NMDAR antibody encephalitis and fluctuating catatonia

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***N*-Methyl D-aspartate receptor (NMDAR) antibody encephalitis has varied presentations and may often be seen in psychiatry because of a range of associated psychiatric manifestations. Here, the authors present a case of prolonged catatonia that occurred in episodes and continued for months before being successfully diagnosed as a cause of NMDAR antibody encephalitis.**

It is well known that catatonia is associated with various physical conditions along with many psychiatric disorders.[1,2] One of the common neurological conditions linked to catatonia is encephalitis,[1] and in recent years NMDAR antibody encephalitis is also being reported more frequently.[3,4] Various symptomatic presentations like psychosis, catatonia, movement disorders, short-term memory deficit and seizures have been reported in patients with synaptic autoimmunity,[4,5,6,7] which often results in patients being seen in different departments before final diagnosis. In such cases, the commonly reported psychiatric manifestations have been auditory and visual hallucinations, delusions, behavioural changes (frequently agitation), along with catatonia[4,7]

We present here the case of a patient with catatonic symptoms that were prolonged and fluctuating, and who was later diagnosed to have NMDAR antibody mediated autoimmune encephalitis. The presentation of the case is discussed in the light of available literature in this area.

Case report

A 21-year-old male of Afro-Caribbean origin presented as withdrawn, with lethargy, decreased talk, decreased interaction, decreased appetite and low mood, following an episode of 'cold and cough'. He was observed to be drowsy and talked in monosyllables after being involuntarily admitted to a psychiatric hospital following a hostile incident in which he picked up two knives that he used to threaten his relatives. Just before this incident the patient had appeared confused and was seen removing his shoes and shorts in his friend's house.

Past history

Around two years previous to this incident, the patient had been admitted to a general hospital with a two-day history of behavioural changes, vacant episodes and odd speech. There was no evidence of previous mental health concerns or substance use. Upon hospital admission the patient became suddenly uncommunicative. He was reported to have a fever by his carers, however he was apyrexial during admission and his observations were stable. He was sleeping for about three to four hours each day, usually during the early hours of the morning.

There was no history of neck stiffness or photophobia; and the general neurological examinations including cranial nerves were normal. The results of a CT Scan of the brain, CSF, MRI brain scan, CT venogram, EEG, thyroid function test, ACE levels, antinuclear antibody test, copper, and ESR were all normal. His B12 and folate levels were slightly low and a urine drug test was negative. At this time an NMDAR antibody test was not carried out.

Psychiatric evaluation suggested behavioural oddities, states of catatonia and being mute. Some oddities in body movements were described as 'unusual physical gestures, hand movements, stereotyped behaviour'; but no specific neurological involuntary movements were noted. The patient was initially prescribed diazepam 4mg and zopiclone 3.75mg per day; and later these were changed to olanzapine, which was gradually increased to 20mg per day, and lorazepam up to 3mg per day.

The patient presented with psychomotor retardation, social withdrawal and mutism most of the time. Occasionally, he uttered a few words after being persuaded to do so and exhibited ambitendence and negativism as well. At times he was also seen to be excitable and aggressive. There was very gradual improvement in his condition after around a month. Delayed reaction time and talking in very short sentences continued, however, and there were no obvious psychotic symptoms. His condition improved approximately six months after initial onset of his symptoms, which had been fluctuating in intensity. Following this his dosage of olanzapine was gradually decreased to 7.5mg over the period of a year.

Progress

In the ward, the patient was aggressive and occasionally attacked other patients. He appeared suspicious and guarded, but mostly remained mute. He was prescribed olanzapine up to 20mg per day and diazepam up to 15mg a day, and there was a slow improvement in his condition. He was discharged after 50 days under the care of home treatment team, as he was deemed to be manageable in a community. However, his symptoms of suspicion, decreased talk, no insight and a reluctance to take medication continued.

At around three weeks after discharge, the patient was readmitted with catatonic symptoms such as mutism, along with gross psychomotor retardation. There were no other psychotic symptoms and he was non-compliant to medications in the community. Following admission, he responded gradually to lorazepam 4mg per day and his antipsychotic was changed to quetiapine, which was gradually increased to 600mg whilst lorazepam was later changed to diazepam 15mg daily. He was discharged after 52 days as an inpatient under the care of a home treatment team.

