

Neuropsychiatric Systemic Lupus Erythematosus: Making the Case for an Expanded Psychiatric Role

Ayol Samuels*, Mirnova E. Ceïde and Naalla Schreiber

Department of Psychiatry & Behavioral Sciences, Montefiore Medical Center/Albert Einstein College of Medicine, New York, USA

*Correspondence to:

Dr. Ayol Samuels, MD
Department of Psychiatry
Montefiore Medical Center/Albert Einstein
College of Medicine, 111 East 210th street
Bronx, NY 10467, USA
Tel: 917 751 2671
E-mail: ayol.samuels@gmail.com

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Abstract

Systemic Lupus Erythematosus can present with psychiatric symptoms. As these symptoms are non-specific and may occur in the absence of clear systemic signs and symptoms of lupus, they are difficult to distinguish from primary psychiatric illnesses. We present the case of a young woman who, on two separate admissions, was treated for a psychiatric illness with no effect and then treated for Neuropsychiatric SLE with remarkable improvement. We discuss the atypical features that a psychiatrist can use to distinguish the two diagnoses and the role of the psychiatrist or neurologist in determining the severity of mental status changes in order to guide treatment.

Introduction

Neuropsychiatric symptoms are common manifestations of Systemic Lupus Erythematosus (SLE) with prevalence estimates ranging from 14% to 80% in adults with SLE [1, 2]. SLE can lead to diverse psychiatric symptoms, including mood and anxiety disorders, acute confusional states, psychosis, and cognitive dysfunction [3]. Although common, Neuropsychiatric SLE (NPSLE) is arguably the least understood of all the lupus manifestations due to lack of clarity from a pathophysiologic, diagnostic, and therapeutic perspective, thereby posing multiple dilemmas in the clinical setting [4].

Case Report

Ms. Z, a 22 years-old South Asian woman with SLE and no other medical history, no past psychiatric history, no toxic habits, and no family psychiatric history presented to our hospital for one month of worsening mouth and body pain with failure to thrive. She could not give a coherent history and was resistant to medical care. On exam, Ms. Z was a poorly groomed, malodorous young woman with pronounced negativism, including flat affect, poverty of speech, psychomotor slowing, and poor eye contact. She denied mood or psychotic symptoms. She was alert and could state her name and age but replied “I can’t say” or “no, no, no” when asked further questions. The remainder of her neurologic exam was unremarkable. As per her family, Ms. Z lost her job and became increasingly isolative, withdrawn, and irritable approximately 9 months prior to admission. They denied depressed mood, increased energy or goal-directed activity, paranoia, and hallucinations. A review of her chart demonstrated a brief period of treatment 3 years prior to admission for SLE (met 4 out of 4 needed criteria with + ANA, + anti-dsDNA, + arthritis, + leukopenia) with low-dose prednisone and hydroxychloroquine.

Upon admission, the rheumatology service treated Ms. Z for what they described as a mild lupus flare, based upon joint findings and positive bloodwork (low c3 and c4, elevated anti-dsDNA, ESR 53, ANA 1:320). Both rheumatology

and neurology believed her psychiatric symptoms were due to Major Depressive Disorder (MDD) and therefore did not include these symptoms in the assessment of the severity of her SLE. The initial treatment protocol consisted of low-dose IV steroids, methylprednisolone 30 mg IV for 5 days, with the subsequent addition of hydroxychloroquine 400 mg daily and an oral prednisone taper from 20 mg daily down to 5 mg daily. This medication regimen ameliorated her polyarthritis but did not improve her mental status. Ms. Z continued to require IV fluids and parenteral nutrition due to her extremely poor oral intake. The psychiatry consult team felt that NPSLE and other medical etiologies should be ruled out first as Ms. Z's psychiatric symptoms were non-specific and highly suggestive of delirium.

