

# A case report: adenosine triggered myocardial infarction during myocardial perfusion stress test imaging in a diabetic patient

Maarten de Mulder <sup>1\*</sup>, Menno van Gameren<sup>1</sup>, Eric A. van Asperen <sup>2</sup>, and Martijn Meuwissen <sup>1</sup>

<sup>1</sup>Department of Cardiology, Amphia Hospital, Breda, Amphia Ziekenhuis, Molengracht 21, 4818 CK, Breda, The Netherlands; and <sup>2</sup>Department of Nuclear Medicine, Amphia Hospital, Breda, Amphia Ziekenhuis, Molengracht 21, 4818 CK, Breda, The Netherlands

Received 5 July 2020; first decision 15 October 2020; accepted 12 March 2021

## Background

Myocardial perfusion imaging (MPI) using single-photon emission computed tomography (SPECT) can in general be used safely in daily clinical practice. However, under the right circumstances, it can lead to serious complications.

## Case summary

A 68-year-old female patient with diabetes and a history of inferior ST-elevation myocardial infarction 8 years earlier, visited our outpatient clinic with atypical chest discomfort. In order to assess whether this is due to myocardial ischaemia, MPI-SPECT was ordered. As it was suspected she would not achieve sufficient exercise levels, pharmacologic stress using adenosine was arranged. During the scan, she developed acute myocardial infarction. Subsequent urgent coronary angiography demonstrated a subtotal stenosis in the proximal left anterior descending coronary artery which was successfully stented. She was still free from angina 4 months later.

## Discussion

The combination of a reduced systemic and coronary perfusion pressure in the presence of an exhausted coronary autoregulation, may be a starting point for local geometrical changes that initiate the classic cascade of thrombus formation and acute occlusion of coronary arteries during MPI-SPECT. This illustrates the need for continuous patient and electrocardiogram monitoring.

## Keywords

Myocardial perfusion imaging • Stress testing • Adenosine • Myocardial infarction • Case report

## Learning points

- Adenosine stress testing leading to acute myocardial infarction is a rare but major side effect.
- In patients undergoing adenosine stress testing, continuous electrocardiograms (ECGs) monitoring should be preferred over symptom driven ECG monitoring.
- The interpretation of chest pain is challenging in (female) diabetic patients.

## Introduction

One of the challenges in daily clinical practice is to objectify the presence and extent of myocardial ischaemia. Myocardial perfusion imaging (MPI) using single-photon emission computed tomography (SPECT) is one of the preferred methods, frequently using pharmacologic stress testing with adenosine. Common side effects of adenosine include flushing, dyspnoea, gastrointestinal discomfort, chest pain, and headache.<sup>1</sup>

\* Corresponding author. Tel: +31 (0)76 595 5000, Email: [m.de.mulderr@gmail.com](mailto:m.de.mulderr@gmail.com)

Handling Editor: Timothy C. Tan

Peer-reviewers: Danny van de Sande and Roman Didier

Compliance Editor: Rahul Mukherjee

Supplementary Material Editor: Vishal Shahil Mehta

© The Author(s) 2021. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact [journals.permissions@oup.com](mailto:journals.permissions@oup.com)

## Timeline

2010		Percutaneous coronary intervention (PCI) right coronary artery for inferior myocardial infarction
2018	August	Recurrence of chest pain
	October	Visit to cardiology outpatient department
	21 November	Myocardial perfusion imaging (adenosine-induced stress)
	21 November	Admission to hospital and PCI left anterior descending coronary artery
	23 November	Discharge from hospital in good condition
2019	March	Free from angina at outpatient clinic

## Case presentation

A 68-year-old female patient with a history of inferior ST-elevation myocardial infarction (STEMI) treated by primary percutaneous coronary intervention (PCI) 8 years earlier visited our outpatient clinic. At that time, a residual intermediate stenosis in the mid left anterior descending coronary artery (LAD) was treated conservatively after discussion in the heart team.

Cardiovascular risk factors were diabetes and current smoking. She complained of atypical chest discomfort. Physical examination was unremarkable besides obesity (body mass index 33). The electrocardiogram (ECG) is shown in [Figure 1A](#). Adenosine stress MPI-SPECT was arranged, as it was suspected she would not achieve sufficient exercise levels.

