t is illegal to post this copyrighted PDF on any website. Delirium and Dysarthria After Titration of Clozapine

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Clozapine is essential for the management of treatmentrefractory schizophrenia,¹ but its use is often limited by side effects such as agranulocytosis, cardiomyopathy, orthostatic hypotension, sialorrhea, and constipation.² We describe a patient who developed severe dysarthria and delirium after receiving clozapine at subtherapeutic doses, adding to existing reports of clozapine-induced delirium,³⁻⁶ stuttering,⁷⁻⁹ and dysarthria.^{10,11}

Case Report

Mr A, a 56-year-old man, had a history of schizophrenia, polysubstance dependence, hepatitis C, obstructive sleep apnea, and hypertension. He was admitted for worsening psychosis, having been discharged 6 days previously following a 19-day psychiatric hospitalization during which he was treated with oral paliperidone 12 mg daily. His medication history included olanzapine, aripiprazole, and quetiapine. Upon admission, paliperidone was continued at 12 mg. Mr A reported some ear, tooth, and throat pain; his vital signs, blood count, and electrolyte levels were within normal limits. Otitis externa was found, so he was given topical ofloxacin with good response.

Despite receiving paliperidone, Mr A continued to have auditory hallucinations and delusions with minimal improvement through hospital day 11. After initial laboratory work, clozapine was initiated at 25 mg at bedtime (qhs), and paliperidone was reduced to 9 mg qhs. His sleep pattern was normal. On day 15, after taking clozapine 75 mg the night prior, he reported mild dysarthria and dry mouth, but denied urinary retention and constipation. On day 16, after taking clozapine 100 mg the night prior, his speech was slurred; he had not slept and accused hospital staff of stealing his wallet. He was disoriented and picking at the air. Mr A's vital signs were within normal limits except for mild hypertension. The physical examination revealed no other neurologic deficits. Laboratory values revealed no leukocytosis, electrolyte disturbance, or evidence of myocarditis. Clozapine was discontinued due to concern that it had caused delirium.

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Paliperidone 9 mg was continued. On day 17, he continued to have insomnia, dysarthria, and delirium. Melatonin was added to his medication regimen.

By day 18, Mr A's dysarthria and delirium had resolved. Because of continued psychosis, clozapine was cautiously restarted at 25 mg. On day 21, with no evidence of delirium or dysarthria, clozapine was increased to 50 mg. On day 23, he exhibited renewed dysarthria. Clozapine was increased to 75 mg qhs. On day 24, his speech was generally unintelligible, though he remained alert and oriented. Clozapine was discontinued due to dysarthria and concern that delirium might reemerge.

Through days 25–28, Mr A's dysarthria improved until his speech normalized. He was transitioned to paliperidone palmitate but continued to have unresolved psychosis. On day 36, after receiving the second loading dose of paliperidone palmitate, he was dispositioned to a board-and-care home.

Discussion

Given the emergence of dysarthria and delirium after initial exposure to clozapine, resolution of symptoms after clozapine cessation, reemergence of dysarthria after reexposure to clozapine, the limited potential of his other medications (topical ofloxacin, paliperidone, and melatonin) to cause delirium, and the low likelihood of undetected infection, stroke, or other acute medical illness, we believe Mr A suffered from clozapine-induced dysarthria and delirium. We speculate that both symptoms resulted from clozapine's anticholinergic effects.

Prior reports^{3–11} have shown development of delirium or dysarthria at clozapine doses above 100 mg. It is important for clinicians to be aware, however, that these conditions may arise even with lower doses and despite conservative titration schedules, as this case illustrates. In such circumstances, efforts to manage patients' psychotic symptoms may be limited to other antipsychotic medications with less anticholinergic effect but also less efficacy.

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