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CASE REPORT
Cardiac imaging

A case report of dipyridamole stress-induced ST depression progressing to ST-elevation myocardial infarction despite intravenous aminophylline: steal, spasm, or something else?

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Background Dipyridamole stress is commonly used for myocardial perfusion imaging and is generally safe. Myocardial ischaemia can occasionally occur and is classically thought to be due to coronary steal as a result of redistribution of flow away from collateral dependent myocardium. Although ischaemia more commonly presents as electrocardiographic (ECG) ST depression and angina, ST-elevation myocardial infarction may occur as a very rare complication.

Case summary We report a case of a patient who developed chest pain and ST depression during dipyridamole infusion. The pain persisted despite intravenous aminophylline with new inferior ST elevation soon after. Coronary angiography showed subtotal right coronary artery occlusion with no collateral supply. The symptoms and ECG changes resolved after percutaneous coronary intervention.

Discussion Coronary steal may not fully account for our patient's presentation given the failure of aminophylline and absent angiographic collaterals. Vasospasm may be triggered by dipyridamole and can directly cause ischaemia or provoke rupture of an unstable plaque. Augmentation of cardiac energetics during vasodilator stress may also play a role.

Keywords Case report • Ischaemia • Infarction • Dipyridamole • Coronary steal • Vasospasm

Learning points

- Myocardial ischaemia can occur during dipyridamole stress testing although myocardial infarction is a rare occurrence.
- Although coronary steal is thought to be the most likely cause for vasodilator-induced myocardial ischaemia, other mechanisms such as coronary vasospasm or spontaneous plaque rupture may play a role.

Introduction

Dipyridamole stress myocardial perfusion imaging (MPI) is generally safe although myocardial ischaemia manifesting as electrocardiographic (ECG) ST depression and angina can occur.[1] ST-elevation myocardial infarction (STEMI) is a rare complication.[1] Coronary steal refers to the shunting of blood flow away from collateral dependent myocardium after vasodilation and is generally believed to be the main mechanism for dipyridamole-induced myocardial ischaemia.[2] As such, presence of angiographic collaterals is a pre-requisite for steal

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to occur[2–4] and symptoms should reverse with aminophylline use.[5,6] We report a case of post-dipyridamole myocardial ischaemia with initial ST depression progressing to STEMI despite intravenous (IV) aminophylline. Coronary angiography revealed a severe stenosis with no collaterals. A literature review and brief discussion on possible alternative mechanisms for this occurrence is also presented.

Timeline

29 July 2011	Developed non-ST-elevation myocardial infarction (NSTEMI). Culprit lesion was a 95% stenosis in the mid-right coronary artery (RCA). Percutaneous coronary intervention (PCI) performed with drug eluting stent (Taxus Element, Boston Scientific). Residual 80% proximal to mid-left anterior descending (LAD) artery disease.
1 August 2011	Staged PCI to LAD with drug-eluting stent (Xience V, Abbott).
21 June 2018	Seen in outpatient clinic for exertional dyspnoea without chest pain. Dipyridamole stress myocardial perfusion imaging (MPI) was ordered.
23 July 2018	Presents for 1 day rest-dipyridamole stress MPI.
09:30 h	Rest component of MPI performed uneventfully.
11:30 h	Initiation of dipyridamole infusion as stress portion of non-invasive MPI (0.56 mg/kg intravenously over 4 min).
11:34 h	Development of chest pain with inferior and lateral ST-segment depression.
11:35 h	Dipyridamole infusion stopped and intravenous aminophylline 250 mg given with no relief.
11:43 h	Development of inferior ST elevation.
12:26 h	Urgent coronary angiogram showed a right dominant circulation, patent LAD and RCA stents with a subtotally occluded distal RCA. PCI to the RCA using a drug-coated balloon (Magic Touch 2.0 × 15 mm, Concept Medicals) resulted in resolution of angina and ST elevations.
26 July 2018	Discharged from hospital.
13 December 2018	Reviewed in clinic. Improvement in exertional dyspnoea. No chest pain.

