Stuck in a rut with the wrong diagnosis

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How would you handle this case?

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Ms. N, age 58, has a history of bipolar disorder with psychotic features. While being treated in the ED for violent behavior, she develops signs of catatonia. How can you best help her?

CASE Aggressive behaviors, psychosis

Ms. N, age 58, has a long history of bipolar disorder with psychotic features. She presents to our emergency department (ED) after an acute fall and frequent violent behaviors at her nursing home, where she had resided since being diagnosed with an unspecified neurocognitive disorder. For several weeks before her fall, she was physically aggressive, throwing objects at nursing home staff, and was unable to have her behavior redirected.

While in the ED, Ms. N rambles and appears to be responding to internal stimuli. Suddenly, she stops responding and begins to stare.

HISTORY Severe, chronic psychosis and hospitalization

Ms. N is well-known at our inpatient psychiatry and electroconvulsive therapy (ECT) services. During the last 10 years, she has had worsening manic, psychotic, and catatonic (both excited and stuporous subtype) episodes. Three years ago, she had experienced a period of severe, chronic psychosis and excited catatonia that required extended inpatient treatment. While hospitalized, Ms. N had marginal responses to clozapine and benzodiazepines, but improved dramatically with ECT. After Ms. N left the hospital, she went to live with her boyfriend. She remained stable on monthly maintenance ECT treatments (bifrontal) before she was lost to follow-up 14 months prior to the current presentation. Ms. N's family reports that she needed a cardiac clearance before continuing ECT treatment; however, she was hospitalized at another hospital with pneumonia and subsequent complications that interrupted the maintenance ECT treatments.

Approximately 3 months after medical issues requiring hospitalization began, Ms. N received a diagnosis of neurocognitive disorder due to difficulty with activities of daily living and cognitive decline. She was transferred to a nursing home by the outside hospital. When Ms. N's symptoms of psychosis returned and she required inpatient psychiatric care, she was transferred to a nearby facility that did not have ECT available or knowledge of her history of catatonia resistant to pharmacologic management. Ms. N had a documented history of catatonia that

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spanned 10 years. During the last 4 years, Ms. N often required ECT treatment. Her current medication regimen prescribed by an outpatient psychiatrist includes clozapine, 300 mg twice daily, and clonazepam, 0.5 mg twice daily, both for bipolar disorder.

EVALUATION An unusual mix of symptoms

In the ED, Ms. N undergoes a CT of the head, which is found to be nonacute. Laboratory results show that her white blood cell count is 14.3 K/µL, which is mildly elevated. Results from a urinalysis and electrocardiogram (ECG) are unremarkable.

After Ms. N punches a radiology technician, she is administered IV lorazepam, 2 mg once, for her agitation. Twenty minutes after receiving IV lorazepam, she is calm and cooperative. However, approximately 4 hours later, Ms. N is yelling, tearful, and expressing delusions of grandeur—she believes she is God.

After she is admitted to the medical floor, Ms. N is seen by our consultation and liaison psychiatry service. She exhibits several signs of catatonia, including grasp reflex, gegenhalten (oppositional paratonia), waxy flexibility, and echolalia. Ms. N also has an episode of urinary incontinence. At some parts of the day, she is alert and oriented to self and location; at other times, she is somnolent and disoriented. The treatment team continues Ms. N's previous medication regimen of clozapine, 300 mg twice daily, and clonazepam, 0.5 mg twice daily. Unfortunately, at times Ms. N spits out and hides her administered oral medications, which leads to the decision to discontinue clozapine. Once medically cleared, Ms. N is transferred to the psychiatric floor.

What would be your first step in treating Ms. N?

a) switch her to a different antipsychotic
b) switch her to a different benzodiazepine
c) increase her benzodiazepine dosage
d) file paperwork for involuntary ECT
e) all of the above
f) b, c, and d

TREATMENT Bifrontal ECT initiated

On hospital Day 3 Ms. N is administered a trial of IM lorazepam, titrated up to 6 mg/d (maximum tolerated dose) while the treatment team initiates the legal process to conduct ECT because she is unable to give consent. Once Ms. N begins tolerating oral medications, amantadine, 100 mg twice daily, is added to treat her catatonia. As in prior hospitalizations, Ms. N is unresponsive to pharmacotherapy alone for her catatonic symptoms. On hospital Day 8, forced ECT is granted, which is 5 days after the process of filing paperwork was started. Bifrontal ECT is utilized with the following settings: frequency 70 Hz, pulse width 1.5 ms, 100% energy dose, 504 mC. Ms. N does not experience a significant improvement until she receives 10 ECT treatments as part of a 3-times-per-week acute series protocol. The Bush-Francis Catatonia Rating Scale (BFCRS) and the KANNER scale are used to monitor her progress. Her initial BFCRS score is 17 and initial KANNER scale, part 2 score is 26.

