Indirect evidence of sympathetic stimulation by regadenoson

G. Ross Farris, MD,[a] Fadi G. Hage, MD, FASNC,[a] Vineet Kumar, MD,[a] Ami E. Iskandrian, MD, MASNC[a]

[a] University of Alabama at Birmingham and VA Medical Center, Birmingham, AL

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INTRODUCTION

Non-invasive pharmacologic stress testing is widely used to evaluate patients with suspected or known coronary artery disease. Regadenoson is the most commonly used coronary vasodilator. It acts by selectively stimulating the A2a receptors, leading to coronary vasodilation. The usual hemodynamic response to regadenoson administration is an increase in heart rate and a decrease in blood pressure.

The increase in heart rate with regadenoson is thought to be due to sympathetic stimulation.[1] The right stellate ganglion is believed to innervate the sinus node while the left stellate ganglion innervates the AV node.[2] According to package insert and current ASNC guidelines, a first-degree AV block (prolonged PR interval) is not a contraindication for regadenoson (or adenosine) use.[3,4] We present a patient where regadenoson caused shortening of the prolonged PR interval providing indirect evidence that it stimulates sympathetic innervation.

CASE PRESENTATION

A 65-year-old man presented to our emergency department complaining of chest pain. His past medical history was significant for hypertension, diabetes mellitus type 2, hyperlipidemia, gout, and atrial flutter post bidirectional cavo-tricuspid isthmus block. He presented with one hour of substernal chest tightness that radiated to his left arm. The pain started at rest and was not made worse with exertion. His medications included amlodipine, carvedilol, fosinopril, furosemide, hydralazine, isosorbide mononitrate, and simvastatin.

The physical examination was normal. Laboratory studies were notable for undetectable Troponin I and creatinine 1.6 mg/dL, which was near the patient's baseline. Initial ECG showed sinus rhythm with first-degree AV block and no ischemic ST/T wave changes.

A stress SPECT myocardial perfusion imaging study was requested. Due to gout, the patient was unable to exercise on the treadmill and regadenoson (0.4 mg IV) was administered. The heart rate increased from 68 to 87 bpm and blood pressure increased from 148/72 to 160/74 mmHg. There were no ischemic ST changes.

No complications were encountered. The stress and rest perfusion images were normal (Figure 1). The left ventricular ejection fraction was normal at 65%. The interesting findings were in the ECG changes. The baseline ECG showed a PR interval of 412 ms (Figure 2). After regadenoson injection, the PR interval decreased to 220 ms (Figure 3) which was maintained for 90 seconds and then reverted to prolonged PR similar to baseline (Figure 4).

DISCUSSION

To our knowledge, this is the first reported case of a decrease in PR interval after regadenoson in a patient with severe first-degree AV block. We believe the improvement in AV conduction with increase in heart rate and blood pressure provides strong indirect evidence of sympathetic stimulation by regadenoson. The improvement in AV conduction also helps us in localizing the site of the block to the AV node and not the His-Purkinje System. The duration of this effect was roughly 90 seconds, which reflects the short duration of action of regadenoson. Our case is consistent with the safety of using regadenoson in patients with narrow QRS and markedly prolonged PR interval. This may

Reprint requests: G. Ross Farris, MD, University of Alabama at Birmingham and VA Medical Center, 1808 7th Ave S, BDB 201, Birmingham, AL 35294; *Grfarris1@uabmc.edu*

