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CASE REPORT
Coronary intervention

Isoprenaline induced myocardial infarction in a patient with high-grade atrioventricular block: a case report

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Background Isoprenaline is widely used in the treatment of symptomatic bradycardia. Myocardial infarction precipitated by the therapeutic use of isoprenaline has not been reported in the literature.

Case summary We describe the case of a 67-year-old male patient who presented to our institution with symptomatic Mobitz type II 2:1 atrioventricular block. He had a several-month history of unexplained syncope. He had several cardiovascular risk factors but did not have a diagnosis of coronary artery disease. On admission, he was symptomatic with dizziness but had no chest pain. High-sensitivity troponin I was normal. After initiation of an isoprenaline infusion, he developed cardiac-sounding chest pain and an ischaemic electrocardiogram. Emergency coronary angiography was performed that demonstrated a severe mid-vessel stenosis in his right coronary artery that was treated with percutaneous coronary intervention and the deployment of one drug-eluting stent. He remained in Mobitz type II 2:1 atrioventricular block 48 hours after the procedure, and a dual-chamber permanent pacemaker was implanted. He was discharged in a stable condition with no further chest pain or bradyarrhythmia.

Discussion To our knowledge, this is the first reported case of myocardial infarction precipitated by the therapeutic use of isoprenaline. Our hypothesis is that isoprenaline increased myocardial oxygen demand and induced a type 2 myocardial infarction in this patient with occult coronary artery disease. Isoprenaline should be used with caution in patients with confirmed or suspected coronary artery disease.

Keywords Case report • Isoprenaline • Myocardial infarction • Bradycardia • High-degree AV block

ESC curriculum 3.2 Acute coronary syndrome • 3.1 Coronary artery disease • 5.7 Bradycardia

Learning points

- Isoprenaline may provoke myocardial ischaemia in patients with underlying coronary artery disease.
- Isoprenaline should be used with caution in patients with suspected or known coronary artery disease.

Introduction

Isoprenaline is a potent non-selective beta receptor agonist used as a pharmacological agent to treat symptomatic bradycardia. It has positive chronotropic and inotropic effects via β-1 adrenergic stimulation, as well as producing vasodilatation via β-2 adrenergic stimulation.[1] It is recommended in the United Kingdom Resuscitation Council Advanced Life Support bradycardia algorithm as an interim measure to treat symptomatic bradycardia, prior to more definitive transvenous pacing.[2] It is also used to induce arrhythmia in electrophysiological studies, as

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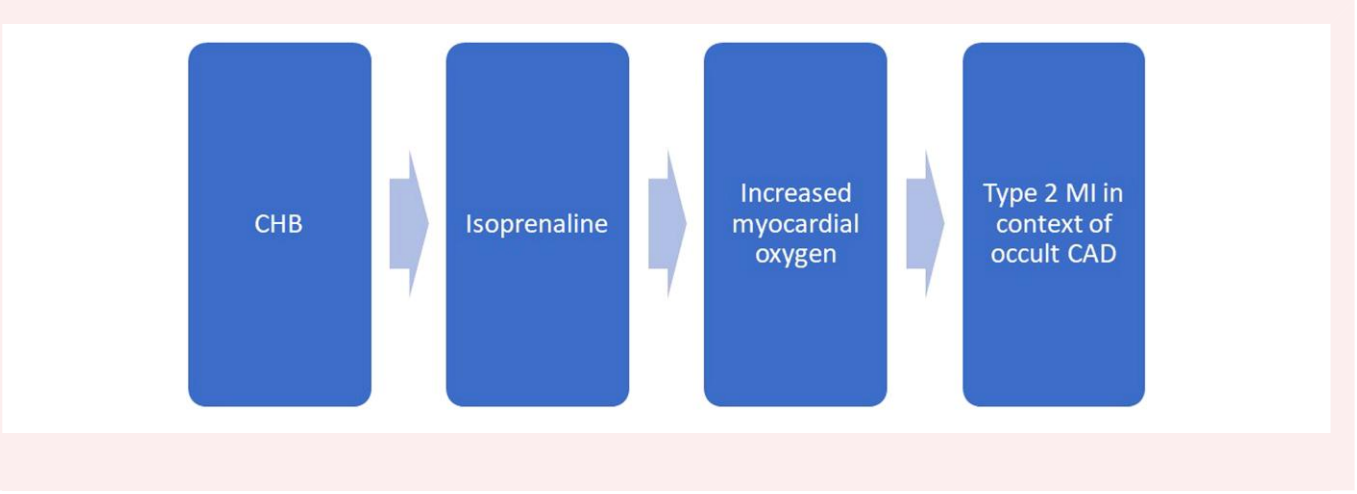
well as having a role in the treatment of ventricular tachycardia storm.[3] Despite the widespread use of isoprenaline in clinical practice, major side effects are rare. Here, we report a case of myocardial infarction precipitated by the use of isoprenaline.