Prior to adenosine administration, the patient denied anginal symptoms. A routine resting ECG was performed ([Figure 1B](#)), that demonstrated mild ST depression in the inferior leads and negative T waves anterior without any pathological Q waves. Subsequently, pharmacological stress using adenosine started, at a standard rate of 0.14 mg/kg/min over 6 minutes. Blood pressure and heart rate were 145/65 mmHg and 63 b.p.m. at rest and at 107/63 mmHg and 66 b.p.m. during maximum hyperaemia, respectively. Profound ST elevation in the anterior leads developed halfway the infusion, [Figure 1C](#), but the patient still denied chest pain. The cardiologist was consulted because of the discrepancy between ECG and clinical presentation. Meanwhile, MPI-SPECT images (using Tc99m-Tetrofosmin) were collected.

The patient was immediately transferred to the coronary care unit (CCU) after consultation with the cardiologist. She was pre-treated with heparin, ticagrelor plus aspirin and subsequently sent for urgent coronary angiography.

Distinct ST resolution was already seen just before coronary angiography (CAG), [Figure 1D](#). CAG showed a diffusely diseased right coronary artery. The left coronary artery contained a subtotal stenosis in the proximal LAD with reduced coronary flow (TIMI 2), [Figure 2](#). No collaterals or angiographic signs of thrombus were visible. The LAD stenosis was treated with two drug-eluting stents with good angiographic result and good coronary flow; TIMI 3 flow.

After PCI, she was admitted to the CCU for further observation. Biochemical markers of myocardial damage were moderately elevated; from CK 154 U/L (ref < 145 U/L) and high sensitive Troponin T of 294 ng/L (ref < 14 ng/L) at admission to the CCU (prior to PCI) and a maximum value of CK 240 U/L (ref < 145 U/L) and high sensitive Troponin T of max 1530 ng/L (ref < 14 ng/L) 6 h later. A pre-discharge echocardiogram demonstrated a mildly depressed left ventricular function with wall motion abnormalities anteroseptal and inferior. The MPI-SPECT stress images demonstrated a severe anterior wall perfusion defect (no rest images were acquired), [Figure 3](#). The summed stress score was 47 and the extent of involved myocardium was 65%.

Two days after admission, she was discharged in a good clinical condition. Four months later, she successfully completed her cardiac rehabilitation program, is free of angina, has stopped smoking and has a normalized ECG, [Figure 1E](#).

## Discussion

We present a female patient with a STEMI triggered by adenosine administration during MPI-SPECT. This is an uncommon (side) effect, in particular in patients without anginal symptoms.<sup>2-4</sup>

