Letters to the Editor

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A Case Report of Methylphenidate-Induced Dyskinesia

Sir: Movement disorders have long been associated with a wide variety of medications and illicit drugs. Dopaminergic agents are well-known precipitants of various dyskinesias, including chorea, choreoathetosis, dystonia, and ballism. For example, levodopa-induced dyskinesias are a relatively common side effect of the treatment of Parkinson's disease, with up to 45% of patients affected after 5 years of such treatment.[1]

Stimulants, such as methylphenidate, have also been associated with dyskinesias. Most case reports, however, implicate large dosages[2] or chronic use of stimulant medications.[3] Another recognized effect of methylphenidate is the development of motor tics in children.[4] In contrast, the case presented here involves the acute development of choreoathetosis in an elderly patient after only 2 small doses of methylphenidate, with rapid resolution of the movement disorder following discontinuation of the offending agent.

Case report. Mr. A is an 87-year-old man with a history of Parkinson's disease, hypothyroidism, and depression. He was admitted to the medical service for progressive weakness and inability to manage his activities of daily living. Mr. A had been diagnosed with Parkinson's disease over 10 years ago. Treatment consisted of 3 tablets of carbidopa/levodopa sustained release, 50 mg/200 mg 3 times per day. Historically, Mr. A's compliance had been suboptimal, but over the prior 6 months, in-home nursing had optimized compliance. The patient was euthyroid on treatment with levothyroxine, 125 mg/day. His depression had been treated successfully with sertraline, 50 mg/day, for approximately 3 years.

Psychiatric consultation was requested to evaluate Mr. A for depression as an etiology for his observed "failure to thrive." Psychiatric assessment revealed a thin, elderly appearing man lying comfortably in bed. A mild pill-rolling tremor and cogwheel rigidity were noted on physical examination. Mr. A denied a subjective feeling of depression and, despite obvious bradykinesia and masked facies, did not appear clinically depressed. However, he was quite cognitively impaired, scoring only 17/30 on the Folstein Mini-Mental State Examination.[5] (Mr. A lost 6 points for time and place disorientation. Immediate recall was intact. Delayed recall was impaired, with loss of 2 points. Attention was impaired on serial 7s, resulting in the loss of 3 points. The last 2 points were lost due to inability to follow a simple 3-step command.) The admission laboratory tests included electrolytes, liver function, thyroid-stimulating hormone, and a complete blood count. The only abnormality found was a mild normocytic anemia, with a hemoglobin level of 11.4 g/dL.

The consultation service assessed Mr. A's primary problem not as a depressive disorder, but rather as a dementing process coupled with advanced Parkinson's disease. A complete laboratory workup for reversible causes of dementia was negative, and a computed tomographic scan of the head revealed cerebral volume loss and areas of periventricular hypodensity.

Mr. A was placed on treatment with methylphenidate, 2.5 mg twice per day, by the medical service to improve appetite and "mood." After only 2 doses of methylphenidate, the patient was found to have significant choreoathetosis and a change in mental status consistent with a delirium. Methylphenidate was subsequently discontinued and quetiapine, 25 mg twice per day, was initiated. Carbidopa/levodopa administration was maintained, although the dosing schedule was adjusted to ensure 8 hours between each dose. Mr. A responded well to the discontinuation of the methylphenidate and the administration of small doses of quetiapine. He experienced a significant resolution of the dyskinesia and a clearing of the delirium. The patient was subsequently discharged to a rehabilitation facility.

Methylphenidate, when given in therapeutic doses, has recently been shown to increase extracellular dopamine in the human brain.[6] This capacity of methylphenidate to increase dopamine within the striatum is the proposed mechanism by which methylphenidate and other stimulants may induce movement disorders. Mr. A's case is complicated by the presence of Parkinson's disease and concurrent therapy with carbidopa/levodopa, an agent known to be associated with iatrogenic dyskinesia. However, the temporal relationship between the start of methylphenidate therapy and the onset of the movement disorder suggests that the stimulant is the etiologic agent behind the observed choreoathetosis. The damage to the basal ganglia inherent in Parkinson's disease may provide a predilection to the development of movement disorders with dopaminergic medications. The development of Mr. A's choreoathetosis early in the course of low-dose methylphenidate treatment may indicate the importance of a "primed" brain in the development of dyskinesia associated with various dopaminergic stimulant medications.

Dr. Heinrich reports no financial affiliation or other relationship relevant to the subject matter of this letter.

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A Case Report of a Manic Episode Triggered by *S*-Adenosylmethionine (SAMe)

Sir: As previously described in the *Companion*,[1] an ever-growing number of Americans seek alternative therapies for their medical problems. Among those alternative therapies is the use of herbal medicines, substances that can elicit changes in mood, cognition, and behavior.[2] S-adenosylmethionine (SAMe) is a natural substance found in all human cells that is involved in methylation reactions such as gene expression and neurotransmitter synthesis, among others.[3] It was shown to have antidepressant effects in a 1988 controlled trial.[4] Here, a case is reported in which a patient with no previous psychiatric history experienced a manic episode following a course of SAMe.

Case report. Ms. A is a 39-year-old woman who, 5 weeks prior to hospitalization, began to use SAMe on a daily basis to "boost" her mood. She had an unremarkable medical history and denied any history of head injury, seizure disorder, or recent illness. She also denied the use of alcohol or illicit substances. Ms. A was admitted to an inpatient psychiatric unit and diagnosed with bipolar I disorder, manic, using DSM-IV criteria.[5] Results of all screening laboratory tests, including a complete blood count, chemistry panel, liver function, erythrocyte sedimentation rate, thyroid-stimulating hormone, rapid plasma reagin, human immunodeficiency virus, urinalysis, urine drug screen, and urine pregnancy test, were within normal limits or negative. The patient stabilized on a combination of risperidone and divalproex sodium extended release within 4 days. Once stable, Ms. A mentioned that for 1 month prior to her manic episode, she had been taking SAMe, 400 mg, on a daily basis. She also related that her mother had a history of bipolar disorder. She remains stable at 3 months.

Antidepressants are known to trigger mania at rates higher than those of placebo.[6] However, in an open multicenter study, Fava et al.[7] treated 195 patients with 400 mg/day of SAMe for 15 days with no reported serious adverse effects. In a smaller open trial of intravenous and oral SAMe treatment, though, Carney et al.[8] reported that 9 of 11 known bipolar patients switched into an elevated mood. This switching was not seen in an even smaller study reported by Lipinski et al.[9] in which 9 depressed patients were treated with SAMe. In a 1994 meta-analysis, Bressa[10] found SAMe to be equally effective as tricyclic antidepressants, with a lower incidence of side effects and no report of SAMe inducing a switch into mania. Switching was not reported in a double-blind study conducted by Bell et al.[11] comparing SAMe with desipramine in a 4-week trial.

The patient described in this letter, who has a positive family history for bipolar disorder, may eventually have had a manic episode not triggered by SAMe, but there is a strong possibility that the episode reported here was triggered secondary to exposure to SAMe. It is imperative that clinicians continue to inquire about their patients' use of herbal medication due to the possibility of changes in mood and behavioral problems. Herbal use should also be considered in the differential diagnosis when primary care providers evaluate patients who present with mood and behavioral changes but have no previous psychiatric history.

Dr. Berigan reports no financial affiliation or other relationship relevant to the subject matter in this letter.

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