Quetiapine-Induced Neuroleptic Malignant Syndrome

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Neuroleptic malignant syndrome (NMS) is a life-threatening condition that most often occurs as an idiosyncratic reaction to antipsychotics and has an incidence of 0.01%–0.02%.[1,2] Typical NMS is characterized by hyperthermia, autonomic dysfunction, altered mental status, and muscular rigidity.[3] We report a case of quetiapine-induced NMS.

Case Report

A 66-year-old man with diabetes mellitus and bipolar I disorder was brought to the emergency department (ED) after 24 hours of psychomotor agitation. He had been treated with a daily dose of lithium 800 mg, quetiapine 400 mg, and venlafaxine 150 mg since his last bipolar disorder relapse with a major depressive episode 5 months earlier. He accidentally took an extra dose of quetiapine 400 mg the night before presenting to the ED. In the ED, he presented with fever (38.6°C), diaphoresis, generalized tremor, muscular rigidity, opisthotonos, fluctuating levels of consciousness, and temporal disorientation. Urine and blood analysis was remarkable for leukocytosis (14.03 x 10^3/μL) and increased creatine kinase (923 IU/L) and C-reactive protein (13.6 mg/dL). His serum lithium level was within the therapeutic range (0.60 mmol/L). Electrocardiogram, chest x-ray, and cranial computed tomography scan were unremarkable. A diagnosis of NMS was assumed, and the patient was admitted to the ED intermediate care unit with monitoring of vital signs. Quetiapine, lithium, and venlafaxine were withheld, and he was started on intravenous (IV) fluids, IV diazepam 10 mg every 8 hours, and IV dantrolene 1 mg/kg. After 48 hours, the patient showed marked improvement, transitioning to an internal medicine ward, where IV treatments were stopped, and he was started on oral lorazepam 2.5 mg every 12 hours. Urine and blood cultures collected at admission were negative. After 3 more days with no NMS signs, lithium was reintroduced (800 mg/d). However, 3 days later he started presenting depressive and psychotic symptoms and was transferred to a psychiatric ward, where he was restarted on venlafaxine, titrated to 150 mg/d. One week later, it was necessary to start an antipsychotic, and risperidone was carefully initiated and slowly titrated to 2 mg/d. The patient showed progressive improvement and was discharged. In the 12 months that followed, he showed no NMS signs.

Discussion

Although some cases of quetiapine-induced NMS have already been published, most had several limitations and short follow-up periods.[4] Our patient presented the classic signs and analytic findings of NMS[3] after an overdosage of quetiapine. An international expert panel consensus proposed diagnostic criteria for NMS, with our patient meeting 5 of 7 criteria and yielding a score of 85/100 of that criteria.[5]

First-generation antipsychotics represent the greatest risk for NMS.[3] However, NMS may occur as a reaction to second-generation antipsychotics and other drug classes.[6,7] Although NMS may occur within the usual therapeutic dose range of antipsychotics, rapid dose titration and higher drug doses are risk factors,[3] as seen in our patient who mistakenly took an extra dose of quetiapine.

Current treatment recommendations are based on case reports and expert opinions.[8,9] The initial approach is to discontinue drugs possibly associated with NMS and start supportive care.[8,9] In more severe cases, pharmacotherapy or electroconvulsive therapy are required.[8,9] Benzodiazepines, dantrolene, bromocriptine, and amantadine are the most beneficial pharmacologic interventions.[8,9]

Even considering that reported rates of recurrence of NMS are as high as 30%,[10] the use of an antipsychotic was inevitable in our patient. When rechallenging a patient with an antipsychotic after NMS, a different drug should be started at a low dose and slowly titrated while monitoring for NMS signs after complete NMS resolution and at least 2 weeks of a washout period.[8,10]

This case emphasizes that clinicians should be highly aware of the possibility of NMS developing, even with a widely used second-generation antipsychotic like quetiapine.

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