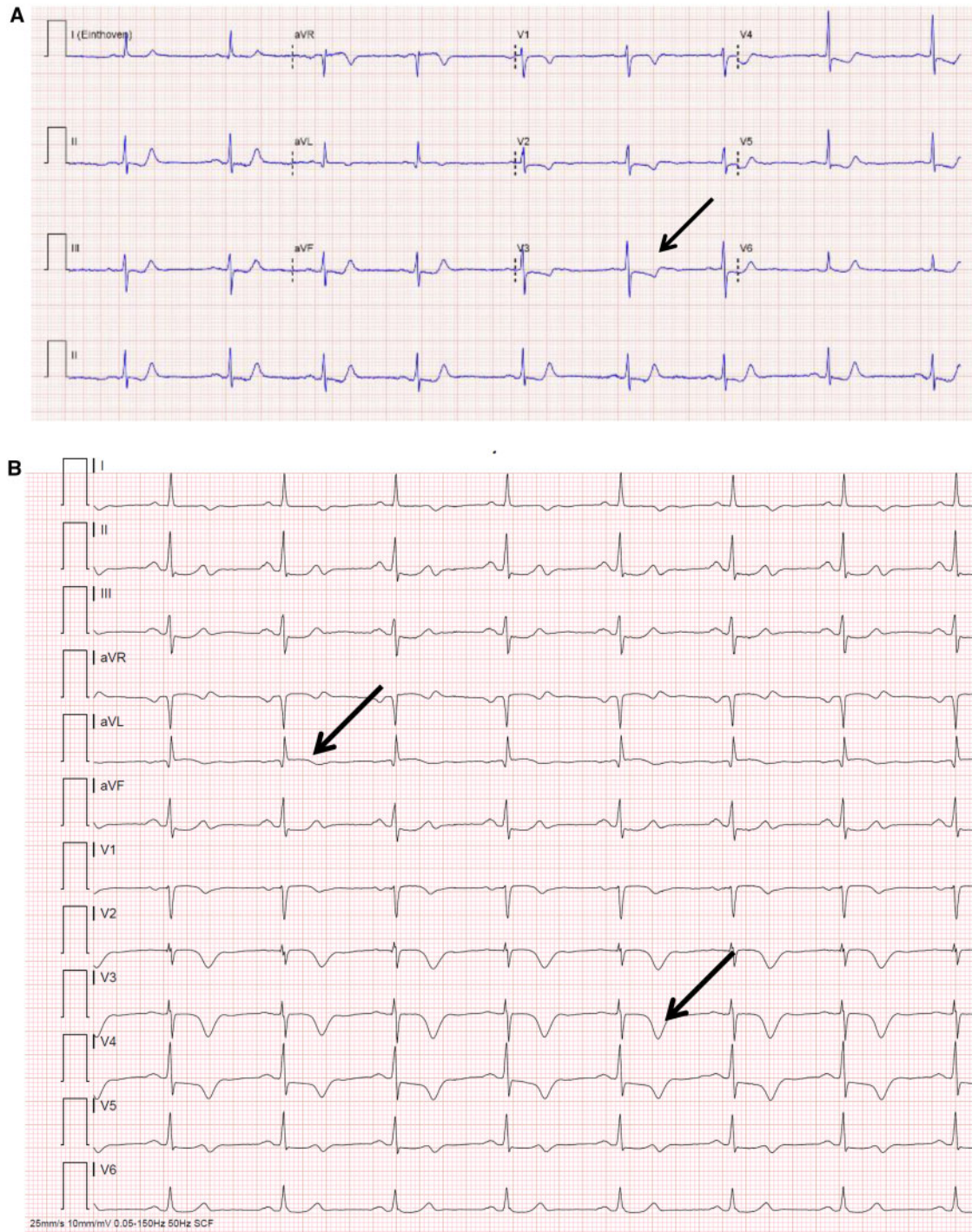
To the best of our knowledge, current literature does not provide an estimate of the amount of acute infarctions during (pharmacological) stress testing. Considering the number of MPI-SPECT scans performed annually, the number of available case reports, the fact that not all clinical events may be recognized as such and subsequently reported and published, hence an estimate cannot be provided. Our patient did not experience anginal chest pain, we assume the atypical presentation was the result of diabetic neuropathy. These atypical complaints may be present two- to five-fold more often in diabetic patients as compared to non-diabetic patients.<sup>5</sup>

This case also illustrates the challenges of interpreting complaints in such patients. In retrospect, it might have been more appropriate to directly order a CAG rather than an MPI-SPECT.