Ms. N spends a total of 61 days in the hospital, which is significantly longer than her previous hospital admissions on our psychiatric unit; these previous admissions were for treatment of both stuporous and excited subtypes of catatonia. This increased length of stay coincides with a significantly longer duration of untreated catatonia. Knowledge of her history of both the stuporous and excited subtypes of catatonia would have allowed for faster diagnosis and treatment.[1]

The authors' observations

Originally conceptualized as a separate syndrome by Karl Kahlbaum, catatonia was considered only as a specifier for neuropsychiatric conditions (primarily schizophrenia)

Clinical Point

Knowledge of Ms. N's history of both the stuporous and excited subtypes of catatonia would have allowed for faster diagnosis and treatment

Table 1

DSM-5 criteria for catatonia[a]

Symptom	Description
Stupor	No psychomotor activity; not actively relating to environment
Catalepsy	Passive induction of posture held against gravity
Waxy flexibility	Slight, even resistance to positioning by examiner
Mutism	No, or very little, verbal response
Negativism	Opposition or no response to instruction or external stimuli
Posturing	Spontaneous and active maintenance of posture against gravity
Mannerism	Odd, circumstantial caricature of normal actions
Stereotypy	Repetitive, abnormally frequent, non-goal-directed activities
Agitation	Without apparent cause
Grimacing	Facial expression of disgust, disapproval, or pain
Echolalia	Mimicking another's speech
Echopraxia	Mimicking another's movements

[a]DSM-5 requires 3 of 12 symptoms to be present, although symptoms may fluctuate with time

Source: Reference 3

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One study found that using a standardized diagnostic instrument for catatonia resulted in a 7-fold increase in diagnosis

as recently as DSM-IV-TR.[2] DSM-5 describes catatonia as a marked psychomotor disturbance and acknowledges its connection to schizophrenia by keeping it in the same chapter.[3] DSM-5 includes separate diagnoses for catatonia, catatonia due to a general medical condition, and unspecified catatonia (for catatonia without a known underlying disorder).[3] A recent meta-analysis found the prevalence of catatonia is higher in patients with medical/neurologic illness, bipolar disorder, and autism than in those with schizophrenia.[4]

Table 1[3] highlights the DSM-5 criteria for catatonia. DSM-5 requires 3 of 12 symptoms to be present, although symptoms may fluctuate with time.[3] If a clinician is not specifically looking for catatonia, it can be a difficult syndrome to diagnose. Does rigidity indicate catatonia, or excessive dopamine blockade from an antipsychotic? How can seemingly contradictory symptoms be part of the same syndrome? Many clinicians associate catatonia with the stuporous subtype (immobility, posturing, catalepsy), which is more prevalent, but the excited subtype, which may involve severe agitation, autonomic dysfunction, and impaired consciousness, can be lethal.[2] The diversity in presentation of catatonia is not unlike the challenging variety of symptoms of heart attacks.

A retrospective study of all adults admitted to a hospital found that only 41% of patients who met criteria for catatonia received this diagnosis.[5] Further complicating the diagnosis, delirium and catatonia can co-exist; one study found this was the case in 1 of 3 critically ill patients.[6] DSM-5 criteria for catatonia due to another medical condition exclude the diagnosis if delirium is present, but this study and others suggest this needs to be reconsidered.[3]

A standardized evaluation is key

Just as a patient who presents with chest pain requires a standardized evaluation, including a pertinent history, laboratory workup, and ECG, psychiatrists may also use standardized diagnostic instruments to aid in the diagnosis of catatonia. One study of hospitalized patients with schizophrenia found that using a standardized diagnostic procedure for catatonia resulted in a 7-fold increase in the diagnosis.[7] The BFCRS is the most common standardized instrument for catatonia, likely due to its high inter-rater reliability.[8]