Summary figure



Case presentation

A 67-year-old male patient was referred to the general cardiology clinic after several episodes of syncope over the preceding 4 months. Comorbidities included hypertension, insulin-dependent diabetes mellitus, hypercholesterolaemia, and a previous ischaemic stroke. His medication included bisoprolol 2.5 mg once daily, amlodipine, bendroflumethiazide, clopidogrel, metformin, ramipril, simvastatin, and insulin. A 12-lead electrocardiogram (ECG) on the day of clinic demonstrated Mobitz type II 2:1 atrioventricular (AV) block, right bundle branch block with QRS duration 137 ms, and no evidence of ischaemia (*Figure 1*). He was referred from clinic directly to the emergency department (ED) of our quaternary cardiac centre for further evaluation and treatment.

On arrival in the ED, he was symptomatic with dizziness but had no chest pain. Clinical examination was unremarkable, apart from a heart rate of 30 b.p.m. Blood pressure was stable at 130/88 mmHg. Repeat ECG again demonstrated Mobitz type II 2:1 AV block. There were also episodes of complete heart block (CHB) on cardiac monitoring. Initial high-sensitivity troponin I was normal at 13 ng/L (reference range <32 ng/L).

Our institution does not routinely offer out-of-hours permanent pacemaker implantation. In light of symptomatic bradycardia and concerning ECG features including a broad QRS duration and intermittent CHB, the patient was started on an isoprenaline infusion at an initial rate of 3 μg/min. On review 90 min after initiation of isoprenaline, the patient complained of severe cardiac-sounding chest pain. Repeat ECG demonstrated an increase in the ventricular rate and new ischaemic changes with ST-segment elevation in lead aVR and widespread ST-segment depression (*Figure 2*). The peak recorded heart rate during isoprenaline infusion was 77 b.p.m. Due to the new ischaemic ECG changes and ongoing chest pain, the primary percutaneous coronary intervention pathway was activated, and he was referred for emergency coronary angiography. He was loaded with aspirin 300 mg and ticagrelor 180 mg prior to the procedure.

Coronary angiography was undertaken via the right radial artery and demonstrated a severe mid-vessel stenosis in a dominant right coronary artery (RCA), with Thrombolysis in Myocardial Infarction (TIMI) 3 flow in the vessel (*Figure 3*, Supplementary material online, *Video S1*). The left coronary system had mild diffuse disease but no significant stenoses (*Figure 4*, Supplementary material online, *Video S2*). In view of ongoing chest pain, it was decided to treat the RCA percutaneously. A transvenous temporary pacing wire was inserted *via* the right femoral vein to the right ventricular apex. After pre-dilatation, the mid-RCA was treated with a 3.5 × 48 mm Xience Pro (Abbott, Chicago, IL) drug-eluting stent (*Figure 5*, Supplementary material online, *Video S3*).

