

Psychosis Unmasking a Diagnosis of Systemic Lupus Erythematosus: a Case Report

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Abstract

Systemic lupus erythematosus (SLE) is an autoimmune disorder that affects multiple organs. Neuropsychiatric SLE (NPSLE) can manifest with a multitude of neurological and psychiatric symptoms. Psychosis is a rare NPSLE manifestation that can occur at any phase of the illness; 21% of SLE-related psychosis cases occur at the onset of SLE, but the evidence base for this is lacking. We report a case of acute-onset psychosis in a woman that led to a diagnosis of SLE, which was substantiated by physical evaluation and laboratory assessments. Assessment of acute-onset psychosis requires consideration of all differential diagnoses, especially in the presence of atypical features. This case also underscores the importance of physical examination and laboratory investigations in psychosis.

Key words: Autoimmune diseases; Lupus erythematosus, systemic; Neuropsychiatry; Psychotic disorders

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disorder that can affect any organ system and has various manifestations. Neuropsychiatric SLE (NPSLE) can present with a multitude of neurological and psychiatric symptoms such as seizures, headache, cerebrovascular disease, aseptic meningitis, cognitive dysfunction, psychosis, and depression.¹ Approximately one-third of patients with SLE in India report neuropsychiatric manifestations.² These may precede, occur concomitantly with, or follow the diagnosis of SLE. Psychotic features associated with NPSLE and primary psychotic disorders are indistinguishable; the psychotic features frequently mask and delay the diagnosis of SLE. Acute psychosis as the initial presenting symptom of SLE is rare in clinical practice.³

In this report, we discuss a case of acute-onset psychosis in a woman that led to a diagnosis of SLE, together with the neurobiological underpinnings and management options. This case highlights the importance of physical examination and laboratory investigations when

psychiatric symptoms present with concomitant physical signs and symptoms.

Case Presentation

In November 2022, a 45-year-old tribal woman with no past, personal, or family history of psychosis presented to the psychiatry outpatient department of the All India Institute of Medical Sciences with an abrupt onset of behavioural abnormalities characterised by fearfulness, incoherent speech, unprovoked outbursts of anger, intermittent delusions of grandeur, auditory hallucinations, restlessness, and insomnia that had been occurring for two days. Her father provided a history of a low-grade fever (37.2°C) and a non-specific headache that preceded the onset of the behavioural abnormalities; there was no apparent psychological stressor. There were fluctuating pains of the small joints and swelling of both legs.

On physical examination, she had pallor. Mental status examination found that she was oriented, had an unkempt and untidy appearance, made poor eye contact, and that her affect was irritable and restricted. There was no evidence of formal thought disorder, though her thought content revealed delusions of grandiosity and persecution. She claimed that she was the incarnation of a Hindu goddess who had the power to eradicate poverty, which had made her neighbours jealous and they had therefore conspired to demean her. Assessment of her perception revealed a second-person auditory hallucination of an unknown woman commanding her to leave her village. There were, however, no hallucinations in any other sensory modality. She underwent a full blood count, which included haemoglobin, haematocrit, total leucocyte count and differential counts, and platelet counts, and was provisionally diagnosed as having brief psychotic disorder, according to the DSM-5.⁴ She was started on oral olanzapine at an escalating dose of

5 to 10 mg/day over 7 days, with a follow-up planned for 10 days later.

She returned after a month (whilst continuing medication) with significant improvement of her psychotic symptoms but with a hyperpigmented erythematous rash over the malar area of her face and the bridge of her nose that had developed 2 weeks previously (Figure). Further evaluation revealed that these rashes had also developed on the anterior aspect of her chest and both arms. She also reported an exacerbation of pains in the small joints but



Figure. Hyperpigmented malar rash on the face

with no gross abnormality on a brief visual inspection. A neurological examination did not reveal any abnormality.

The new-onset rash and previously reported joint pains and pallor, along with the acute psychosis, aroused suspicion of possible SLE, which prompted a referral to the general medicine specialist. She underwent a panel of laboratory investigations including a full blood count, erythrocyte sedimentation rate, C-reactive protein, lactate dehydrogenase, and extractable nuclear antigen antibody profile; various abnormalities were revealed (Table). However, tests of her liver and renal functions and serum electrolytes were within normal limits. She was advised to undergo magnetic resonance imaging of the brain, but she could not afford it. Taking into consideration the findings of anaemia, psychosis, arthralgia, a hyperpigmented malar rash, and the positive extractable nuclear antigen antibody profile (fulfilling >4 of 11 of the Systemic Lupus International Collaborating Clinics diagnostic criteria⁵), a diagnosis of SLE was made. She was started on oral methotrexate 7.5 mg once weekly, deflazacort 12 mg/day, and hydroxychloroquine 300 mg/day, along with continuation of the olanzapine at a dose of 10 mg/day. Her psychotic symptoms improved, with waxing and waning signs and symptoms of SLE.