The primary medical team, in conjunction with the rheumatology and neurology consult services, initiated a complete medical and neurological work-up to rule out other causes of mental status change. This work-up included an EEG, MRI, lumbar puncture, and blood-work. CSF results were negative for signs of infection or acute inflammation. Laboratory workup revealed normal thyroid function tests, vitamin B12, folic acid, basic metabolic panel, complete blood count, and anti-TPO antibodies. HIV testing and syphilis screen were negative. EEG was normal and a CT scan of the chest, abdomen and pelvis to rule out an ovarian teratoma or a malignancy was unremarkable. Brain MRI showed non-specific punctate white matter lesions. Two pertinent positive findings included Anti-Ribosomal P antibodies that were elevated at greater than 8 (normal < 1) and the presence of oligoclonal bands in the CSF.

Based on these inconclusive findings, rheumatology recommended a trial of psychotropic medications as the first-line treatment for Ms. Z as they remained convinced that her psychiatric symptoms were not severe and likely related to a primary psychiatric illness. The patient did not respond to trials of haloperidol up to 1 mg total daily dose, olanzapine up to 10 mg at bedtime, or sertraline up to 50 mg daily. She had a marked dystonic reaction after receiving an additional 1 mg IV haloperidol, which was given for agitation.

One month into the hospitalization, the patient's sibling visited and reported that Ms. Z was confused, disoriented to time and place, and had poor verbal comprehension in her native language. This new collateral information from her sibling, in conjunction with Ms. Z's lack of response to psychotropic medication, persuaded the medical team and multiple consulting services that the patient's presentation was most consistent with an episode of delirium, likely secondary to NPSLE. At that time, a 3-day course of high-dose pulse steroids consisting of methylprednisolone 1,000 mg daily was given to treat delirium from NPSLE. Ms. Z had marked improvement in her clinical status. She was discharged one week later on prednisone 50 mg daily and mycophenolate 500 mg Q12 for her SLE. She was off all psychotropic medication, with better social function and intact cognition, including orientation and memory.

Approximately 3 weeks later, Ms. Z was brought back to the hospital for refusing food, social withdrawal, headache, and tearfulness. Given her increase in psychiatric symptoms

off psychotropic medication and her normal blood work and physical exam, with reported good compliance to prednisone and mycophenolate, the medical services were again concerned for a primary psychiatric illness like depression. As there was no medical intervention offered, Ms. Z was transferred to the psychiatry floor for management of presumed MDD. Ms. Z remained on the psychiatry floor for 3 weeks and was sequentially treated with trials of aripiprazole up to 15 mg daily and mirtazapine 15 mg QHS, and later olanzapine up to 20 mg daily with concurrent lorazepam at 2 mg Q12 for possible catatonia. Additionally, her mycophenolate was increased to 1500 mg Q12 and her prednisone was lowered to 40 mg daily. Ultimately, the inpatient psychiatric team felt there was no improvement on psychotropic medications, and they believed Ms. Z's presentation was again the result of NPSLE and not an underlying primary psychiatric disorder.

Ms. Z was transferred back to the medicine service for another course of high-dose pulse steroids. This time she was treated with 1,000 mg methylprednisolone IV for 5 days. Two days into this treatment, Ms. Z exhibited improved grooming, ameliorated cognition, increased verbal fluency, and better socialization with her family. She was discharged one month after admission, on definitive SLE treatment including oral methylprednisolone and mycophenolate, and all psychotropic medications were titrated off as an outpatient. She maintained her treatment gains exclusively on immunosuppressants for SLE and no longer required psychiatric follow up.

Discussion

While our case is not a unique presentation of NPSLE, it highlights the difficulties of differentiating the psychiatric presentations of NPSLE from primary psychiatric conditions. NP manifestations are the presenting symptoms in up to 50% of cases of lupus and are often present without other systemic signs and symptoms of SLE [5]. There is no laboratory or radiological biomarker for establishing a diagnosis of NPSLE. MRI, EEG, and CSF findings are often absent or non-specific and may be present in patients with SLE regardless of symptomatology [6, 7]. The presence of anti-ribosomal P antibodies can point to a lupus-related psychosis but is by no means conclusive [6, 8, 9]. Thus NPSLE remains a diagnosis of exclusion [3].