Case presentation

A 67-year-old lady with hypertension and dyslipidaemia presented in mid 2018 with a 6 month history of New York Heart Association (NYHA) functional Class II exertional dyspnoea with no chest pain. She was on daily Aspirin 100 mg after a non-ST-elevation myocardial infarction in 2011 requiring left anterior descending and right coronary artery (LAD and RCA) percutaneous coronary intervention (PCI) with drug-eluting stents. A 1-day rest-dipyridamole stress MPI was ordered, with the rest MPI completed uneventfully with no perfusion defects seen (*Figure 1*). She was asymptomatic with a normal baseline ECG (*Figure 2*) before 0.56 mg/kg of IV dipyridamole was infused over 4 min for stress. During the final minute of the infusion, she developed angina and her ECG showed sinus tachycardia with ST depression (*Figure 3*). Dipyridamole infusion was stopped and IV aminophylline 250 mg was given with no relief. At 9 min post-dipyridamole, new inferior ST elevation with reciprocal ST depression in I, aVL was noted (*Figure 4*). The rhythm remained in sinus tachycardia with no atrioventricular block. She did not receive any medications before her urgent transfer to the cardiac catheterization laboratory where oral Ticagrelor 180 mg and intra-arterial (through radial arterial sheath) Glyceryl trinitrate 200 mcg were given on table. Coronary angiography showed a right dominant circulation, patent LAD, and RCA stents with a subtotally occluded distal RCA (*Figure 5* and Supplementary material online, *Videos S1–S4*). There was no significant disease in the rest of the LAD and circumflex vessel. No collaterals supplying the RCA could be visualized angiographically. In view of the small vessel size, the procedurist performed PCI to the RCA using a drug-coated balloon (Magic Touch 2.0 × 15 mm, Concept Medicals) rather than a stent. Percutaneous coronary intervention resulted in resolution of angina and ST elevation. The post-PCI serum troponin I was 1575 ng/L. A transthoracic echocardiogram showed left ventricular ejection fraction of 50% with RCA territory hypokinesia. The patient was discharged well after 4 days.

Discussion

Myocardial ischaemia with angina and ECG changes after vasodilator stress is uncommon.[1,7] ST depression is observed more frequently whereas occurrences of ST elevation are limited to isolated case reports.[5–10] To our knowledge, this is the first reported case of dipyridamole-induced ECG ST depression progressing to ST elevation despite the use of aminophylline. The elevated serum troponin and inferior wall motion abnormalities seen on the echocardiogram despite an earlier normal rest MPI indicates that myocardial infarction did occur post-dipyridamole stress. However, the mechanism of STEMI in this case may not be related to the classical 'coronary steal', in which ischaemia occurs when dipyridamole-induced coronary vasodilation results in redistribution of flow away from collateral dependent myocardium.[8] The presence of angiographic collaterals, which was not seen in our patient, appears to be a pre-requisite for coronary steal to occur.[2–4,11] Moreover, as seen in previous case reports, the ischaemic signs and symptoms are expected to improve with IV aminophylline should steal phenomenon be present.[5,6] Instead, our patient had persistent chest pain with evolution of ST depression to ST-segment elevation after IV aminophylline, which is not consistent with the pathophysiology of coronary steal.

Apart from steal, coronary spasm has also been implicated in vasodilator-induced myocardial ischaemia. ST-segment elevation post-adenosine stress has been reported to occur in the presence of normal coronaries and is attributed to coronary vasospasm secondary to activation of adenosine A1 receptors.[9] Qamruddin also reported a case of ST elevation occurring 13 min after regadenoson injection. Angiography revealed a non-occlusive but functionally significant LAD stenosis. Interestingly, the post-stress myocardial perfusion

