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Case Report

Myocardial Ischemia Induced by Regadenoson Administered for Myocardial Perfusion Imaging in Combination with Modest Physical Activity

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Abstract

Adenosine has been widely used in radionuclide stress myocardial perfusion imaging. However, adenosine has many adverse effects due to the activation of the widely distributed receptors. Therefore, an effort has been made to develop a selective receptor agonist (regadenoson). Pharmacologic stress with regadenoson is generally considered to be safe. The hemodynamic effects of regadenoson peak within few minutes after administration. However, it is important to be aware that serious adverse events can occur at a later time point. In this case we reported myocardial ischemia due to pharmacologic stress induced by regadenoson in combination with modest physical activity.

Keywords: Regadenoson; Pharmacologic stress; Myocardial perfusion imaging; Ischemia

Abbreviations

ECG: Electrocardiogram; MPI: Myocardial Perfusion Imaging; PLA: Postero-Lateral Artery; RCA: Right Coronary Artery

Introduction

Adenosine is a naturally occurring ligand of four distinct types of receptors (A_1, A_{2A}, A_{2B} and A_3), and because of its ability to increase myocardial blood flow, adenosine has been widely used in radionuclide stress Myocardial Perfusion Imaging (MPI). However, adenosine has several adverse effects (e.g. dyspnea, headache, chest pain, and flushing), which has been attributed to the activation of the widely distributed A_1, A_{2B} and A_3 receptors. Therefore, an effort has been made to develop a selective A_{2A} receptor agonist (regadenoson). Despite its high selectivity for A_{2A}, regadenoson has a relatively low affinity for this receptor, thus regadenoson binding is readily reversible, the onset of its action is rapid, and the duration of action is brief [1]. The ADVANCE-MPI trials established non-inferiority of regadenoson compared to adenosine for detection of reversible myocardial perfusion defects, and further, that regadenoson was better tolerated than adenosine [1]. In this case report, we present a case of late onset myocardial ischemia due to administration of regadenoson in combination with modest physical activity.

Case Presentation

A 77-year-old Caucasian man with coronary artery disease was referred to MPI following a single episode of chest pain two months earlier without effect of nitrolingual spray. He was scheduled for a physical stress MPI using an ergometer bicycle, however, the physical stress was terminated prematurely about 5 minutes after the commencement of the test due to exhaustion of the legs. During the physical stress, he did not experience any chest pain and no ischaemic ECG changes were observed. The study was conducted with intravenous injection of 0.4 mg regadenoson without any significant adverse events, and in particular, neither chest pain nor ischaemic ECG changes were observed during a recovery period of 5 minutes (Figure 1A). According to our local MPI guideline, he was instructed

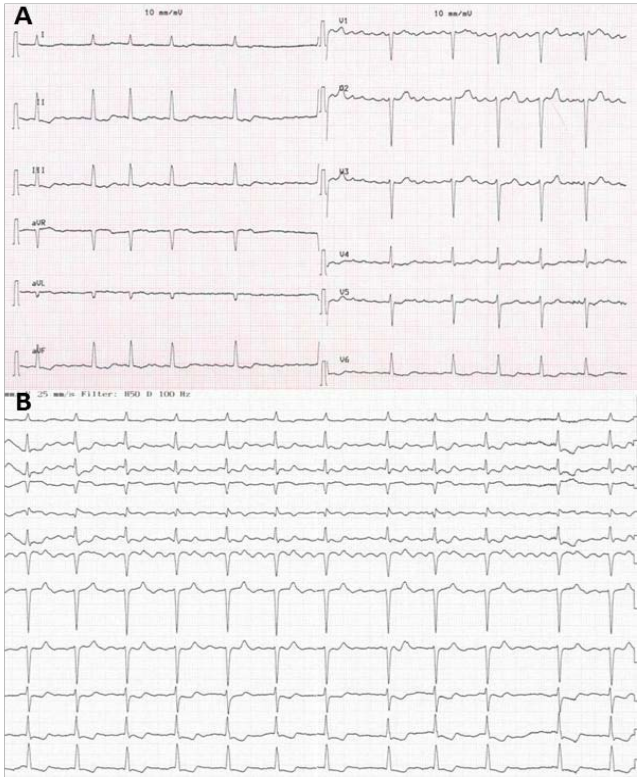

Figure 1: Electrocardiogram (ECG) (A) taken 3 minutes after regadenoson administration shows atrial fibrillation without significant ST-depression. ECG (B) taken approximately 30 minutes after regadenoson administration shows atrial fibrillation and significant ST-depression in leads II, III, aVF, and V4-V6.