The patient remained stable in the coronary care unit. Echocardiography showed normal left ventricular systolic function with an ejection fraction of 60% and mild mitral and tricuspid regurgitation. Repeat high-sensitivity troponin I was elevated at 2021 ng/L. After 48 h, the patient remained in Mobitz type II 2:1 AV block and had intermittent loss of capture from the temporary pacing wire. Therefore, a dual-chamber permanent pacemaker (Abbott, Chicago, IL) was inserted via the left axillary vein.

He was discharged on Day 8, after completing a course of intravenous antibiotics for a lower respiratory tract infection. He had no further chest pain or arrhythmia prior to discharge. He was discharged with a plan for 12 months of dual antiplatelet therapy and follow-up in clinic. Interrogation of the pacemaker 5 weeks after implant demonstrated 99% ventricular pacing.

Discussion

There are several factors in this case to suggest that the therapeutic use of isoprenaline led to myocardial infarction and ischaemia in this patient with high-grade AV block. Before this admission, our patient reported no angina and had no prior diagnosis of ischaemic heart disease. However, he had several risk factors for underlying coronary artery disease including insulin-dependent diabetes, hypertension, and hypercholesterolaemia. Although we cannot definitively prove causation, our hypothesis is that the use of isoprenaline increased myocardial oxygen demand and provoked myocardial ischaemia and a type 2 myocardial infarction due to oxygen demand/supply mismatch in this patient with occult coronary artery disease. It is unlikely that the heart block seen in this patient was the result of ischaemia, as he had no chest pain or ischaemic changes on his ECG prior to the initiation of isoprenaline. Furthermore, he had TIMI 3 flow in the RCA despite a severe stenotic lesion. Finally, despite the resolution of ischaemia with

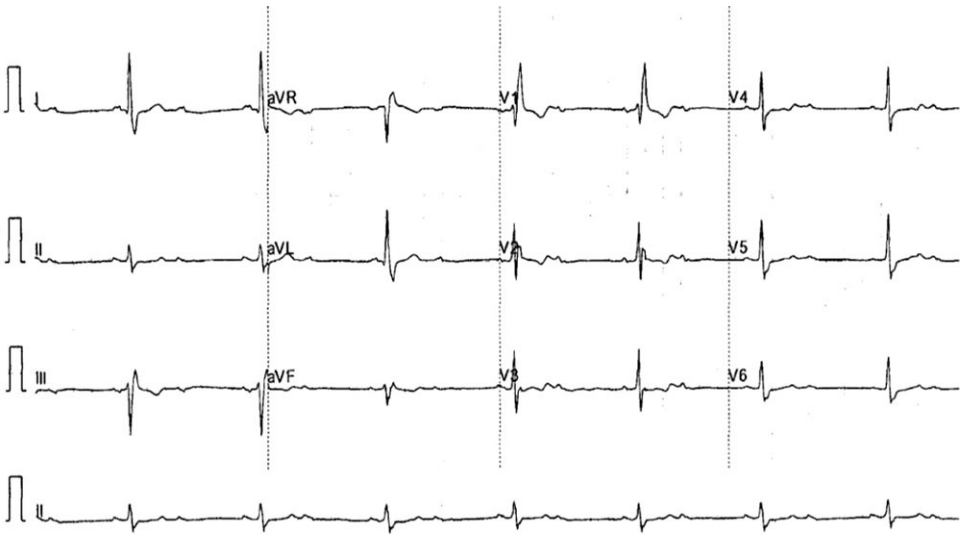


Figure 1 Electrocardiogram showing second-degree heart block.