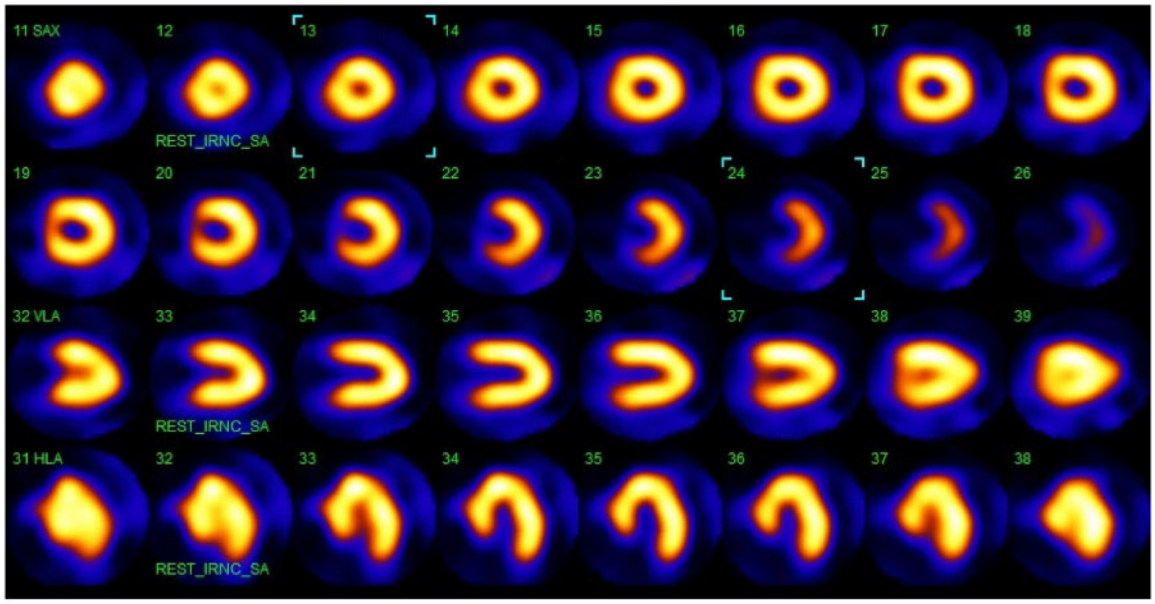

Figure 1 Normal rest myocardial perfusion performed prior to stress testing.