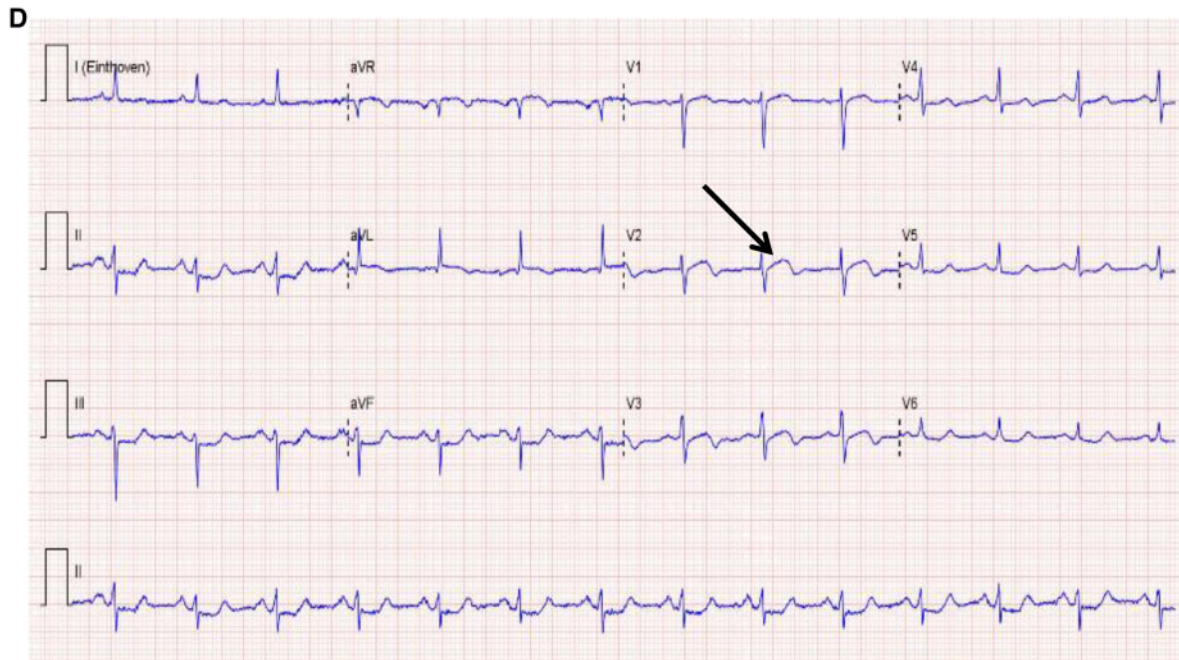
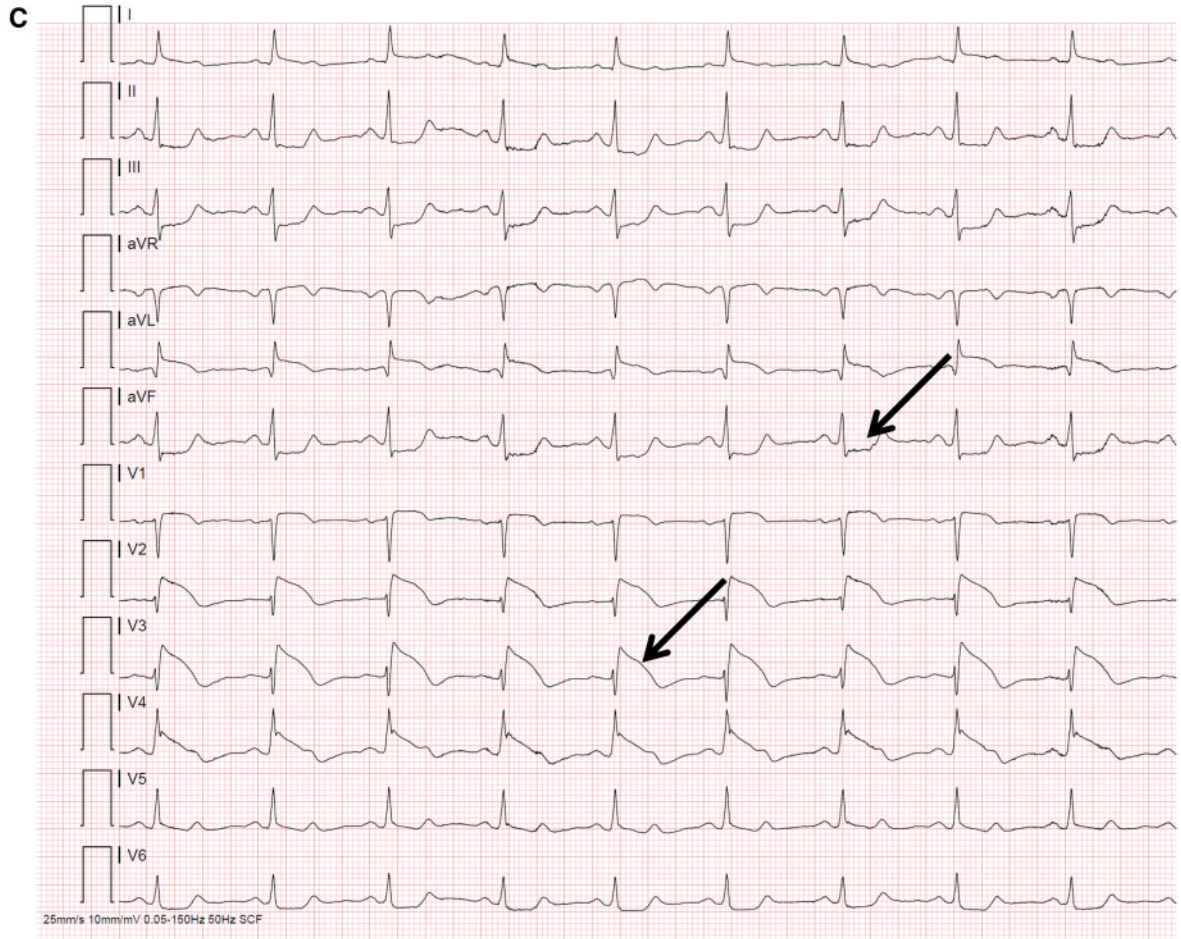
Several mechanisms may underlie the transient transmural ischaemia in our patient.