However, the patient's mental state continued to fluctuate, with occasional mutism, restricted affect, withdrawal, psychomotor retardation, suspiciousness, poor appetite and increased sleep. He also exhibited bouts of anger and physical aggression and was almost mute during reviews, but occasionally scribbled a few words on paper when given the option. After approximately seven weeks following discharge from the ward he was involuntarily admitted again following a bout of aggression where he elbowed a glass door shouting and screaming. He was treated with olanzapine 20mg per day and received 12 ECT treatments. This resulted in some improvement in the symptoms, but he needed prompting to engage in activities of daily living.

During this psychiatric admission, the patient's ECG, MRI brain, EEG, U&E, LFT, TFT, lipid profile, FBC, B12 folate, ferritin, and ANA were all normal. However the serum NMDAR antibodies were positive so the possibility of NMDAR encephalitis was considered and he was referred to the neurology department. There was no obvious focal neurological deficit though his Addenbrooke's cognitive examination (ACE) score was 77/100, which was significantly low. His CSF NMDAR antibodies test was negative; however a repeat serum NMDAR test was positive.

Neurologists confirmed that the patient had autoimmune antibody mediated NMDAR encephalitis and he received IV immunoglobulin therapy (Privigen) 45g per day for five days. A repeat score of ACE before the immunoglobulin treatment was 90/100.

The patient recovered clinically and continued to remain stable, with no recurrence of symptoms within 24 months of observation following immunoglobulin treatment, and with a repeat ACE score of 96/100. The olanzapine dose was gradually decreased.

Discussion

The patient presented primarily with catatonic features, mostly mutism; and occasionally ambitendence and negativism. Associated symptoms were lethargy, increased sleep, appetite disturbance and hostility. There were no specific delusions and hallucinations, although he was guarded and suspicious. Mood symptoms were not observed. The intensity of the features fluctuated, but they continued for a long time. Although benzodiazepines, antipsychotics and ECT were helpful, the improvement in the patient's symptoms was not lasting. However, his condition did improve following the immunoglobulin therapy for anti-NMDAR encephalitis. There were no more catatonic symptoms, lethargy, suspiciousness or aggressive behaviour; he became more active and his social interactions improved.

It has been reported that anti-NMDAR encephalitis develops and resolves as a multistage process, with most patients having a viral-like prodrome, followed by the development of alterations in memory, behaviour and cognition, psychosis, seizures, dyskinesia (orofacial, limb and trunk), and autonomic and breathing instability.[6]

While there were many similarities to the previously reported presentations of such cases, there were a few interesting observations to be made from this example. The flu-like symptoms suggestive of a possibility of viral infection were not prominent, and although oddities in body movements were noted, specific examples of dyskinesia were not described. There was also no altered sensorium, seizure activity, autonomic instability or hypoventilation, which are symptoms that have been described in many other cases.[6] Furthermore, many patients with anti-NMDAR encephalitis have abnormalities in EEG, MRI, CSF, - however these were not observed in the index patient. A proportion of patients with anti-NMDAR encephalitis are reported to have tumours,[8] however there was no report of any tumour in this case. However, there were cognitive disturbances as observed by the dwindling ACE scores, which improved following interventions.

In this case, it was most striking that the patient presented with a

catatonia that was prolonged and fluctuating. It appeared that the patient had had two distinct episodes lasting several months before being diagnosed with anti-NMDAR encephalitis. Understandably, the catatonia was partially responsive to the usual treatments.

Variations in the presentation of catatonia and its response to treatment are common.[9] However, some features may guide clinicians about the possibility of encephalitis. It is important to identify these patients early, as a considerable proportion may develop severe sequelae that can result in death.[10] A study has reported some differentiating features that show psychiatric patients can exhibit a stuporous type of catatonia more frequently, whilst neurological patients demonstrate a mixed form of catatonia with more complications, longer hospitalisations, and more days with catatonia.[1] The index case had a similar presentation as the latter. Anti-NMDAR encephalitis may be suspected for acute presentations of catatonia where there are atypical presentations with viral-like prodrome, oddities in movements, or when the symptoms are not responding adequately to the usual treatment. There is clearly a need for psychiatrists to become familiar with this illness considering its presentation and possible consequences.

In conclusion, this case highlighted that anti-NMDAR encephalitis may present with prolonged and fluctuating catatonic symptoms of varying severity. Early clinical suspicion and appropriate investigation is the key to diagnose this condition. Whilst immunoglobulin therapy can lead to clinical recovery, patients may require psychiatric intervention to control the symptoms. As observed in this case, the psychiatric interventions may range from using benzodiazepines, antipsychotics and ECT, along with intensive community support and hospitalisation. Overall it also suggests a strong case for collaboration between neurologists and psychiatrists.

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Declaration of interests

No conflicts of interest were declared.

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