

## THE CLINICAL PICTURE

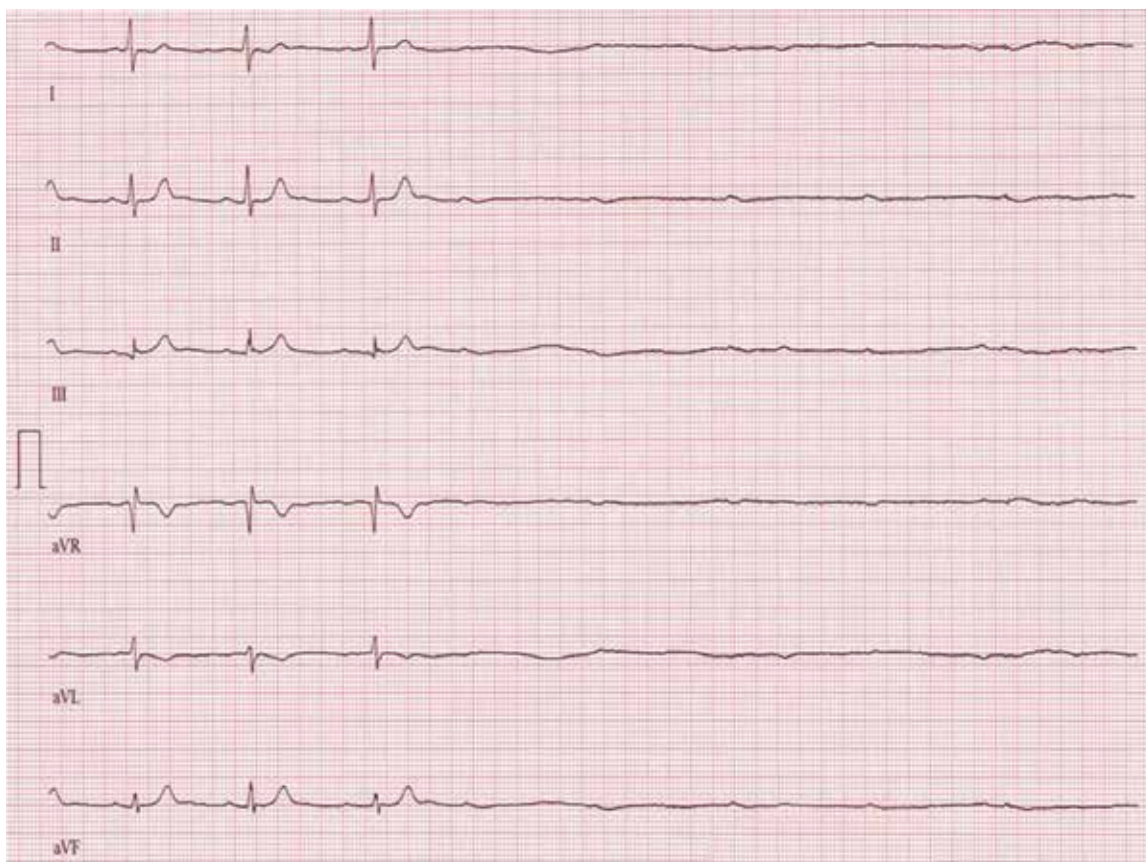
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# The Clinical Picture

## Syncope during a pharmacologic nuclear stress test



**FIGURE 1**

**A** 60-YEAR-OLD WOMAN was referred for pharmacologic nuclear stress testing before treatment for breast cancer. She had hypertension, diabetes mellitus, coronary artery disease, and a remote history of stroke, and she was taking clonidine (Catapres), labetalol (Normodyne, Trandate), furosemide (Lasix), hydralazine, valsartan (Diovan), insulin, and the aspirin-dipyridamole combination Aggrenox. Her vital signs and

electrocardiogram before the stress test were normal.

The stress test was started with a standard protocol of adenosine (Adenoscan) infused intravenously over 4 minutes. For the first 2 minutes, she was stable and had no symptoms, but then sinus pauses and second-degree atrioventricular block type 2 developed, after which her heart stopped beating (**FIGURE 1**). The infusion was immediately stopped, but she became unresponsive and remained pulseless.

Cardiopulmonary resuscitation was started, aminophylline 100 mg was given intravenously, and she

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regained a pulse and blood pressure within a few minutes. She was then transferred to the emergency room, where she returned to her baseline clinical and neurologic status without symptoms.

## ■ AN UNRECOGNIZED DRUG INTERACTION

Asystole occurred in this patient because of the interaction of intravenous adenosine with the dipyridamole in the medication Aggrenox. Although adenosine, given during pharmacologic stress testing, is known to interact with various medications, the potential for this interaction may be overlooked if the culprit is present in a combination drug. Aggrenox is commonly given for secondary stroke prevention and should be discontinued before pharmacologic nuclear stress testing.

Pharmacologic stress testing involves two commonly used stress agents, adenosine and regadenoson (Lexiscan), which cause coronary vasodilation through their action on A2A receptors in the heart. Coronary vasodilation results in flow heterogeneity in the region of a stenotic artery, which can be detected with nuclear perfusion agents. In addition, adenosine has a short-lived effect on the A1 receptors that block atrioventricular conduction.<sup>1</sup>

Dipyridamole (Persantine) is contraindicated when either adenosine or regadenoson is used. Dipyridamole enhances the effect of exogenous and endogenous adenosine by inhibiting its uptake by cardiac cells, thus enhancing the action of these coronary vasodilators.<sup>2</sup> Atrioventricular block is common during adenosine stress testing but is transient because adenosine has a short half-life (< 10 seconds), and complete heart block or asystole, as seen in this patient, is rare. Giving intravenous adenosine or regadenoson to patients on dipyridamole may have a marked effect on adenosine receptors, so that profound bradycardia and even asystole leading to cardiac collapse may occur. No data are available on the specific interaction of dipyridamole and regadenoson.

Even though the pharmacodynamics of the interaction between dipyridamole and adenosine are known,<sup>3</sup> few reports are available detailing serious adverse events. The contraindication to pharmacologic stress testing in patients taking dipyridamole is noted in the American Society of Nuclear Cardiology Guidelines for stress protocols,<sup>4</sup> which advise discontinuing dipyridamole-containing drugs at least 48 hours before the use of adenosine or regadenoson. Similarly, the American Heart Association guidelines<sup>5</sup> for the management of supraventricular tachycardia recommend an initial dose of 3 mg of adenosine rather than 6 mg in patients who have been taking dipyridamole.

The dose of aminophylline for reversing the adverse effects of adenosine or regadenoson is 50 to 250 mg intravenously over 30 to 60 seconds. But since these adverse effects are short-lived once the infusion is stopped, aminophylline is usually given only if the adverse effects are severe, as in this patient.

Pharmacologic nuclear stress testing with adenosine receptor agonists (eg, adenosine or regadenoson) is contraindicated in patients taking dipyridamole or the combination pill Aggrenox because of the potential for profound bradyarrhythmias or asystole. ■

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IV adenosine or regadenoson can cause profound bradycardia and asystole in someone on dipyridamole