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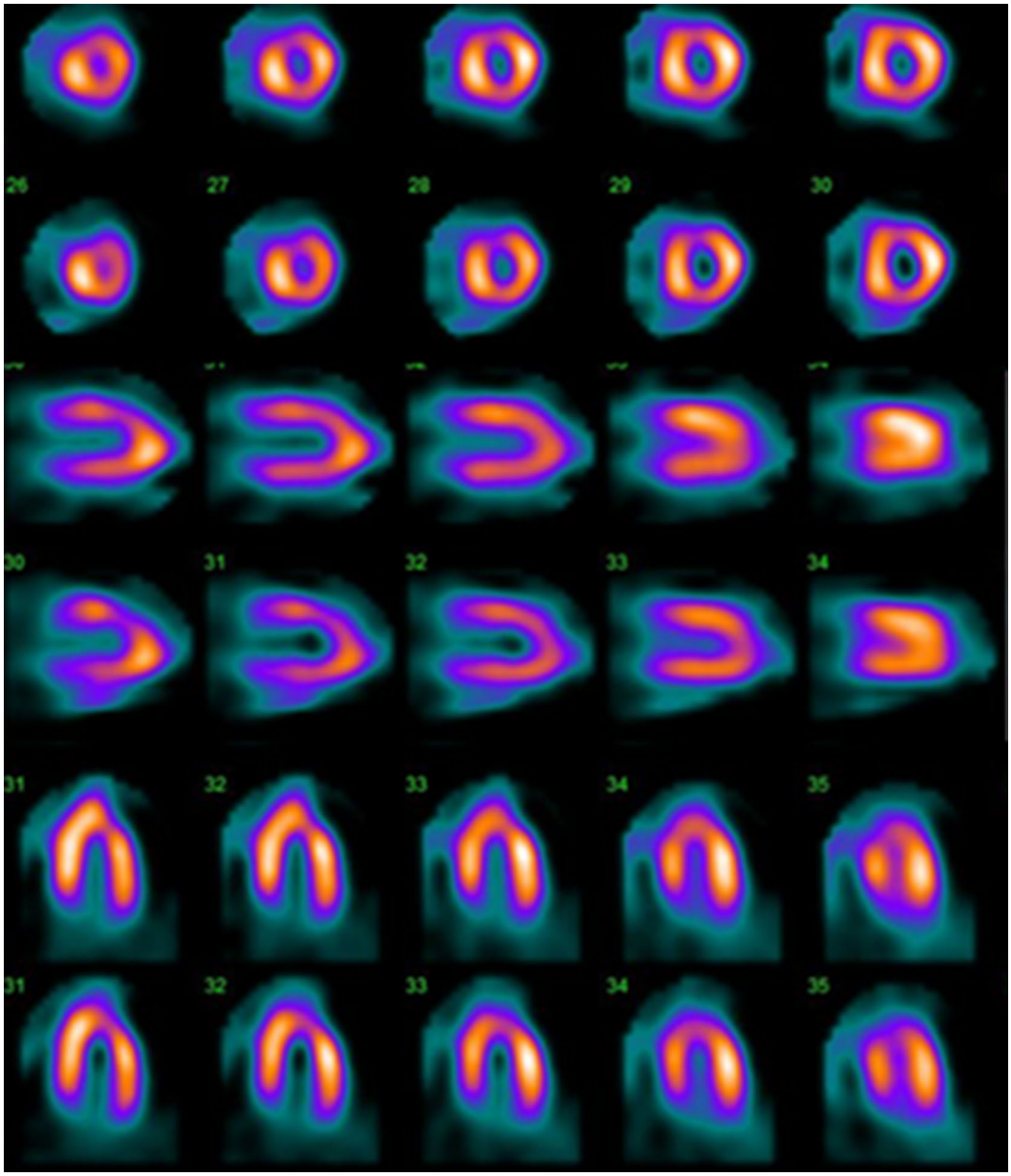

Figure 1. The stress and rest perfusion images showed normal perfusion pattern. The left ventricular wall motion and thickening (not shown) and ejection fraction were normal.