Discussion

Neuropsychiatric events occur in 30% to 40% of patients with SLE. Of these, 50% to 60% experience neuropsychiatric events either at the point of disease onset

Table. Results of laboratory tests

Test	Value	Normal range
Haemoglobin, g/dL	6.8	12.5-15
Mean corpuscular volume, fL	62.0	80-100
Mean corpuscular haemoglobin, pg	19.0	27-34
Mean corpuscular haemoglobin concentration, g/dL	31.0	30-36
Peripheral blood smear	Microcytic hypochromic anaemia	-
Erythrocyte sedimentation rate	130 mm (first hour)	0-15 mm/hour (men); 0-20 mm/hour (women)
C-Reactive protein, mg/dL	5.1	<1.0
Lactate dehydrogenase, U/L	782	140-280
Extractable nuclear antigen antibody profile		
Antinuclear antibody	++++ in 1:40 primary dilution (endpoint titre, 1:2560)	-
Anti-double stranded DNA	+++ in 1:10 primary dilution (endpoint titre, 1:80)	-
Sjögren syndrome-related antigen A antibodies	++	-
Ro-52 antibodies	+++	-
Anti-histone antibodies	+	-
Nucleosome antibodies	++	-

or within the first year of diagnosis.⁶ It can manifest with neurological and psychiatric symptoms, which are classified into 19 neuropsychiatric manifestations by the American College of Rheumatology.⁷ Psychosis is an uncommon neuropsychiatric manifestation, occurring in 2% to 3% of patients with SLE.⁸ It is considered a NPSLE manifestation by both the Systemic Lupus International Collaborating Clinics 2012 diagnostic criteria and the European League Against Rheumatism / American College of Rheumatology 2019 classification criteria.^{5,9} However, mood disorders are not considered to be manifestations because of their lower specificity in SLE.

New-onset acute psychosis has multiple causes. The type of onset, clinical manifestation, associated physical findings, and abnormal laboratory parameters can provide clues to the cause. This needs an observant eye to delineate the cause for such a clinical presentation of psychosis. Our patient presented with acute-onset psychosis as the primary symptom, along with a history of fever and non-specific small joint pains; however, the latter two symptoms did not raise the attending psychiatrist's suspicion of SLE. Although commencing antipsychotic therapy was necessary for timely management, further investigations to rule out or confirm other potential causes of the psychosis in the presence of these secondary signs and symptoms was key. In our patient, a follow-up visit revealed a new-onset rash, along with persistent small joint arthralgia and fever that occurred before the initial visit, and laboratory-confirmed anaemia, which prompted a diagnosis of SLE, which was later confirmed. Interestingly, although NPSLE is not uncommon, psychosis as the initial presenting symptom of SLE has not often been reported.

A case series from 2015 reported details of three patients who initially presented with psychosis and were then diagnosed with SLE 6 to 9 months later.³ Treatment resistance in all three cases, along with development of neurological signs and dermatological and systemic symptoms prompted consideration of 'organicity', which necessitated further investigation. All three patients responded to immunological treatments for SLE. A case report in 2010 reported acute-onset psychosis in a Chinese woman in the second trimester of pregnancy who was extensively investigated and diagnosed as having SLE.¹⁰

A comprehensive study of SLE-related psychosis found that 21% of previously undiagnosed patients with SLE initially presented with psychosis.¹¹ In cases of new-onset psychosis, a high degree of clinical suspicion is needed to foresee the underlying disorder. Therefore, autoimmune disorders, particularly SLE, should be considered in young women presenting with acute psychosis. Systemic symptoms and laboratory findings, such as anaemia and raised erythrocyte sedimentation rate, can provide important information about the underlying diagnosis.

There are several hypotheses regarding the aetiopathogenesis of psychosis in SLE. In a systematic review, environmental insults (evidenced by DNA

methylation due to ultraviolet rays, neuronal damage due to inflammation and ischaemia), genetics, inflammation, thrombosis, treatment with corticosteroids, psychosocial stress, blood-brain barrier dysfunction, and elevated levels of cytokines, chemokines, and autoantibodies were all described as possible aetiologies for NPSLE.⁸ Over 20 autoantibodies are associated with NPSLE, some of which are specific to psychosis. These include anti-double stranded DNA, anti-N-methyl-D-aspartic acid receptor 2, and anti-ribosomal P glycoprotein autoantibodies. The proposed mechanisms include autoantibody-induced blood-brain barrier dysfunction (causing the brain to be exposed to exogenous and endogenous toxins), microangiopathy, and caspase mediated neuronal apoptosis.⁸

There are few differences in SLE manifestations between those with neuropsychiatric symptoms and those without. The presence of some autoantibodies is higher in those with NPSLE than in those without,⁸ and patients with NPSLE are reported to have more renal manifestations of the disease.¹²

In terms of management, although antipsychotics are effective, patients with SLE-related psychosis also respond to immune modulators and corticosteroids that are typically indicated for the treatment of SLE.¹³ Although corticosteroids are known to induce psychosis, immunomodulators for SLE (eg, cyclophosphamide, azathioprine, methotrexate, and mycophenolate mofetil) can also cause neuropsychiatric symptoms,⁸ requiring the treating clinician to determine whether such symptoms are due to the SLE itself or iatrogenic. In our patient, psychosis developed even before SLE was diagnosed, thus ruling out the possibility of iatrogenesis. Antipsychotics prescribed at typical doses for the treatment of primary psychotic disorders may often lead to extrapyramidal symptoms; thus, when prescribed, antipsychotics should be given in lower doses. Our patient responded well to olanzapine at a dose of 10 mg/day even before corticosteroids and immunomodulators were started. She responded well with the treatment regimen of antipsychotic, corticosteroids, and immunomodulators.

Conclusion

Psychosis can be the first presenting symptom of SLE. A high degree of clinical suspicion is needed when acute-onset psychosis presents with other clinical signs and symptoms of SLE in women.

Contributors

All authors designed the study, acquired the data, analysed the data, drafted the manuscript, and critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of Interest

All authors have disclosed no conflicts of interest.

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Data Availability

All data generated or analysed during the present study are available from the corresponding author on reasonable request.

Ethics Approval

The patient was treated in accordance with the tenets of the Declaration of Helsinki. The patient provided written informed consent for all treatments and procedures and for publication.

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