Case Report

Extrapyramidal Symptoms With Concomitant Use of Amitriptyline and Amiodarone in an Elderly Patient

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ABSTRACT

Background: Amitriptyline is a tricyclic antidepressant useful for the treatment of depression. Amiodarone is a class III antiarrhythmic agent used for the treatment of cardiac dysrhythmias.

Objective: The objective of the current report is to describe the case of a previously asymptomatic patient receiving amitriptyline who developed extrapyramidal symptoms within 1 month of initiating concomitant treatment with amiodarone for atrial fibrillation.

Case summary: An 82-year-old, right-handed, white woman was brought to the medical center's emergency department with speech difficulty suggesting stroke. She was noted to have continuous orobuccal dyskinesias, upper and lower extremity shaking, and dry mouth. Once it was determined that no other focal neurologic findings indicated stroke, her medications were reviewed. The patient had been taking amitriptyline 50 mg/d for the past year for insomnia without any adverse events. However, 1 month before presentation, she also initiated treatment with amiodarone 200 mg/d for atrial fibrillation and had developed the symptoms of concern shortly thereafter. The patient's amitriptyline treatment was discontinued and she received benzotropine for extrapyramidal symptoms from amitriptyline toxicity. She experienced complete resolution of dysarthric speech and limb shaking within 2 days. A total score of 7 was achieved using Naranjo's adverse drug reaction causality algorithm, suggesting amitriptyline was a probable cause of these adverse events.

Conclusion: This was a probable case of extrapyramidal symptoms in an elderly woman who began using amiodarone while also taking amitriptyline. (*Am J Geriatr Pharmacother.* 2010;8:595–598) © 2010 Elsevier HS Journals, Inc.

Key words: adverse events, amiodarone, amitriptyline, antiarrhythmic, antidepressant, drug interaction, extrapyramidal.

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INTRODUCTION

Extrapyramidal symptoms are considered to be a rare adverse event related to the use of tricyclic antidepressants.[1] One such tricyclic antidepressant, amitriptyline, is a commonly used drug, especially among older patients. Piecoro et al[2] reported that amitriptyline was inappropriately prescribed in 7.6% of those aged ≥65 years with prescriptions for the drug, based on a cross-sectional retrospective review of the records of >64,000 Medicaid recipients. Amiodarone, a commonly used antiarrhythmic agent (especially among older patients, in whom the incidence of dysrhythmias such as atrial fibrillation is high[3]), is known to interact with several medications via its effect on the cytochrome P450 (CYP) system.[4] A search of PubMed and the Cochrane library using the search terms *amiodarone* and *amitriptyline interaction*, *amitriptyline toxicity*, and *extrapyramidal symptoms* for published reports regarding possible drug reaction between amitriptyline and amiodarone was performed and did not yield any reports of such interactions.

CASE SUMMARY

An 82-year-old, right-handed, white woman with a history of hypertension, coronary artery disease, osteoporosis, iron deficiency anemia, esophageal stricture, peptic ulcer disease, atrial fibrillation, appendectomy, cholecystectomy, partial gastrectomy, right colectomy, syncope, and transient ischemic attacks had been hospitalized 1 month earlier with bilateral hand numbness and had undergone evaluation for stroke. Magnetic resonance imaging of the brain indicated old left thalamic lacunar infarction but no acute infarction. Neurologic exam at the time of hospital admission was significant for bilateral dysmetria of arms (dysmetria of the right arm was greater than that of the left), discrete right arm weakness, and mild dysarthria. Some verbal perseveration and decreased fluency were noted without paraphasic errors, and the patient was discharged after the remainder of the stroke work-up (computed tomography of the head without contrast, plus magnetic resonance imaging of the brain) produced unremarkable results.

Three days after discharge, the patient was readmitted for new onset atrial fibrillation with heart rate >140 beats/min. At that time, a heparin drip and warfarin 3 mg were initiated, but they were later discontinued because of recurrent gastrointestinal hemorrhage and reductions in hemoglobin (from 11 to 8 g/dL) and hematocrit (from 34% to 27%). She was discharged in stable condition with a prescription for amiodarone 200 mg/d.

Three weeks later, the patient returned to the hospital with a chief complaint of garbled speech. The patient's daughter had noticed that her mother's speech was garbled to the point of being indistinguishable for 2 to 3 days. The stroke team was consulted but the patient was found to have fully intact mental status. She had been experiencing intermittent difficulty speaking and expressing herself for the past few weeks, with gradual worsening. She was experiencing shaking of the extremities (shaking in the upper body was greater than that in the lower body), dry mouth, and the feeling of being dehydrated. The patient reported she had no facial drooping, focal weakness, sensory disturbance, double/blurred vision, tongue biting, or incontinence. She had marked and persistent orobuccal dyskinesias with chewing, lip smacking, fly-catching tongue movements, dry mouth, and intermittent bilateral extremity jerking (more marked in the upper body than the lower body), dysmetric movements in upper extremities bilaterally, slightly reduced strength in the extremities, and normal muscle tone. She did not have any new neurologic deficits compared with her 2 previous admissions. Both the patient and her daughter confirmed that the extremity weakness was not new. Thus, the patient's slurred speech seemed to be related to the continuous orobuccal dyskinesias. It was noted that she had been taking amitriptyline 50 mg/d for insomnia for the past year. Her other medications included alendronate 70 mg weekly for osteoporosis, aspirin 81 mg/d, bumetanide 0.5 mg/d as a diuretic, calcitriol 0.25 µg/d, cholecalciferol 1000 U/d, cyanocobalamine 1000 µg every 3 months, lidocaine 5% transdermal patch (12 hours on and 12 hours off) for back pain, ferrous sulfate 325 mg/d for iron deficiency anemia, pantoprazole 40 mg/d for gastroesophageal reflux disease, simvastatin 40 mg/d for hyperlipidemia, tiagabine 4 mg TID for neuropathic pain, tizanidine 2 mg in the morning and 4 mg at noon and night for backache, tolterodine tartrate 4 mg/d, and oxycodone controlled-release 10 mg BID as needed for pain. The only recent change in her medication regimen was the addition of amiodarone 200 mg/d 1 month earlier, and suspicion was raised for amitriptyline toxicity related to impaired metabolism of the agent by amiodarone.[4–7]

The probability of an adverse drug reaction to amitriptyline was calculated using Naranjo's causality algorithm and yielded a score of 7 (scores for causality: <0, doubtful; 1–4, possible; 5–8, probable; >9, definite), suggesting that amitriptyline was a probable cause of the patient's extrapyramidal symptoms.[8] Furthermore, using the drug interaction probability scale