Statins Can Produce Ataxia in Bipolar Disorder: Two Case Reports

To the Editor: Aggressive cholesterol reduction via HMG-CoA reductase inhibitors (statins) in individuals at risk for vascular disease is currently standard of care, perhaps even the modal intervention, given compliance issues with diet and exercise changes. These recommendations, however, do not generally cite the results of large double-blind trials suggesting modest adverse central nervous system (CNS) effects of insomnia[1] and cognitive impairment[2] with statin use. Sporadic case reports of more severe CNS effects (dementia, irritability, and central fatigue) have also appeared, suggesting important individual vulnerabilities. We report 2 cases of acute ataxia coincident with statin onset in individuals with bipolar disorder, referencing these reports to the growing literature on mitochondrial encephalopathies.

Case 1. Mr A, a 52-year-old man, had good control of his bipolar disorder since 2000 on treatment with lamotrigine 700 mg and topiramate 400 mg daily. He presented in 1999 with a modal weekly frequency of alternating hypomania and severe depression found subsequently to be completely unresponsive to lithium, dopamine antagonists, and tamoxifen.

In 2008, Mr A reported in follow-up new-onset ataxia, requiring decreased dosing of lamotrigine to 400 mg at the cost of decreased mood stability. Addition of atorvastatin 20 mg to his chronic regimen was noted. Subsequent discontinuation of this agent resulted in complete cessation on his ataxia at interval 6-month follow-up.

Case 2. Ms B, a 64-year-old woman, was seen in consultation in 2008 for subacute onset of gait and writing ataxia in the context of psychiatric polypharmacy: zolpidem 20 mg/d, carbamazepine 1 g/d, and lamotrigine 450 mg/d. She had been maintained for decades on 1 g/d of carbamazepine for ultradian mood instability.

Ms B fell on the examiner at his desk upon entering the office, and during history-taking, she held her head in her hands, citing postural instability. Her husband noted progressive cognitive slowing coincident with simvastatin addition 2 years prior. Simvastatin discontinuation resulted in complete cessation of ataxia and cognitive complaints at 4 weeks.

Statins can have profound effects on mitochondrial function as assessed by muscle biopsy on individuals receiving simvastatin.[3] I suggest the hypothesis, conceptually consistent with the concept that statins may act as unmasking agents for latent neuromuscular disorders, that neuropsychiatric statin intolerance suggests preexisting CNS metabolic disorder.[4] Individuals with bipolar disorder, as a group, have been reported to have components of metabolic dysfunction as evidenced by animal knockout models (polyG),[5] elevated lactic acid in cerebrospinal fluid[6] and magnetic resonance spectroscopy,[7] and elevated joint prevalence with systemic mitochondrial disorders.[8]

Bipolar disorder symptoms distribute on a polygenetic dimensional continuum. It would be of interest to ascertain whether common CNS symptoms associated with mitochondrial disorders, such as pain, rage, hyperekplexia, migraine, irritable bowel, and myoclonus, predict statin intolerance in bipolar patients.

Delayed clinical offsets and onsets of drug side effect may complicate individual diagnoses. Statin myopathy has a bimodal temporal onset, with the later peak occurring 12 months after use.[9] The concern arises, analogous to initial experience with antidepressant use in bipolar disorders, that short-term drug trials significantly understate risks of chronic use. Use of lipophilic statins (simvastatin > lovastatin > atorvastatin > rosuvastatin) with preferential CNS relative to hepatic targeting may pose higher risks of adverse effects.[1,3]

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