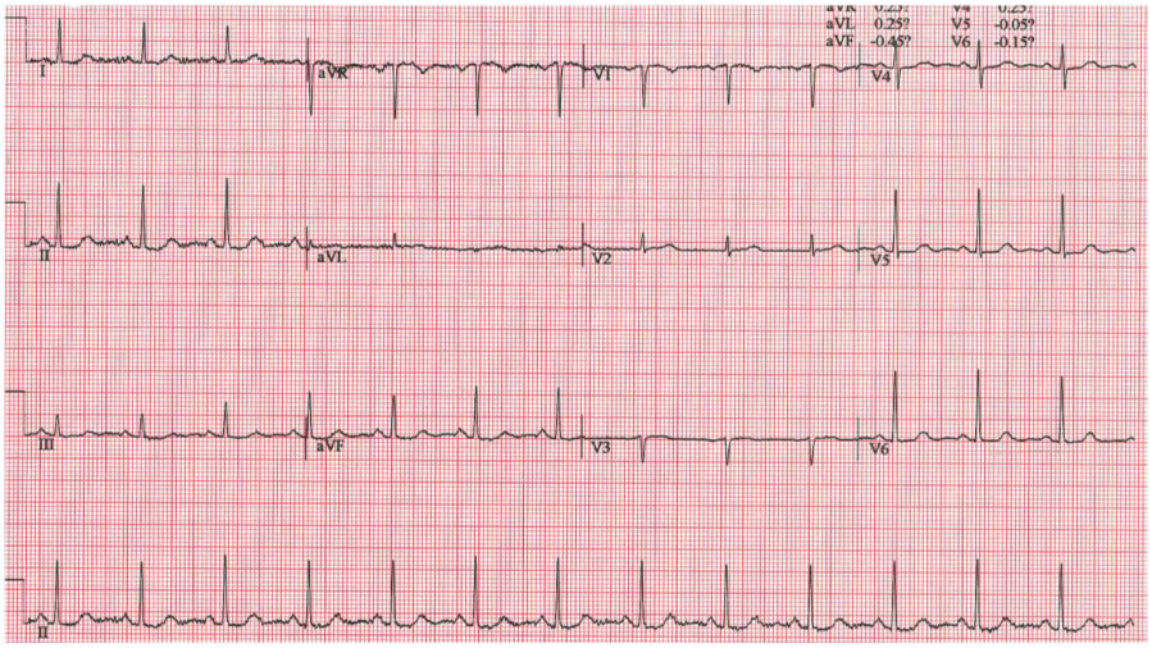

Figure 2 Patient's baseline resting electrocardiogram showing no significant abnormalities.

images were normal, illustrating that ischaemia did not occur at the time of vasodilator stress and that coronary vasospasm occurred after cessation of the pharmacological effects of the vasodilator.[12] Our patient, however, did not exhibit angiographic evidence of coronary vasospasm despite having ongoing chest discomfort and ST elevation. This makes vasospasm a less likely possibility although it cannot be completely excluded given that intracoronary nitroglycerine was not administered prior to PCI.

Spontaneous fissuring or rupture of an unstable plaque is the typical mechanism for myocardial infarction. This can occur post-

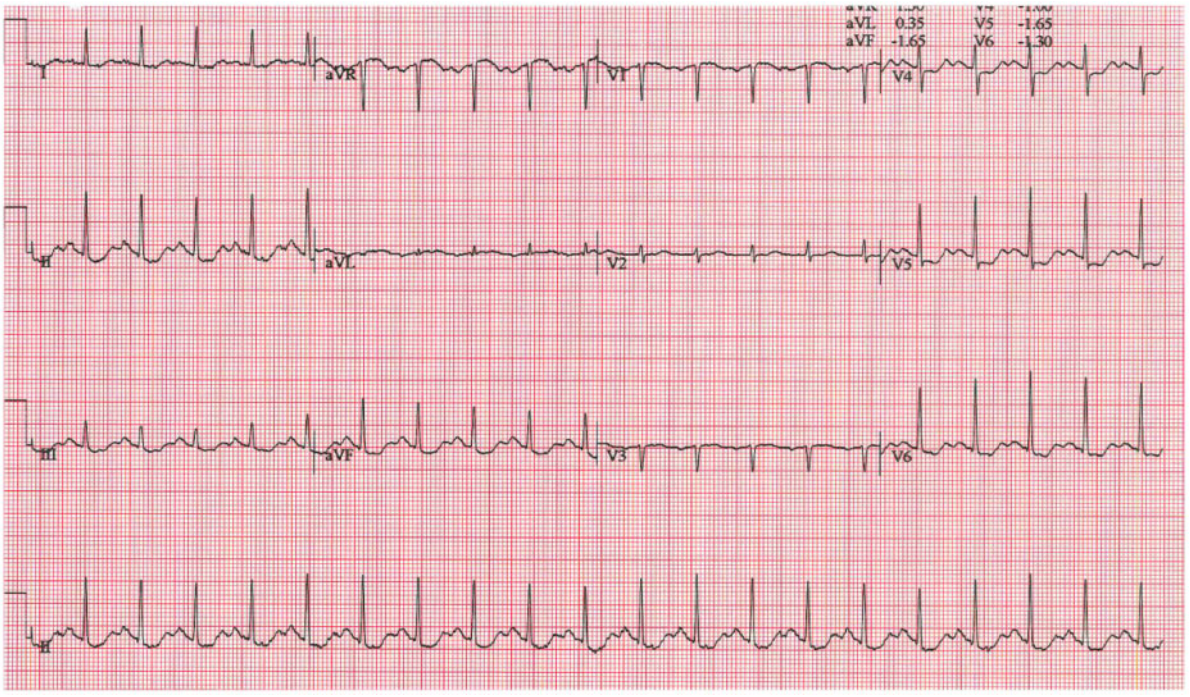

Figure 3 Electrocardiogram performed when patient developed angina during the final minute of dipyridamole infusion, showing new ST depression in inferior and lateral leads.