Table 2

Causes of catatonia

Category	Prominent examples
Psychiatric disorders	Schizophrenia spectrum, mood, obsessive-compulsive, autism spectrum
Cerebrovascular	Aneurysms, arteriovenous malformation, subdural hematomas
Tumors	Angiomas, frontal lobe tumors, paraneoplastic diseases
Infections	HIV/AIDS, viral encephalitis, bacterial sepsis
Metabolic causes	Cushing's disease, hyperparathyroidism, diabetic ketoacidosis, uremia
Toxins	Coal gas, tetraethyl lead poisoning
Drug-induced	Antipsychotics, antidepressants, anticonvulsants, lithium, hallucinogens, corticosteroids, baclofen, stimulants, metoclopramide
Related to drug withdrawal	Dopaminergic agents, GABAergic agents, sedative-hypnotics, clozapine

GABA: gamma aminobutyric acid

Source: Reference 13

Other scales include the KANNER scale and Northoff Catatonia Scale, which emphasize different aspects of the disease or for certain clinical populations (eg, the KANNER scale adjusts for patients who are nonverbal at baseline). One study suggested that BFCRS has lower reliability for less-severe illness.[9] These differences emphasize that psychiatry does not have a thorough understanding of the intricacies of catatonia. However, using validated screening tools can lead to more consistent diagnoses and continue important research on this often-misunderstood illness.

Dangers of untreated catatonia

Rapid treatment of catatonia is necessary to prevent mortality. A study of patients in Kentucky's state psychiatric hospitals found that untreated catatonia with resultant death from pulmonary embolism was the leading cause of preventable death.[10] A 17-year retrospective study of patients with schizophrenia admitted to 1 hospital found that those with catatonia were >4 times as likely to die during hospitalization than those without catatonia.[11] The significant morbidity and mortality from untreated catatonia are typically attributed to the consequences of poorly controlled movements, immobility, autonomic instability, and poor/no oral intake. Reduced oral intake can result in malnutrition, dehydration, arrhythmias, and increased risk of infections. Furthermore, chronic catatonic episodes are more difficult to treat.[12] In addition to the aggressive management of neuropsychiatric symptoms, it is vital to evaluate relevant medical etiologies that may be contributing to the syndrome (***Table 2***[13]). Tracking vital signs and laboratory values, such as creatine kinase, electrolytes, and complete blood count, is required to ensure the medical condition does not become life-threatening.

Treatment options

Studies and expert opinion suggest that benzodiazepines (specifically lorazepam, because it is the most studied agent) are the first-line treatment for catatonia. A lorazepam challenge test—providing 1 or 2 mg of IV lorazepam—is considered diagnostic and therapeutic given the high rate of response within 10 minutes.[14] Patients with limited response to lorazepam or who are medically compromised should undergo ECT. Electroconvulsive therapy is considered the gold-standard treatment for catatonia; estimated response rates range from 59% to 100%, even in patients who fail to respond to pharmacotherapy.[15] Although highly effective, ECT is often hindered by the time

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Clinical Point

Benzodiazepines, specifically lorazepam, are the first-line treatment for catatonia

Table 3

Treatment of catatonia

Treatment	Advantages	Disadvantages
Lorazepam	Best studied Considered a first-choice agent Improvements can occur in minutes; may be diagnostic Oral/IM/IV formulations available	Could worsen comorbid delirium Oversedation, disinhibition may occur Minority of patients show minimal or no response
Electroconvulsive therapy	Rapid and thus an important consideration in malignant or life-threatening catatonia	Requires sedation Logistical challenges Stigma
Clozapine[a]	May help treat underlying psychotic and neuroleptic malignant syndrome symptoms	Multitude of dangerous adverse effects May only be beneficial for psychotic spectrum illness
Other second-generation antipsychotics[a]	May ameliorate psychotic symptoms	May only be beneficial for schizophrenia spectrum disorders High-potency agents could worsen catatonia
Zolpidem[a]	Alternative to lorazepam if benzodiazepines are not tolerated or are ineffective Can have rapid response	Could worsen comorbid delirium Oversedation, disinhibition may occur Minority of patients show minimal or no response
Amantadine[a]	Fairly well-tolerated Good adjunctive agent to GABA agonists	May worsen psychosis and delirium Response may take days to 1 week
Memantine[a]	Fairly well-tolerated Good adjunctive agent to GABA agonists	May worsen psychosis Response may take days to 1 week
Topiramate[a]	Fairly well-tolerated	Potential decreased appetite

[a]Indicates limited research conducted, largely based on case reports or expert opinion

GABA: gamma-aminobutyric acid

Source: References 14-18

required to initiate treatment, stigma, lack of access, and other logistical challenges.

