Severe Catatonia Following Sudden Withdrawal of Quetiapine

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Catatonia is a syndrome characterized by psychomotor abnormalities. It is hypothesized to be associated with γ-aminobutyric acid (GABA) hypoactivity and involves functional alterations between the basal ganglia, thalamus, and cortex.[1–3] First-line treatments are benzodiazepines or electroconvulsive therapy (ECT).[1,2] Dopamine-blocking drugs should be avoided, as they can worsen or precipitate catatonia.[1,2] We present a case depicting the development of severe catatonia after stopping quetiapine. Withdrawal catatonia is an uncommon condition with onset shortly after stopping a drug, primarily associated with benzodiazepines and clozapine.[2]

Case Report

We present the case of a 66-year-old woman treated in the inpatient unit for severe psychotic depression. She was previously diagnosed with recurrent depressive disorder and had a prior hospitalization because of psychotic depression. We established a history of psychotic symptoms for 3 months, characterized by delusions of ruin and somatic concerns, concomitant with a severely depressed mood and anhedonia. On the 28th day of combined treatment with escitalopram (20 mg) plus quetiapine (600 mg), she developed intolerable side effects, namely severe lower limb edema and drowsiness. Upon evaluation, the internist physician advised the discontinuation of quetiapine. We discontinued quetiapine within 3 days, using low-dose olanzapine (5 mg/d) to prevent withdrawal symptoms. She developed a sudden catatonic syndrome 3 days later, scoring 28 points on the Bush-Francis Catatonia Rating Scale (BFCRS).[4] Beyond the classic symptoms of extreme hypoactivity, nonresponse to painful stimuli, no speech, negativism, rigidity, waxy flexibility, and refusal to eat or drink, she presented autonomic instability, namely hypertension and tachycardia. We did not find alterations during the physical and neurologic examination. She required urgent intubation for nutritional support and the utilization of a urinary catheter due to acute urinary retention. She stayed under close monitoring. We excluded major medical precipitants, namely metabolic, infectious, or neurologic conditions, and all ancillary examination results were within normal limits (Table 1). Finally, we considered a differential diagnosis between neuroleptic malignant syndrome, serotonin syndrome, and malignant or severe catatonia, depicted in Table 1, and established a diagnosis of severe catatonia. At this point, we suspended olanzapine. ECT was not readily available. Treatment with clonazepam 1 mg (titrated to 8 mg) was started, with a significant improvement in overall symptoms on the first day, as her BFCRS score decreased from 28 to 20 points. One week later, the patient still presented psychomotor retardation, and the delusional ideas of somatic concerns emerged once more. We decided to introduce clozapine, slowly titrated to 100 mg/d, with excellent clinical response. On day 15, she improved significantly, presenting with only mild psychomotor retardation and no psychotic features. Her BFCRS score decreased to 0 points.

Discussion

Withdrawal symptoms associated with quetiapine, such as agitation, dysphoria, insomnia, and hypertension, have been previously reported.[5] Still, to our knowledge, this is the first report of withdrawal catatonia due to quetiapine discontinuation. Withdrawal catatonia is mainly described with benzodiazepines and clozapine.[1,2] Both medications are used as treatments for catatonia, suggesting the occurrence of "rebound" catatonia when discontinuing medications used to treat it. This phenomenon is possibly comparable to the emergence of psychosis after antipsychotic withdrawal, which is mainly associated with clozapine and occurs in approximately 20% of treatment-resistant patients who suddenly discontinue it.[6] This may be related to the supersensitivity of dopamine receptors and cholinergic, serotonergic, and GABAergic systems.[1,2,6] Similar to clozapine, quetiapine has a rapid dissociation from the D_2 receptor and complex multireceptor interaction.[7] There is some evidence that dopamine D_2 receptor blockage is related to causing or worsening catatonia syndrome.[6] We speculate that olanzapine initiation or the olanzapine plus quetiapine withdrawal could have worsened the catatonia features in this case. There are successful reports of quetiapine being used to treat schizophrenia with catatonic stupor.[8] A combined effect of quetiapine and benzodiazepines is described in the treatment of catatonia.[8] The etiology of withdrawal catatonia is not fully understood, and further research is required to understand the role that quetiapine may play in it.

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Table 1. Differential Diagnosis for Catatonia

	Catatonia	Malignant Catatonia	Neuroleptic Malignant Syndrome	Serotonin Syndrome
In favor				
	Behavioral prodrome characterized by psychotic depression Normal laboratory values 6 of 12 *DSM-5* criteria are met (stupor, waxy flexibility, mutism, negativism, posturing, and grimacing) Mental status changes with predominant catatonic signs and mutism Normal CT scan Evident clinical response to treatment with benzodiazepines	Behavioral prodrome characterized by psychotic depression 6 of 12 *DSM-5* criteria are met (stupor, waxy flexibility, mutism, negativism, posturing, and grimacing) Rapid progression, within a few days Autonomic instability, with tachycardia and high blood pressure Mental status changes with predominant catatonic signs and mutism Normal CT scan Evident clinical response to treatment with benzodiazepines	Rapid progression, within a few days Autonomic instability, with tachycardia and high blood pressure Mental status change with predominant catatonic signs and mutism Normal CT scan	Rapid progression, within a few days Autonomic instability, with tachycardia and high blood pressure Mental status change
Against				
	Autonomic instability, with tachycardia and high blood pressure	Absence of typical symptoms such as hyperthermia and muscular rigidity at physical examination Blood tests with normal serum CK No other laboratory findings	Clinical picture develops after the discontinuation of an antipsychotic medication Presence of signs, such as posturing and grimacing, not generally observed in NMS Absence of typical symptoms such as hyperthermia and muscular rigidity at physical examination Blood tests with normal serum CK No other laboratory findings	No changes in serotonergic drugs were made Absence of typical features such as nausea, vomiting, and diarrhea, but also shivering, hyperreflexia, myoclonus, and ataxia Presence of signs, such as posturing and grimacing, not generally observed in NMS Normal neurologic examination Antidepressant medication was continued, and the clinical picture evolved positively

Abbreviations: CK = creatine kinase, CT = computed tomography, NMS = neuroleptic malignant syndrome.

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