CASE REPORT

THE PATIENT
23-year-old woman

SIGNS & SYMPTOMS
– Syncopal episode
– Sinus bradycardia
– History of bipolar disorder

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THE CASE

A 23-year-old woman with past medical history of bipolar II disorder and a REM-specific seizure disorder that resolved at age 9 presented after a syncopal episode. The patient reported an initial sensation of lightheadedness while at work, which was followed by a syncopal episode with brief (1-2 min) loss of consciousness and a minor head injury.

She denied other prodromal symptoms including chest pain, shortness of breath, palpitations, and nausea. She also did not experience convulsions, urinary/bowel incontinence, or confusion upon regaining consciousness.

She denied previous syncopal episodes. However, she reported that, 2 weeks prior, there had been an event similar to that of her presenting complaint. During that episode, she experienced lightheadedness and a fall without loss of consciousness.

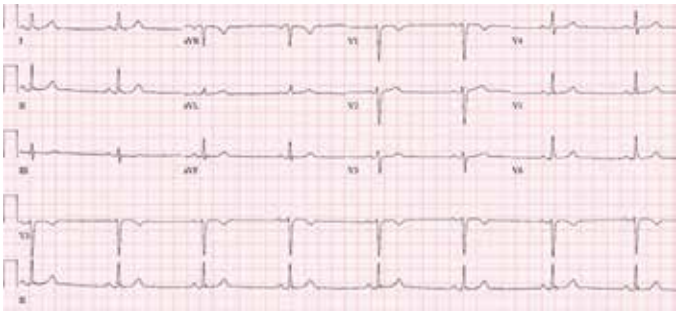
The patient had been prescribed a regimen of sertraline 100 mg/d and aripiprazole 10 mg/d to maintain mood stability. She had self-discontinued these medications about 8 months prior to presentation. A recent return of her depressive features had prompted a restart of this regimen 1 week before her first fall, without an initial taper upward.

While in the emergency department, she became bradycardic (heart rate, 38 beats/min) and hypotensive (blood pressure, 70/40 mm Hg). She subsequently became increasingly somnolent and had 1 episode of emesis. An electrocardiogram (EKG) revealed sinus bradycardia without other acute abnormalities (**FIGURE**).

Blood work including a basic metabolic panel, complete blood count, and cardiac enzymes were all within normal limits. Computed tomography of the head revealed no intracranial pathology. Her vitals were initially unresponsive to a fluid bolus but improved and stabilized after administration of intravenous atropine 0.5 mg.

Aripiprazole was held and sertraline was decreased to 75 mg on hospital Day 1, with close monitoring of her mood. Cardiology was consulted and followed the patient during her stay. The patient was monitored on telemetry for 3 days, exhibiting only sinus bradycardia with a stable heart rate of 45-55 beats/min. Systolic blood pressures were stable within 120 to 130 mm Hg. Transthoracic echocardiogram performed on hospital Day 2 was unremarkable, revealing a normal left ventricular ejection fraction of 65% and no wall motion abnormalities. She had no recurrence of the syncope or emesis.

FIGURE
EKG revealed sinus bradycardia in a 23-year-old woman with recent syncope



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THE DIAGNOSIS

Given her benign cardiac work-up and symptom onset coinciding with the abrupt resumption of high doses of aripiprazole after an 8-month abstinence, the patient's presentation was attributed to a rather uncommon adverse drug reaction to aripiprazole. This has only been described in a few case reports.

DISCUSSION

Aripiprazole (Abilify) is an atypical antipsychotic frequently used in the treatment of psychiatric conditions, including bipolar disorder and schizophrenia. While the specific therapeutic mechanism is unknown, it is believed that drug efficacy is related to partial agonism at dopamine D_2, serotonin 5-HT_{1A}, and serotonin 5-HT_{2A}.[1] As aripiprazole works on a variety of receptors involved in other physiologic processes, clinical adverse effects have been reported, most of which are associated with the adrenergic alpha$_1$ receptors.[1] These include cognitive impairment and seizures. Cardiovascular adverse effects of aripiprazole include orthostatic hypotension, cardiac arrhythmia, prolonged QT interval, and syncope.[1-5]

Selective serotonin reuptake inhibitors (SSRIs) such as sertraline (Zoloft) have also been shown to cause cardiac arrhythmia and syncope.[6] Although sertraline may have contributed to the patient's cardiac symptoms, it is more likely that the aripiprazole was the direct cause, as she remained asymptomatic while on a therapeutic dose of sertraline. Furthermore, aripiprazole is primarily metabolized though hepatic CYP2D6, which sertraline has been shown to inhibit.[1,7] Therefore, the concomitant use of sertraline with no initial taper of either medication likely led to an increased effective dose of aripiprazole in our patient and subsequently to her presentation.

Few prior cases have identified aripiprazole as a cause of antipsychotic-associated bradycardic response.[8] Based on the Adverse Drug Reaction Probability Scale, often referred to as the *Naranjo Scale*, we believe this to be a probable adverse response in our patient.[9] Bradycardia followed a reasonable temporal sequence after aripiprazole use with a response previously described in the literature. Symptoms also improved after discontinuation of the drug and other etiologies of the bradycardia were ruled out.

Our patient was discharged with a 30-day cardiac event monitor and a scheduled appointment with Cardiology.

THE TAKEAWAY

As this case suggests, there may be an association between aripiprazole and symptomatic bradycardia. Therefore, family physicians should inquire about aripiprazole use in patients who present with cardiac symptoms and consider tapering this medication if other causes cannot be identified. Additionally, given the potential cardiac adverse effects of atypical antipsychotics, physicians may consider ordering baseline and follow-up EKGs to monitor for arrhythmias in patients prescribed aripiprazole. This may be especially prudent when an atypical antipsychotic is combined with an SSRI, as potential cardiac adverse effects may occur more frequently. JFP

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