Adenosine is one of the most potent vasodilators of the resistance vessels by stimulating vascular smooth muscle cells to relax, leading to a decrease of the microvascular resistance and up to four to five times increased coronary blood flow in normal coronary arteries.<sup>1</sup> However, in our patient the pre-existing intermediate coronary stenosis progressed to a critical stenosis with an exhausted coronary autoregulation, i.e. further vasodilatation is not possible. Furthermore, IV adenosine infusion leads to a significant reduced systemic blood pressure, and in the presence of an exhausted autoregulation, a decreased perfusion pressure and thus myocardial ischaemia. Moreover, these changes in coronary pressure and flow may induce geometric modification of the coronary artery and stenosis.<sup>6</sup> In a highly vulnerable plaque, this vasomotion (e.g. partial vessel collapse) might be the last push to further destabilize it, break its thin cap and subsequently start the classic cascade of plaque rupture with thrombus formation and vessel occlusion.

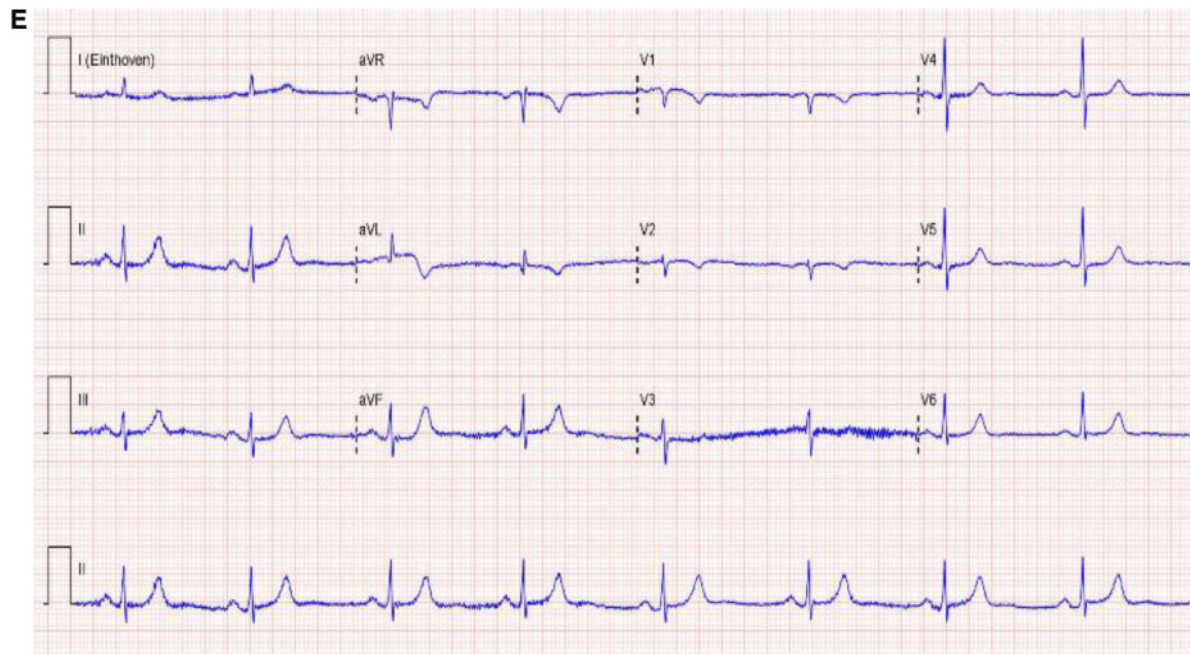
It has also been suggested that (active) coronary vasospasm, provoked by adenosine, can be the initiator of these anatomic changes.<sup>7</sup> A comparable conclusion was drawn in a recently



