Aripiprazole-Induced Parkinsonism in a Child: A Case Report

To the Editor: Parkinsonism is a neurologic syndrome that manifests as any combination of 6 cardinal features: tremor at rest, rigidity, bradykinesia/hypokinesia, flexed posture, loss of postural reflexes, and the freezing phenomenon.[1] At least 2 of these features, with at least 1 being either tremor at rest or bradykinesia, must be present for a definitive diagnosis of parkinsonism.[1] The biochemical abnormality in parkinsonism is reduced dopaminergic neurotransmission in the basal ganglia.[1]

In 1954, Steck[2] first described neuroleptic-induced parkinsonism in patients taking chlorpromazine. This observation was confirmed by Gade and Heinrich[3] in 1955. The prevalence of neuroleptic-induced parkinsonism is difficult to ascertain because of heterogenous patient populations, variable drug regimens, and other factors that make this distinction extremely difficult. In most cases, however, it is second only to Parkinson's disease as the most common cause of parkinsonism.[4,5,6] Various medications such as neuroleptics, selective serotonin reuptake inhibitors, lithium, valproic acid, calcium channel blockers, antiarrhythmics, procholinergics, chemotherapeutics, amphotericin B, estrogen, and others have been implicated.[4] To our knowledge, we are reporting the first published case of aripiprazole-induced parkinsonism.

Case report. A 12-year-old white boy presented to the emergency department in 2010 with chief complaints of excessive drooling, generalized slowing of body movements, and difficulty in walking with stiffness in arms and legs for 3 days. His psychiatric history was significant for posttraumatic stress disorder (PTSD; nightmares, flashbacks, numbing, avoidance, and sexually acting-out behavior) due to physical and sexual abuse, attention-deficit/hyperactivity disorder (ADHD; hyperactivity, impulsivity, and inattention), oppositional defiant disorder (ODD), and mood disorder not otherwise specified (longstanding history of mood dysregulation, mood swings, and excessive irritability). On mental status examination, he described his mood as "sad." His affect was blunted, his speech was limited to short response, and he denied having audiovisual hallucinations. He was not delirious. On physical examination, he was found to have bradykinesia, lip smacking, flexed posture, and cogwheel rigidity. There was no past history of illicit substance or alcohol abuse. There was no family history of movement disorders.

His outpatient medications included lisdexamfetamine 70 mg orally every morning and guanfacine 1 mg orally every morning. Within 3 days of initiation of benztropine 1 mg orally twice daily and aripiprazole 5 mg/d orally, he developed classic parkinsonian symptoms, ie, bradykinesia, cogwheel rigidity, and flexed posture. After emergency department stabilization, he was admitted to the inpatient psychiatry unit with an additional diagnosis of neuroleptic-induced parkinsonism. Findings from his routine blood work including complete blood cell count with differential, comprehensive metabolic profile, and drug screen as well as noncontrast head computed tomography scan were within normal limits. All medications were stopped except benztropine 1 mg orally twice daily, and amantadine 100 mg orally twice daily was given, which led to symptom resolution within 72 hours. After release from the hospital, he was rechallenged with an antipsychotic, quetiapine extended release (XR) 50 mg orally every evening, with reemergence of parkinsonian symptoms. Quetiapine XR was discontinued, with dramatic resolution of parkinsonian symptoms.

A PubMed search for the years 1954 to 2010 with the keywords *antipsychotics*, *aripiprazole*, *parkinsonism*, and *children* was performed, and a Google Scholar search incorporating the same keywords and range of years was also conducted. To our knowledge, only 2 case reports of drug-induced parkinsonism in children[7,8] have been published.

Neuroleptic-induced parkinsonism results from a diminution in dopamine activity.[9] This can be induced by depletion of dopamine in presynaptic stores (eg, during reserpine treatment), dopamine-blocking agents (eg, antipsychotics), and the atypical calcium-blocking agent cinnarizine.[9] Dopamine-2 blockade in nigrostriatal dopamine system results in parkinsonian symptoms in patients who are taking antipsychotics.[10] This effect is frequent with typical antipsychotics, being strong D_2 blockers, compared to atypical antipsychotics, which are relatively weak D_2 blockers.[11] Absence of tremor and reversibility are typical of drug-induced parkinsonism rather than Parkinson's disease.[12]

This syndrome usually subsides with dose reduction or medication cessation.[9] As such reduction or cessation is not always possible, alternative strategies include switching from a high-potency D_2 blocking agent (eg, fluphenazine) to a lower-potency first-generation antipsychotic or second-generation antipsychotic agent (eg, quetiapine). According to the literature, aripiprazole, a partial D_2 agonist, may also decrease the risk of acute extrapyramidal symptoms.[9] Adjunctive anticholinergic agents, eg, benztropine or dopamine agonists such as amantadine, are effective agents to alleviate extrapyramidal symptoms (EPS).[9]

Physicians should look for the symptoms of parkinsonism and movement disorders in children who are on treatment with antipsychotics, either typical or atypical. Incidence of EPS appears to be greater for typical antipsychotics. Among atypical antipsychotics, hierarchy of EPS risk is risperidone > olanzapine = ziprasidone = aripiprazole > quetiapine > clozapine.[10,13] If challenged by a neuroleptic again, patients may have reemergence of parkinsonian symptoms.

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