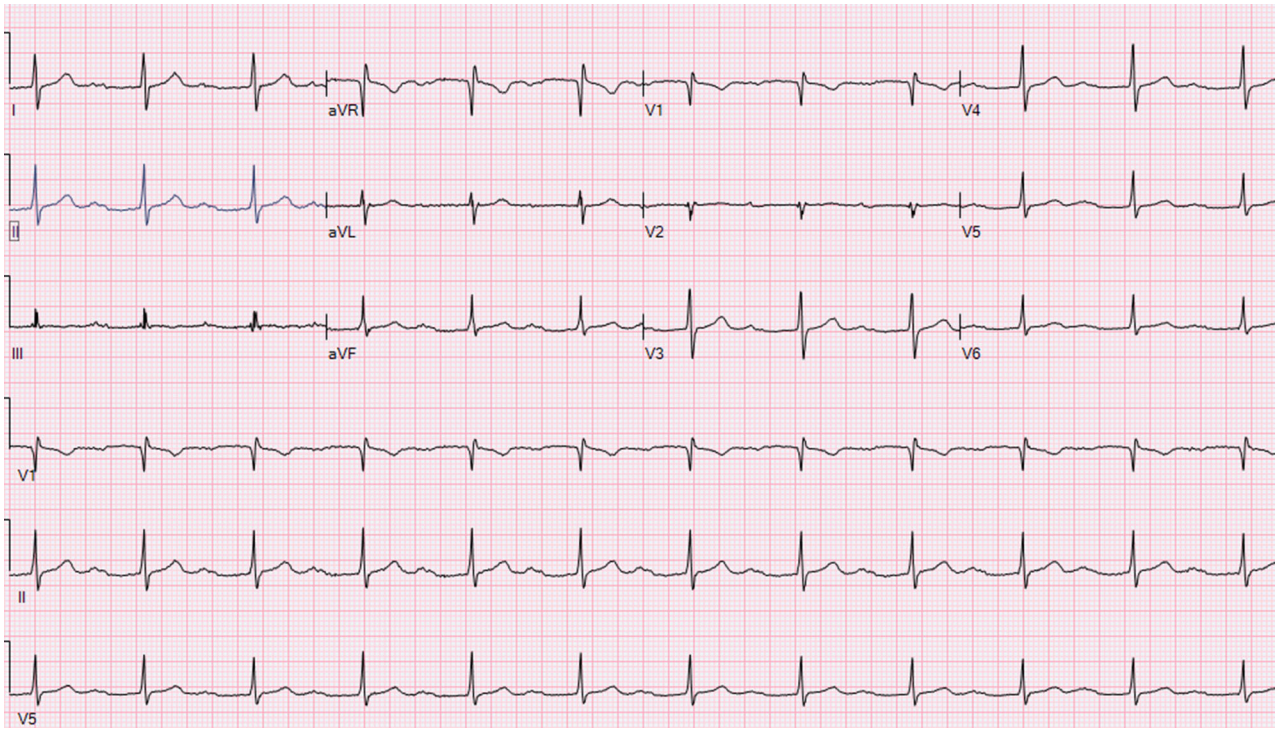

Figure 2. This ECG obtained prior to infusion of regadenoson demonstrates a markedly prolonged PR interval of 412 ms.

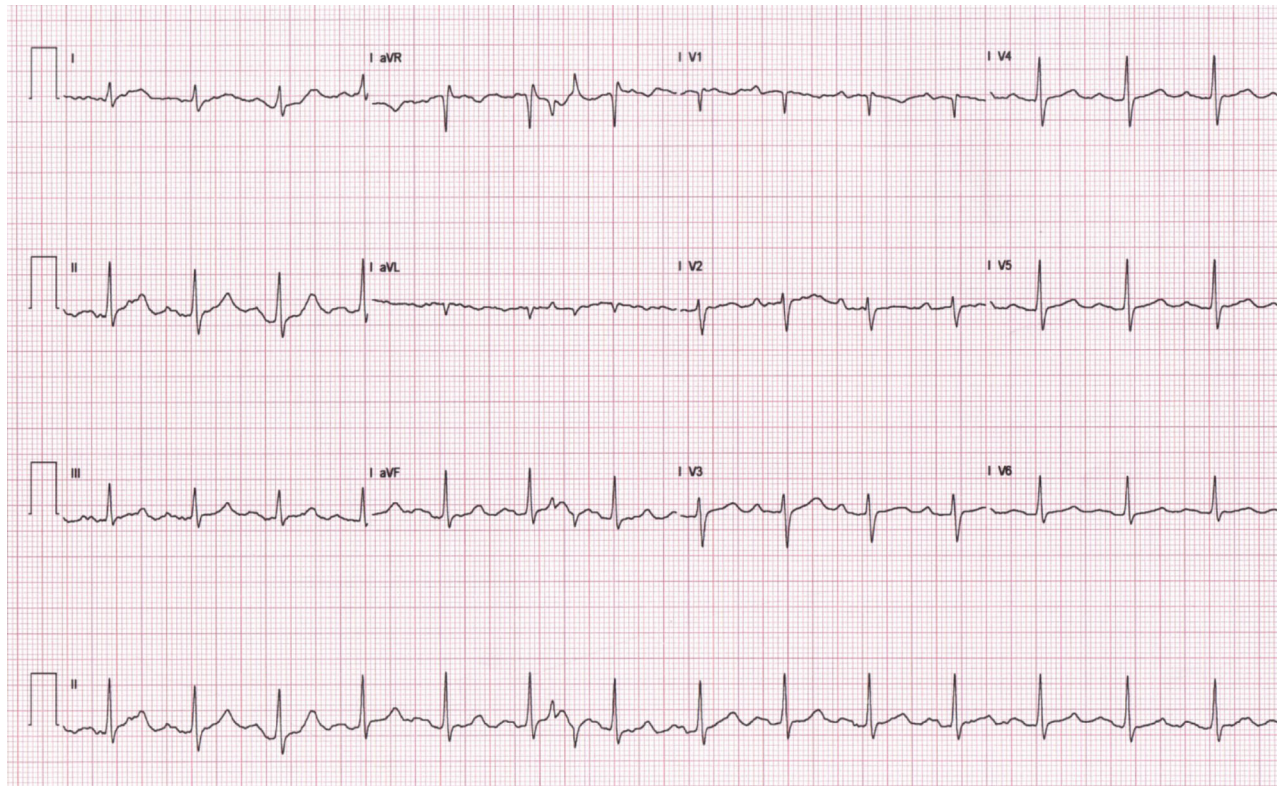

Figure 3. This ECG was obtained approximately 52 seconds after administration of regadenoson, and the PR interval has shortened by approximately 200 ms.

