Pearls & Oy-sters: An unusual neuropsychiatric manifestation of systemic lupus erythematosus

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Pearls

- Catatonia is a syndrome characterized by abnormal behavior, movement, and response to external stimuli. It can occur in systemic lupus erythematosus (SLE) without evidence of structural abnormalities on imaging.
- Diagnosis is made clinically based on the dominance of ≥3 symptoms listed in the DSM-5 (table).
- The underlying cause should be treated in addition to any catatonia-specific treatment (benzodiazepines, electroconvulsive therapy). Prognosis is generally good and is related to the effectiveness of treating the underlying condition.

Oy-sters

- Catatonia is a rare neuropsychiatric manifestation of many medical disorders, and it is not limited to patients with a history of psychiatric illness. Careful consideration of various etiologies that can resemble or contribute to catatonia is required.
- A clinical response to a benzodiazepine challenge may be useful in supporting the diagnosis, but a lack of response does not rule out catatonia.
- Malignant catatonia, presenting with fever and autonomic instability, is an emergency with a high mortality rate (~20%) and should not be missed.

Case report

A 21-year-old man without relevant medical or medication history presented with a 1-month new-onset history of fevers, arthralgias, malar rash, and malaise. Over the course of a week, he became confused, started speaking incoherently, and then stopped verbalizing altogether. He acutely stopped eating, drinking, or ambulating to use the bathroom.

On neurologic examination, he was nonverbal and staring forward, but on occasion would spontaneously look around the room. He had irregular purposeless movements in all 4 limbs. On other occasions, he was observed to sway his head forwards and backwards, and alternate in a flexor and extensor position of his wrists repetitively. The movements were not constant, and he would occasionally lie on his bed without any movements for hours on end. He did not consistently follow commands and he did not mimic movements.

Investigations

Bloodwork showed anemia, thrombocytopenia, and lymphopenia. He had elevated anti-double-stranded DNA, antichromatin, antiribosomal protein, and antiribonucleoprotein antibodies. His complement levels (C3, C4) were depressed. He was diagnosed with systemic lupus erythematosus (SLE).

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Table Clinical manifestations and diagnosis of catatonic disorder due to another medical condition, adapted from DSM-5[4]

Diagnostic criteria for catatonic disorder due to another medical condition (fulfills criteria A–E)	
A. The clinical picture is dominated by at least 3 of the following (items 1–12):	
Feature	Description
1. Stupor	Lack of psychomotor activity
2. Catalepsy	Maintenance of postures passively induced against gravity
3. Waxy flexibility	Initial rigidity prior to reduction of resistance to positioning by examiner
4. Mutism	Very little to no verbal output
5. Negativism	Lack of response to instructions or external stimuli
6. Posturing	Spontaneous maintenance of postures
7. Mannerism	Performing odd depictions of normal actions
8. Stereotypy	Repetitive purposeless stereotyped movements
9. Agitation	Unpredictable and not influenced by external stimuli
10. Grimacing	Odd or forced facial expressions
11. Echolalia	Mimicking others' speech
12. Echopraxia	Mimicking others' movements
B. There is clinical evidence that the disturbance is due to another underlying medical condition.	
C. The disturbance is not better explained by a primary psychiatric cause.	
D. The disturbance does not exclusively occur during the course of delirium.	
E. The disturbance causes significant distress or functional impairment.	

MRI of the brain on initial presentation showed 2 small nonspecific foci of white matter hyperintensity of the right parietal and left frontal lobe with no gadolinium enhancement (figure e-1, links.lww.com/WNL/A469). Magnetic resonance angiography of the head and neck was normal and did not show evidence of vasculitis or other vascular abnormalities.

Thirty-minute EEG studies were repeated twice, 1 week apart. There were no spikes or epileptiform discharges. The studies were performed during the patient's ongoing abnormal hyperkinetic movements, revealing additional muscle artifacts. The only abnormality was mild to moderate background generalized slowing (figure e-2, links.lww.com/WNL/A469).

Lumbar puncture showed 7×10^6/L erythrocytes with 0 nucleated cells in the CSF sample. Glucose level in the CSF was 70 mg/dL (3.9 mmol/L) and the protein level was elevated at 78.3 mg/dL.

Levels of sodium, potassium, chloride, bicarbonate, urea, creatinine, albumin, calcium, magnesium, L-lactate, phosphate, random glucose, and bilirubin were normal. Coagulation studies including international normalized ratio, partial thromboplastin time, antiphospholipid immunoglobulin G and immunoglobulin M, Klaus fibrinogen, and lupus anticoagulant testing were normal. Thyroid-stimulating hormone, aminotransferases, alkaline phosphatase, and γ-glutamyl transferase were in the normal ranges. CSF venereal disease research laboratory (VDRL) test, hepatitis B surface antigen, hepatitis C antibody, and CSF/blood bacterial culture testing were negative, and CSF/serum anti–NMDA receptor antibody tests were negative.

Treatment

Due to the time course of the patient's systemic symptoms coinciding with his neurologic symptoms, he was treated for confirmed systemic and possible neuropsychiatric lupus with corticosteroids, cyclophosphamide, and IV immunoglobulin. Due to a lack of improvement in cognitive status after 2 weeks, 2 courses of 1 g/course IV rituximab were administered.

One night, the nurse paged the resident on-call due to increased agitation and amplitude of the patient's purposeless movements in all 4 limbs. Lorazepam 2 mg was provided, which reduced the patient's agitation and movements. Remarkably, after approximately 5 minutes, the patient sounded a word for the first time.

