prone to develop steroid-induced psychosis if there is concurrent lupus nephritis causing hypoalbuminemia.[11,12] On the contrary, the presence of anti-P_0 antibody, neuroinflammatory markers in CSF, disease activity marker in blood, responsiveness to immunosuppressive agents and temporality with the underlying disease point towards the diagnosis of NPSLE.[11,12,14,15]

Although 80% acute psychotic episodes present within 1 year of diagnosing,[10] the first-time presentation of SLE with acute psychosis as its predominant manifestation is even rarer and can cause substantial difficulty and delay in accurate diagnosis and treatment.[4,16-21] MRI brain does not show any abnormality in 42% cases despite having signs and symptoms of active disease.[22] Chandra *et al.* reported a diagnostic delay of 6-9 months from disease onset in three cases of neuropsychiatric lupus, previously diagnosed as primary psychiatric illness.[3] Delusion, paranoid ideation, visual and auditory hallucinations are common psychotic symptoms and frequently accompanied by concomitant cognitive dysfunction and depression.[10,23] Cutaneous manifestations have been described as commonest non-NPSLE symptom in lupus psychosis,[10] as also evident in the patient. Young adult, juvenile and pediatric patients are particularly at risk of developing psychosis related to SLE.[24,25]

The standard treatment for NPSLE is pulse methylprednisolone therapy.[11] Our patient responded well with methylprednisolone, but had a recurrence in follow-up. Therefore, she was given monthly cyclophosphamide therapy that has been the best second-line agent having greater efficacy than methylprednisolone with comparable safety.[26] The target should always be to administer glucocorticoids at minimal dose and use of mycophenolatemofetil and azathioprine as a steroid-sparing agent as maintenance therapy. Intravenous immunoglobulin, plasmapheresis, rituximab, and newer biological such as belymumab and tofacitinib are potential third-line agents to treat lupus psychosis.[11] Apart from immunosuppressive therapy NPSLE patients frequently need psychopharmaceuticals, particularly at its acute presentation. Moreover, SLE patients do have a higher psychological burden and are associated with an increased risk of suicide.[27] Thus, liaison with psychiatrists for the best outcome is recommended. Generally, atypical antipsychotics are well tolerated.[28]

Conclusion

The message through this case report is that organic disorders should be kept in mind while evaluating acute psychosis as they generally harbor reversible causes with a better outcome. Among young females with acute psychosis, autoimmune disorders should be considered. Subtle systemic accompaniments and laboratory features like anemia, thrombocytopenia, increased CRP should be taken with utmost importance as more often than not they serve as the potential clue to the final diagnosis. Primary care physicians, internists, neurologists should be aware of isolated psychiatric manifestations of SLE. Psychosis in a primary setup is seldom attributed as a manifestation of a systemic disease with considerable delay in diagnosis and instituting prompt therapy for a reversible disease. Heightened suspicion among primary care physicians can thus play an important role in early diagnosis and prompt referral of patients with SLE.

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Conflicts of interest

There are no conflicts of interest.

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