Table 3[14-18] highlights the advantages and disadvantages of treatment options for catatonia. Some researchers have suggested a zolpidem challenge test could augment lorazepam because some patients respond only to zolpidem.[14] The efficacy of these medications along with some evidence of anti-*N*-methyl-D-aspartate medications, such as amantadine and memantine, suggest that there is an underactivation of gamma-aminobutyric acid (GABA) and overactivation of glutamate in the brain,[16] with some researchers noting the similarity between catatonia and the fear response.[17] Consequently, excessive dopamine D2 antagonism or withdrawal of dopamine agonists can either bring on or worsen the symptoms of catatonia, with researchers identifying an overlap between neuroleptic malignant syndrome and catatonia.[18] Although some studies suggest that second-generation antipsychotics (SGAs), particularly lower-potency agents such as olanzapine, may help treat catatonia, other studies suggest using caution when initiating in patients without an underlying psychotic illness. The treating clinician may want to consider switching a patient receiving a high-potency

Related Resource

- Freudenreich O, Francis A, Fricchione GL. Chapter 9. Psychosis, mania, and catatonia. In: Levenson, James L, ed. The American Psychiatric Association Publishing textbook of psychosomatic medicine and consultation-liaison psychiatry. 3rd ed. American Psychiatric Association Publishing; 2019.

Drug Brand Names

Amantadine • Symmetrel	Lithium • Eskalith, Lithobid
Aripiprazole • Abilify	Lorazepam • Ativan
Baclofen • Ozobax	Metoclopramide • Reglan
Bupropion ER • Wellbutrin XL	Memantine • Namenda
Clonazepam • Klonopin	Topiramate • Topamax
Clozapine • Clozaril	Zolpidem • Ambien

antipsychotic to one with a lower potency, lowering the dose of high-potency agent, or discontinuing the medication altogether.

Ms. N was ultimately diagnosed with bipolar disorder, current episode mixed, with psychotic and catatonic features. Ms. N had symptoms of mania including grandiosity, periods of lack of sleep, delusions as well as depressive symptoms of tearfulness and low mood. The treatment team had considered that Ms. N had delirious mania because she had fluctuating sensorium, which included varying degrees of orientation and ability to answer questioning. However, the literature supporting the differentiation between delirious mania and excited catatonia is unclear, and both conditions may respond to ECT.[18] A diagnosis of catatonia allowed the team to use rating scales to track Ms. N's progress by monitoring for specific signs, such as grasp reflex and waxy flexibility.

OUTCOME Return to baseline

Before discharge, Ms. N's BFCRS score decreases from the initial score of 17 to 0, and her KANNER scale score decreases from the initial score of 26 to 4, which correlates with vast improvement in clinical presentation. Once Ms. N completes the acute ECT treatment, she returns to her baseline level of functioning, and is discharged to live with her boyfriend. She is advised to continue weekly ECT for the first several months to ensure clinical stability. This regimen is later transitioned to biweekly and then monthly. Electroconvulsive therapy protocols from previous research were utilized in Ms. N's case, but ultimately the lowest number of ECT treatments needed to maintain stability is determined clinically over many years.[19] Ms. N is discharged on aripiprazole, 15 mg/d; bupropion ER, 300 mg/d (added after depressive symptoms emerge while catatonia symptoms improve midway through her lengthy hospitalization); and memantine, 10 mg/d. Ideally, clozapine would have been continued; however, due to her history of nonadherence and frequent restarting of the medication at a low dose, clozapine was discontinued and aripiprazole initiated.

More than 1 year later, Ms. N remains stable and continues to receive monthly ECT maintenance treatments.

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Clinical Point

ECT is considered the gold-standard treatment for catatonia, with estimated response rates ranging from 59% to 100%

Bottom Line

Catatonia should always be considered in a patient who presents with acute neuropsychiatric symptoms. Rapid diagnosis with standardized screening instruments and aggressive treatment are vital to prevent morbidity and mortality.

Clinical Point

Once Ms. N completes the acute ECT treatment, she returns to her baseline level of functioning and is discharged

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