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The patient started taking 1 mg twice daily of lorazepam, which was titrated to 2 mg thrice daily. He showed substantial improvement in the above symptoms over the next 4 weeks and was subsequently discharged.

The patient completed a total of 6 courses of monthly cyclophosphamide as an outpatient. Oral prednisone therapy was gradually tapered and replaced with ongoing azathioprine maintenance therapy. He was gradually tapered down to lorazepam 1.5 mg three times daily over 6 months, with plans for further tapering with close psychiatric follow-up.

The patient had excellent response to azathioprine therapy with no clinical evidence of SLE recurrence. Although his 3-month follow-up revealed some minor subjective issues with short-term memory, his 6-month follow-up demonstrated a return to his behavioral and cognitive baseline.

Diagnosis

Due to the patient's symptoms of mutism, prolonged passive immobility, excessive purposeless motor activity, repetitive stereotyped movements, agitation, and substantial acute improvement with benzodiazepine therapy, his features were consistent with catatonia as a neuropsychiatric manifestation of SLE.

Discussion

Lifetime prevalence of neuropsychiatric symptoms in SLE has been estimated to range from 80% to 91%.[1,2] Neurologic manifestations include cognitive dysfunction, stroke, seizures, headache, neuropathy, and movement disorders. Psychiatric manifestations include depression, psychosis, anxiety, mania, phobias, delirium, and catatonia. These psychiatric symptoms can occur without any evidence of cerebritis or structural abnormalities.

Catatonia can present at any time in SLE, either as the initial presentation or during relapse. The syndrome is characterized by decreased responsiveness to environmental stimuli, movement disturbances, and disorganized behavior. It is often associated with mood disorders and psychosis, but can rarely occur in many medical and neurologic conditions including HIV infection, stroke, head trauma, organ failure, meningoencephalitis, and hypercalcemia.[3,4]

According to the DSM-5, catatonia is diagnosed based on clinical dominance of at least 3 symptoms, with full details in the table.[4] Malignant presentations with fever and autonomic instability also exist.[5]

A positive lorazepam challenge can aid the diagnosis. Partial and temporary improvement after a few minutes of 1 or 2 lorazepam 1–2 mg IV doses represents a positive test.[5] One study of 21 catatonic patients showed 24% did not respond to lorazepam treatment,[6] and therefore a negative test does not rule out the syndrome.

Potential etiologies that are associated with catatonia or can resemble catatonia including infection, metabolic abnormalities, organ failure, medication effect including neuroleptic malignant syndrome, mass lesions, stroke, autoimmune conditions such as stiff-person syndrome or anti-NMDA encephalitis, delirium, dementia, movement disorders such as severe parkinsonism, and seizures should be considered or excluded.[5]

A recent review noted significant symptom overlap between catatonia and other syndromes of altered mental state (AMS), such as hypoactive delirium or akinetic mutism, leading to diagnostic uncertainty.[7] Symptoms overlap to such a degree that some patients who meet criteria for catatonia can also meet criteria for a diagnosis of delirium.[7] This has led some to suggest delirium and catatonia may exist on a continuum, with both diagnoses being applicable in certain presentations of AMS.[7] However, our case exhibited a positive response to a lorazepam challenge, lacked significant structural abnormalities on imaging, and while he exhibited fluctuations in movements, he did not have fluctuating sensorium, thus suggesting he is better conceptualized as having catatonia over delirium or akinetic mutism.

Treatment of catatonia first includes treatment of the underlying cause in conjunction to any catatonia-specific therapy. Reports have shown that catatonia in SLE can remit during treatment of SLE with steroids or cyclophosphamide.[8] In persistent cases where catatonia-specific treatments were needed, high-dose benzodiazepines and electroconvulsive therapy (ECT) were commonly used to good effect.

For nonmalignant catatonia, treatment with benzodiazepines is first-line. It is typically initiated with lorazepam 1–2 mg every 4–12 hours, increasing daily, and total daily doses of 8–24 mg are common. Response can be seen within 3–7 days on adequate doses.[5] There is no consensus on duration of treatment after remission, and when therapy is tapered off symptoms may re-emerge.[5] ECT can be used concurrently if benzodiazepines alone fail to achieve remission or if rapid response, such as in malignant catatonia, is required.[5] Malignant catatonia is an emergency, with risk of significant morbidity and a mortality rate estimate of 20%.[9]

Treatment response in catatonia has mainly been studied in case series and open prospective trials, generally showing good efficacy of benzodiazepines and ECT.[5,8] Exceptions may exist in prolonged catatonic cases and in patients with schizophrenia.[5] Overall, the long-term prognosis appears to be most closely associated with severity and success in treatment of the underlying psychiatric or medical disorder.[9]

Although associated with a multitude of medical and psychiatric conditions, catatonia is challenging to recognize as its presentation can mimic other neurologic causes affecting movement, behavior, and cognition. This can affect patient morbidity, as prolonged catatonia increases the risk of malnutrition, pulmonary emboli, and cerebrovascular events

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secondary to immobility.[10] Since catatonia can be a sequela of neuropsychiatric manifestations of systemic disease, proper recognition and treatment by clinicians is necessary to improve patient outcomes.[1]

Author contributions

David Dongkyung Kim: study concept and design, preparation of manuscript. Charles Ho: study concept and design, preparation of manuscript. Rebecca King: study supervision, critical revision of manuscript for intellectual content. Sarah A. Morrow: study supervision, critical revision of manuscript for intellectual content.

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