When Nothing Stops Catatonia Except Electroconvulsive Therapy and Maybe A New Savior, Clozapine

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Catatonia occurs during the course of different psychiatric and medical disorders, with an estimated prevalence of 10% in some inpatient populations.[1] When catatonia is recognized, the treatment of choice is lorazepam or electroconvulsive therapy (ECT). However, it is not uncommon for patients with excited catatonia to be treated with antipsychotics to manage their aggression and excitement.

We present a case of catatonia that was initially not recognized and failed treatment with several antipsychotics, resulting in the development of neuroleptic malignant syndrome (NMS) and rhabdomyolysis.

Case Report

A 26-year-old man with a diagnosis of bipolar disorder, with history of multiple and lengthy hospitalizations and recent history of NMS in association with haloperidol, presented to the emergency department (ED) with worsening paranoia and agitation. He had been discharged from another inpatient facility 5 days prior after being hospitalized for over a month due to similar symptoms. He had been discharged on aripiprazole 2 mg twice/day, clonazepam 1 mg in the morning and 2 mg at bedtime, olanzapine 20 mg by mouth in the morning, and prazosin 1 mg 3 time/day and was reported to be compliant with treatment following discharge. He presented with agitation, and he attacked multiple staff in the ED. He was initially treated with chlorpromazine 100 mg intramuscular (IM), and this was followed by confusion, tachycardia, fever, and a creatine kinase (CK) level of 7,013 U/L. He was subsequently transferred to the medical floor for management of NMS, and he was treated with lorazepam 2 mg 3 times/day and valproic acid 500 mg twice/day. NMS resolved in 4 days, and his CK level dropped to 749 U/L. He was transferred back to the psychiatry department, as his agitation, periodic excitement, and paranoia continued. Attempts to treat him with olanzapine, aripiprazole, risperidone, fluphenazine, and lithium resulted in significant rhabdomyolysis with elevation of CK > 2,000 U/L, elevation of myoglobin, and normalization of levels following discontinuation despite the persistence of agitation and aggression. Valproic acid was continued, as his levels stabilized at 88 g/mL with minimal effect on his aggression and excitement.

His diagnosis was revisited, and he was noted to exhibit some catatonic features including mutism, excitement, staring, impulsivity, posturing, combativness, grimacing, and mannerism with a calculated Bush-Francis Catatonia Rating Scale[2] of 14. Hence, while maintaining him on valproic acid 500 mg twice/day, he was started on lorazepam, and the dose was increased gradually to 30 mg/day, which was given as a standing dose or IM as needed with no response. Trials of diazepam 20 mg twice/day and zolpidem 10 mg were not successful. Consent for ECT was obtained from his family. His symptoms improved significantly after the third round of bilateral ECT. However, ECT was stopped after the fifth round due to provider unavailability. Unfortunately, his symptoms recurred 2 days later. Attempts to transfer him to other facilities for ECT failed due to his escalating aggression. Clozapine was started and increased gradually to 150 mg twice/day with no adverse events noted. His aggression, catatonia, and psychosis improved, and he was discharged 1 week later on valproic acid 500 mg twice/day and clozapine 150 mg twice/day.

Discussion

Catatonia and NMS share similar pathology, symptoms, and treatment modalities.[3] Several experts[4–6] developed operational criteria for NMS with a significant overlap and proposed a set of clinical and laboratory criteria for diagnosis that involved fever, rigidity, recent use of antipsychotics, alteration of mental status, autonomic nervous system instability, and other laboratory abnormalities such as rhabdomyolysis, leukocytosis, and other changes. However, some cases of incipient NMS did not fulfill the suggested previous criteria, and recently the *DMS-5*[7] addressed this problem by eschewing the strict parameters for diagnosis and rather described the array of signs and laboratory abnormalities and encouraged a reliance on clinical judgment for diagnosis.

Literature is replete with cases of catatonia preceding NMS, especially when antipsychotics are used, and the treatment of catatonia with lorazepam can result in masking some core

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features of NMS, making the diagnosis more challenging.[8] Some authors[9,10] recommend against the use of antipsychotics altogether during catatonia, while the Maudsley guidelines[11] recommend using atypical antipsychotics during catatonia when NMS is ruled out. Some studies[12,13] on the use of schizophrenia with catatonic signs showed good response to antipsychotics. Other research showed good response of schizophrenia patients with catatonic features to clozapine.[14] Although not common, few reports linked clozapine to NMS, while evidence of improvement of catatonia with clozapine use is now accumulating.[15–17]

Antipsychotic-induced rhabdomyolysis can occur in the context of NMS or serotonin syndrome, but it has also been described independent of the 2 conditions, with 1 study[18] estimating the frequency to be up to 10% in the absence of NMS or extrapyramidal symptoms.

Our patient developed rhabdomyolysis and NMS following the use of several antipsychotics. While it might be difficult to exclude agitation, restraints, and IM injections from the etiology of rhabdomyolysis, the normalization following discontinuation of antipsychotics despite persistence of aggression, absence of rhabdomyolysis with lorazepam injections, and presence of catatonic symptoms all suggest their role. It is also difficult to separate early NMS manifested with rhabdomyolysis from antipsychotic-induced rhabdomyolysis. However, due to the recent history of NMS with haloperidol and chlorpromazine, antipsychotics were discontinued.

Our patient failed high doses of lorazepam and trials of diazepam and zolpidem. His catatonic symptoms responded favorably to ECT. However, as ECT became unavailable, clozapine adequately and safely treated catatonia without causing significant adverse events.

Our case reinforces the need for caution when using antipsychotics in the management of patients with catatonia, as it can trigger NMS. When needed, clozapine might be a safer option, especially when benzodiazepines fail and ECT is unavailable.

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