Whereas excluding infections, electrolyte abnormalities, and medication effects is typically possible, excluding a primary psychiatric condition, such as major depressive disorder or schizophrenia, is more difficult as these are also diagnoses of exclusion, which affect a similar demographic as those with SLE [6]. It is important, then, to look for distinguishing clinical features of NPSLE compared with primary psychiatric conditions. In 1999, the American College of Rheumatology delineated 19 possible NP manifestations of SLE, which included psychosis, mood disorder, anxiety disorder, and cognitive disorder [3]. These categories, though, were non-specific and no guidance was given on distinguishing them from psychiatric syndromes. It is due to this lack of specificity and low inter-rater reliability that studies of prevalence for NPSLE vary so drastically [10].

In the case of Ms. Z, while her symptoms might have suggested a major depressive disorder, she did not have the cardinal symptoms of depressed mood or classic anhedonia. And while her behavior could have been characterized as disorganized, she lacked definitive symptoms of schizophrenia, like delusions or hallucinations. Actually, her symptoms of mood lability and isolative, bizarre behavior did not cluster into any specific category of a primary mental illness. Additionally, Ms. Z would consistently say “I can’t say,” which was highly suggestive of the cognitive impairment that her sibling ultimately confirmed. Lastly, Ms. Z’s high sensitivity to EPS from low doses of IV haloperidol was quite atypical and has been linked to several neuropsychiatric conditions [11]. The psychiatry team favored the diagnosis of NPSLE early in both admissions because of these clinical features.

Based on our case, we suggest that the neurologist or psychiatrist should be a key member of the treatment team when negotiating the complexities of the diagnosis and treatment of suspected NPSLE. Several possible features of atypicality might be used to distinguish NPSLE from primary psychiatric syndromes. Acute onset and rapid progression, as seen during the second presentation of Ms. Z, might indicate NPSLE as most primary psychiatric disorders have an insidious onset and gradual progression. The presence of cognitive impairment, in particular alterations in attention or orientation, can indicate NPSLE and are less likely in primary psychiatric disorders. Psychiatric syndromes in DSM 5 consist of core signs or symptoms, in addition to a cluster of other manifestations, which may be lacking in NPSLE, as was the case with Ms. Z. Furthermore, as with Ms. Z, heightened sensitivity to the extrapyramidal side effects (EPS) of antipsychotics can indicate neuropsychiatric autoimmune diseases, like NPSLE [11].

Even when a diagnosis of NPSLE is heavily supported, the necessary treatment is not always clear. Treatment choices should be guided by a good assessment of the severity of a patient’s NP symptoms; however, levels of severity are not clearly defined in existing literature [3, 10]. Severe symptoms should be treated with high-dose IV steroids followed by IV cyclophosphamide as first line treatments and rituximab, IVIG, or plasmapheresis as second line treatments. When symptoms are mild to moderate, though, patients may be treated with symptomatic treatment, like antipsychotics or antidepressants, as was initially suggested with Ms. Z [10, 12]. Due to a lack of clarity in the literature, and possibly due to a lack of experience in assessing psychiatric symptomatology on the part of medical and rheumatology teams, these services may not appreciate the severity of a patient’s psychiatric symptoms, as was the case with Ms. Z.

Conclusion

The consultation-liaison psychiatrist or neurologist should play a crucial role in the diagnosis and management of NPSLE when it manifests with psychiatric symptoms. The psychiatrist can highlight atypical clinical features that would

favor a diagnosis of NPSLE and can assess the severity of a patient’s cognitive, emotional, and behavioral symptoms. An enhanced psychiatric and neurologic role could minimize prolonged morbidity, including multiple hospitalizations and exposure to psychotropic medications, for patients with severe psychiatric manifestations of NPSLE.

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