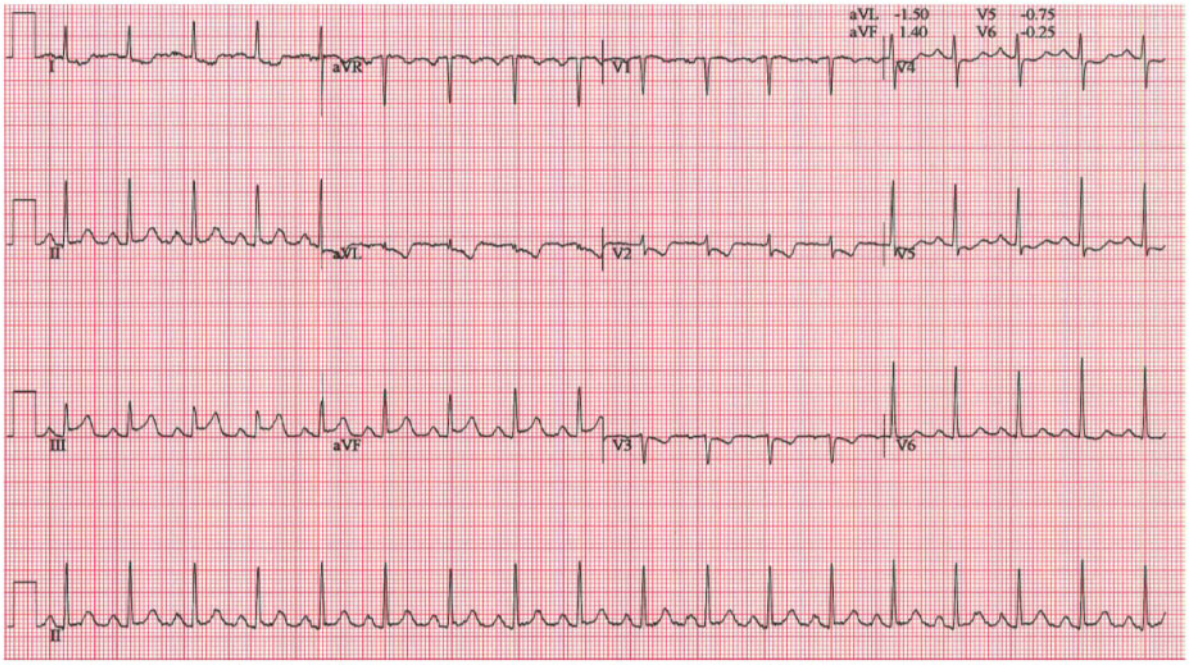

Figure 4 Electrocardiogram 9 min post-dipyridamole infusion, showing new ST elevation in the inferior leads with reciprocal ST depression in I, aVL.