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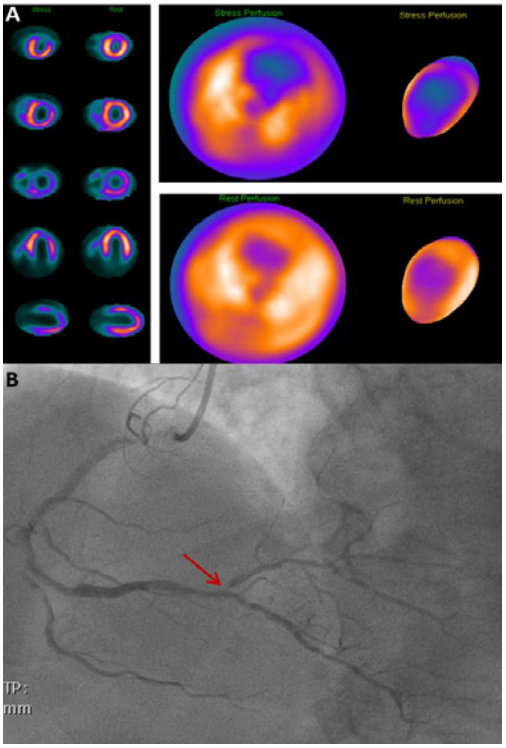

Figure 2: Myocardial perfusion imaging (A) before (rest) and after (stress) regadenoson administration shows a reversible (about 10%) anterolateral perfusion defect. Coronary angiography (B) shows a 99% stenosis (arrow) of the posterolateral branch from the right coronary artery.

to walk up and down the department's corridor for 20 minutes before the scan. This was not expected to cause any problems, since he was used to walk at least two kilometers on a daily basis. Five minutes after starting walking he experienced increasing chest pain. After 10-15 minutes of walking he contacted our staff due to severe chest pain. The ECG was repeated and demonstrated significant ST-depression in anterolateral leads (Figure 1B), blood pressure and heart rate were 200/100 mmHg and 77 bpm, respectively. His chest pain was partly relieved by nitrolingual spray followed by normalization of the ischaemic ECG changes. In consultation with a cardiologist it was decided to perform the MPI and subsequently hospitalize the patient. At the time of admission, his chest pain was ongoing, however, to a significantly lesser extent, and plasma troponin levels were slightly elevated (23ng/l, reference interval: <14ng/l). He was given the diagnosis unstable angina pectoris and treatment was initiated, accordingly. The resting MPI was conducted the next day. The MPI detected reversible ischemia in the anterolateral wall (Figure 2A). On the third day he was referred to coronary angiography, demonstrating a 99% stenosis of the Posterolateral Artery (PLA) from the right coronary artery (RCA, right dominant anatomy) (Figure 2B). The PLA stenosis was reduced to 60% using drug-eluting balloon therapy. He was discharged the following day. At three months follow-up he was doing well with only rare use of nitrolingual spray.

Discussion

In a recent Danish study evaluating safety and tolerability of regadenoson for myocardial perfusion imaging in 232 patients, 90% experienced one or more adverse events [2], but only two patients were hospitalized, both due to ECG changes (transient ST-depression of 1 mm in leads I, and V3–V6 and non-sustained ventricular tachycardia, respectively). The Food and Drug Administration analyzed its Adverse Event Reporting System and reported 26 myocardial infarctions and 29 deaths after regadenoson administration during the period June 2008 to April 2013, and the majority of events occurred within 6 hours of drug administration [3].

Our patient was hospitalized immediately after the pharmacologic stress MPI. A possible mechanism could be coronary collateral-dependent steal due to a significant stenosis. It has previously been postulated that a sudden drop in blood pressure due to the vasodilatory effect of regadenoson can lead to acute ischemia [3], however, our patient had a stable blood pressure for five minutes after regadenoson administration, and the blood pressure was significantly increased when he presented with severe chest pain.

In contrast to the physical stress test alone, the patient developed angina when conducting modest physical activity at least 10 minutes after regadenoson injection. In rodent studies, A_{2A} receptors are abundant in the splanchnic vasculature and A_{2A} receptor activation leads to vasodilation [4]. The combination of modest physical activity and the regadenoson-induced splanchnic vasodilation may have led to an increase in myocardial oxygen demand possibly inducing the patient's angina pectoris due to the significant PLA stenosis.

Conclusion

Pharmacologic stress with regadenoson is generally considered to be safe. The hemodynamic effects of regadenoson peak within few minutes after administration. However, it is important to be aware that serious adverse events can occur at a later time point. In this case we reported late onset myocardial ischemia due to pharmacologic stress induced by regadenoson in combination with modest physical activity.

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