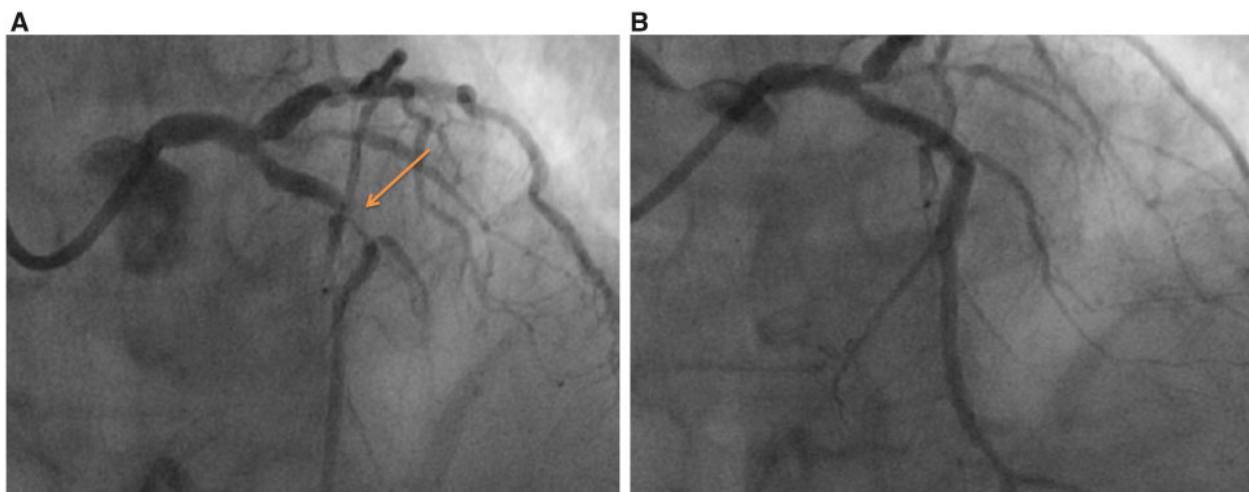
**Figure 1** (A) Outpatient electrocardiogram (prior to admission). Note the negative T waves in the anterior leads (arrow) and the absence of inferior pathological Q waves (where she had myocardial infarction 8 years earlier). (B) Resting electrocardiogram prior to adenosine administration. The T waves in the anterior leads are now profoundly negative (arrow) and very subtle ST elevation in aVL is visible (arrow). (C) Electrocardiogram 5 min after start of adenosine administration. Up to 4 mm ST-segment elevation develops anterior (lead V1–V4) and in lead I and aVL, the inferior leads II, III, aVF are markedly depressed. This fits with a proximal LAD lesion, if aVR was elevated (more than V1) left main obstruction would be suspected. (D) Electrocardiogram prior to coronary angiography. The ST elevation has resolved, but subtle 'shouldering' (arrow) remains. Furthermore, there is now a terminal negative T wave, rather than a clear negative T-wave prior to adenosine. The inferior ST-segment depression has resolved only partially. (E) Outpatient electrocardiogram (4 months after admission). The ST-segment changes have disappeared, the T waves have returned to near normal, only V1 and V2 are negative. Remember that at the outpatient electrocardiogram prior to admission (A), she had negative T waves in V3–V5 as well. Negative T in aVL is unchanged compared to A.