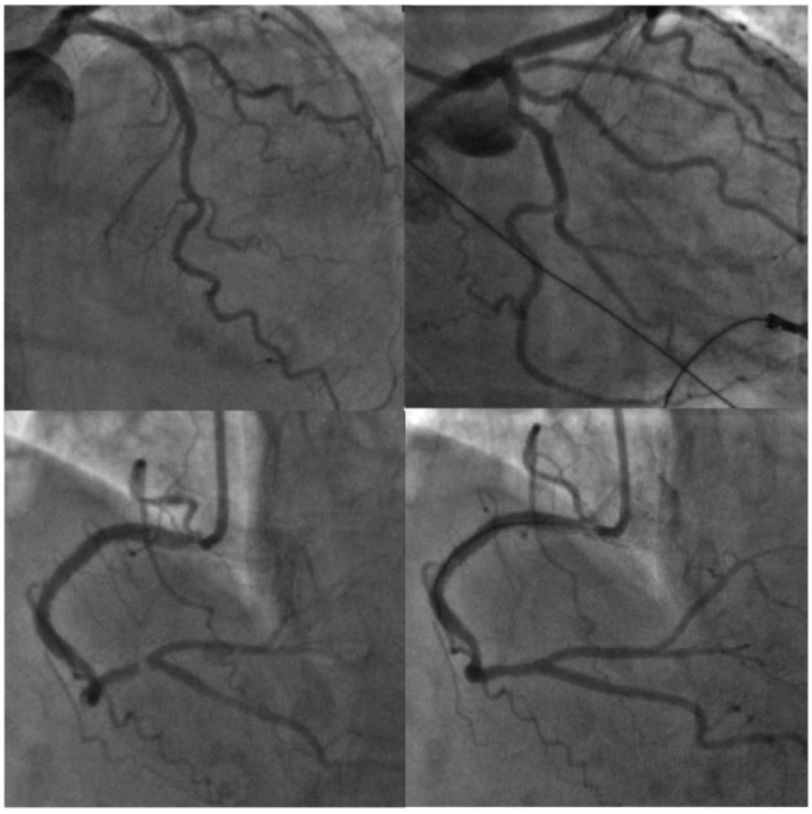

Figure 5 (Top left and top right) Coronary angiogram of the left system showing non-obstructed coronaries (see Supplementary material online, *Videos S1* and *S2*). (Bottom left) Coronary angiogram showing subtotal occlusion in distal right coronary artery (see Supplementary material online, *Video S3*). (Bottom right) Angiographic results post-drug coated balloon angioplasty to the lesion (see Supplementary material online, *Video S4*).

exercise stress and has been attributed to repeated vasospasm from circulating catecholamines resulting in plaque rupture and subtotal coronary occlusion.[13] Increased flexing of atherosclerotic coronary arteries during exertion may also play a role.[14] Although these mechanisms have not been conclusively demonstrated in the setting of vasodilator stress, Kwai *et al.*[10] reported a case of ST-segment elevation post-oral dipyridamole that persisted despite aminophylline but resolved only after IV streptokinase. This case highlights the possibility of dipyridamole-induced coronary thrombosis as the cause of STEMI. Although coronary vasospasm may have been the inciting event resulting in plaque rupture, we postulate that augmentation of cardiac energetics post-dipyridamole[15] may possibly result in a hyperdynamic state similar to exercise that can provoke rupture of an unstable plaque.

In summary, our patient developed myocardial ischaemia with ST-segment depression soon after dipyridamole infusion that progressed to inferior ST-segment elevation myocardial infarction. Steal phenomenon is unlikely to be the cause in view of the failure of IV aminophylline and absent angiographic collaterals. Coronary vasospasm was not angiographically evident but may have been present initially which resulted in the preceding ST-segment depression. The subsequent ST-segment elevation with subtotal coronary occlusion is likely due to unstable plaque rupture secondary to coronary vasospasm and/or increased cardiac work from dipyridamole stress. Apart from being a valuable addition to the limited existing literature on post-vasodilator myocardial infarction, this case also illustrates the importance of warning patients of the possibility of myocardial infarction when taking consent for pharmacological stress. Continuous procedural cardiac monitoring is recommended for all patients even if the indication is not for typical chest pain, as seen in our patient who had exertional dyspnoea as an angina equivalent. Further work, especially in the field of intracoronary imaging, is needed to better understand the pathophysiology of this rare but clinically significant entity.

Lead author biography

Dr Min Sen Yew is a consultant cardiologist in Tan Tock Seng Hospital, Singapore. He underwent fellowship training in nuclear cardiology and cardiovascular computed tomography at the Royal Brompton Hospital, London. His clinical interest is in multimodality cardiac imaging, including nuclear cardiology, cardiac computed tomography, as well as cardiac magnetic resonance imaging

Supplementary material

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

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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