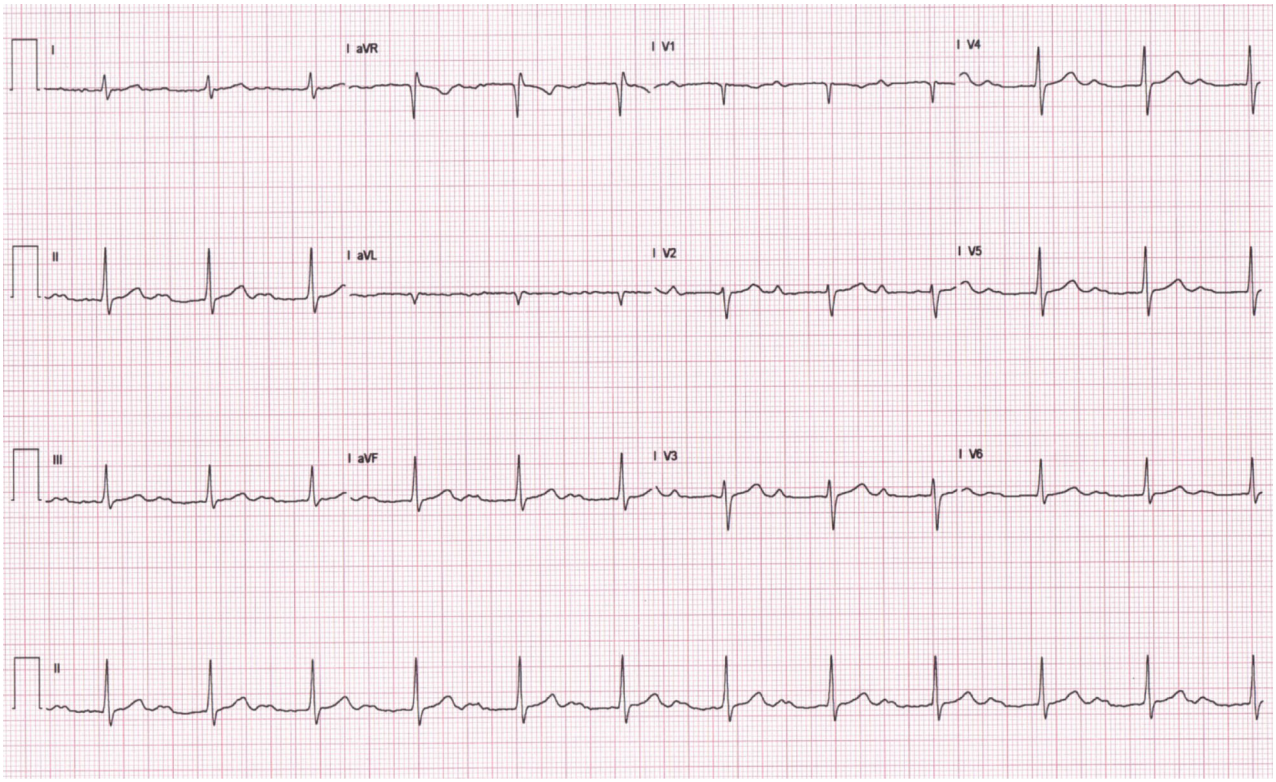

Figure 4. This ECG was obtained approximately 5 minutes after regadenoson infusion, and the PR interval has nearly returned to baseline.

also be applicable for Mobitz Type 1 second-degree AV block when the level of block is at the level of the AV node and not the His-Purkinje System. This can usually be ascertained on 12 lead ECG. Additionally, prior preclinical and clinical studies have demonstrated the dissociation of the heart rate and blood pressure responses seen with regadenoson.[5,6] The heart rate, but not the blood pressure, response to vasodilator stress has been shown to associate with poor outcomes.[1,7,8]

Disclosure

G. Ross Farris, Fadi G. Hage, Vineet Kumar, and Ami E. Iskandrian have no conflicts of interest to disclose.

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