**Figure I** Continued.



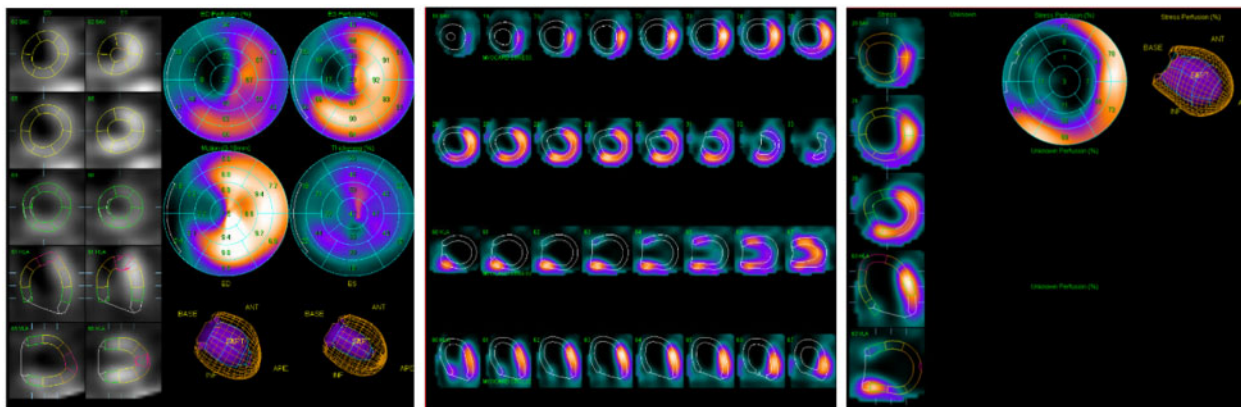
**Figure 1** Continued.



**Figure 2** Still frame of coronary angiography demonstrating pinpoint stenosis of the proximal left anterior ascending coronary artery (arrow), prior to (A) and after percutaneous coronary intervention (B).

published case report, although dipyridamole was used in their patient.<sup>8</sup> The authors assumed that dipyridamole may trigger vasospasm which can directly lead to ischaemia or provoke rupture of an unstable plaque. However, then we would expect to observe myocardial infarction more often, given the frequent use of adenosine in daily practice.

Finally, coronary steal by collateral vessels has been proposed as mechanism.<sup>9</sup> After adenosine, a proportionately greater increase in blood flow of the normal vascular bed is seen as compared to the relatively low fixed flow of the collateral bed, which cannot compensate further for the fall in pressure at the origin. And thus the myocardial area after a stenosis, which was protected by collaterals, then



**Figure 3** Myocardial perfusion stress imaging demonstrating major antero-septal ischaemia.

falls short of perfusion. However, no angiographically visible collateral vessels were present in our patient.

The above described mechanisms may occur at any time point during adenosine infusion, depending on the particular circumstances in that specific patient. Therefore, we agree with the earlier mentioned case reports, that continuous ECG monitoring rather than at pre-specified time points, should be standard of care. In this light, it is interesting to note that in the current 2018 ASNC (American society of nuclear cardiology) SPECT imaging guidelines, the ECG is only mentioned in relation to gated imaging.<sup>10</sup> Many technical matters are discussed, yet suggestions for patient monitoring during the scan are not.

Apart from taking potential side effects into account when ordering a test, it is even more important to consider its diagnostic accuracy. In this respect, several matters have to be taken into account. When an exercise perfusion test is ordered, the physician has to make a rough assessment of the exercise potential of the patient. With insufficient exercise performance due to comorbidities (e.g. arthrosis or pulmonary disease) the test result will be unreliable and a pharmacologic stress test should be ordered. Second, MPI SPECT is designed to detect regional differences in myocardial perfusion during (pharmacologic) exercise and rest. However, when all regions are affected, such as in three-vessel disease, the ischaemia can be balanced between vascular beds and the test can (falsely) be negative.

A relative recent meta-analysis calculated a sensitivity of 80% and specificity of 83% for the detection of coronary artery disease using attenuated corrected MPI SPECT.<sup>11</sup> In 2007, a pooled analysis of studies published between 1980 and 2007 reported the sensitivity and specificity of various imaging modalities for the detection of viable myocardium in that era. Magnetic resonance imaging and MPI SPECT were more or less comparable with a sensitivity 80–85% and specificity 60–65%. The sensitivity of fluorodeoxyglucose–positron emission tomography was much better (92%), with a comparable specificity (60%).<sup>12</sup>

## Conclusion

In summary, adenosine stress MPI SPECT generally is very safe. However, adenosine infusion may lead to myocardial ischaemia and infarction in severe stenotic coronary arteries. This could occur due to a combination of a reduced systemic and coronary perfusion pressure in the presence of an exhausted coronary autoregulation in a subcritical coronary stenosis. This may then be a starting point for local geometrical changes that initiate the classic cascade of thrombus formation and vessel occlusion. Moreover, this case underscores the need for standard close ECG monitoring, rather than only symptom driven ECG's and in particular in diabetic patients.

## Lead author biography



In 2018, Maarten de Mulder finished his training with a special interest in device cardiology and heart failure at the Erasmus University Medical Centre (Rotterdam, The Netherlands). Since then he works as a practicing cardiologist in the Amphia Hospital, Breda, The Netherlands.

## Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

## Acknowledgements

We would like to thank Jeroen Schaap and Sander Ijsselmuiden for their help in composing this manuscript.

**Slide sets:** A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

**Consent:** The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

**Conflict of interest:** None declared.

**Funding:** None declared.

## References

1. Layland J, Carrick D, Lee M, Oldroyd K, Berry C. Adenosin physiology, pharmacology and clinical application. *JACC Cardiovasc Interv* 2014;**7**:581–591.
2. Reyes E, Wechalekar K, Loong CY, Underwood SR. Acute myocardial infarction during adenosine myocardial perfusion imaging. *J Nucl Cardiol* 2004;**11**: 97–99.
3. Raza AJ, Khan NUA, Mustafa JS, Movahed A. ST segment elevation during adenosine pharmacological stress testing in a patient with coronary artery disease. *Am Heart Hosp J* 2009;**7**:122–124.
4. Polad JE, Wilson LM. Myocardial infarction during adenosine stress test. *Heart* 2002;**87**:E2.
5. Nesto RW, Phillips RT. Asymptomatic myocardial ischemia in diabetic patients. *Am J Med* 1986;**80**:40–47.
6. Siebes M, Campbell CS, D'Argenio DZ. Fluid dynamics of a partially collapsible stenosis in a flow model of the coronary circulation. *J Biomech Eng* 1996;**118**: 489–497.
7. Golzar J, Mustafa SJ, Movahed A. Chest pain and ST-segment elevation 3 minutes after completion of adenosine pharmacologic stress testing. *J Nucl Cardiol* 2004; **11**:744–746.
8. Li KFC, Ho HH, Yew MS. A case report of dipyridamole stress-induced ST depression progressing to ST elevation myocardial infarction despite intravenous aminophylline: steal, spasm or something else? *Eur Heart J Case Rep* 2019;**3**: 1–6.
9. Gould KL. Coronary steal, is it clinically important? *Chest* 1989;**96**:227–228.
10. Dorbala S, Ananthasubramaniam K, Armstrong IS, Chareonthaitawee P, DePuey EG, Einstein AJ et al. Single photon emission computed tomography (SPECT) myocardial perfusion imaging guidelines: instrumentation, acquisition, processing, and interpretation. *J Nucl Cardiol* 2018;**25**:1784–1846.
11. Huang JY, Huang CK, Yen RF, Wu HY, Tu YK, Cheng MF et al. Diagnostic performance of attenuation-corrected myocardial perfusion imaging for coronary artery disease: a systematic review and meta-analysis. *J Nucl Med* 2016;**57**: 1893–1898.
12. Schinkel AFL, Bax JJ, Poldermans D, Elhendy A, Ferrari R, Rahimtoola SH. Hibernating myocardium: diagnosis and patient outcomes. *Curr Probl Cardiol* 2007;**32**:375–410.