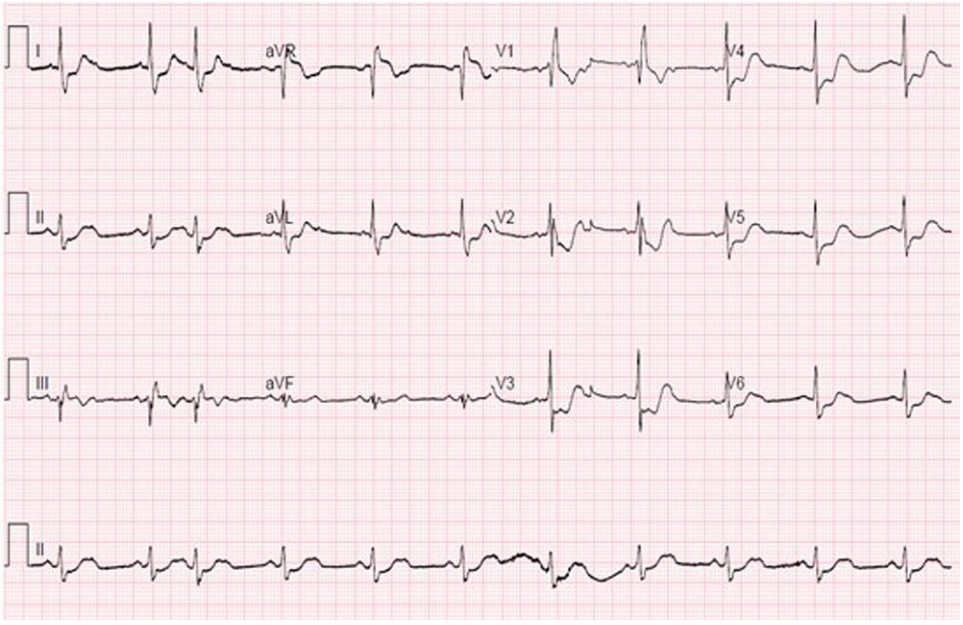


Figure 2 Ischaemic electrocardiogram after isoprenaline.

percutaneous coronary intervention, a pacing check at 5 weeks identified 99% ventricular pacing.

Isoprenaline administration is widely used to generate a model of myocardial infarction in animal studies. Administration of isoprenaline in male Sprague Dawley rats has been shown to induce adverse cardiac changes including ST-segment elevation on ECG, elevated cardiac biomarkers, and an increase in inflammatory markers on histological examination.[4] The mechanism of myocardial damage in these experimental models is thought to be related to the development of reactive oxidative species.[5] Other deleterious effects of isoprenaline include left ventricular hypertrophy and the increased expression and activity of angiotensin-converting enzyme, which are both associated with the development of heart failure.[6,7]

Despite the adverse effects in animal models, isoprenaline is widely used in clinical practice, without many adverse cardiovascular events reported. In a historic study, Wexler *et al.*[8] reported the development of ischaemic ECG changes in volunteers with coronary artery disease who were infused with isoprenaline. However, none of the patients in this very small study reported any chest pain or shortness of breath, and the ECG changes all resolved shortly after cessation of isoprenaline. Kumar *et al.*[9] and Duong *et al.*[10] both reported cases of chest pain

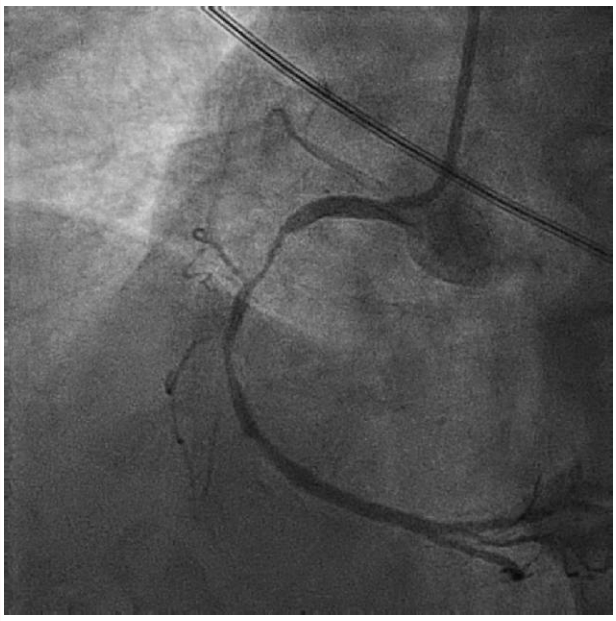


Figure 3 Left anterior oblique projection of the right coronary artery showing significant mid-vessel stenosis.

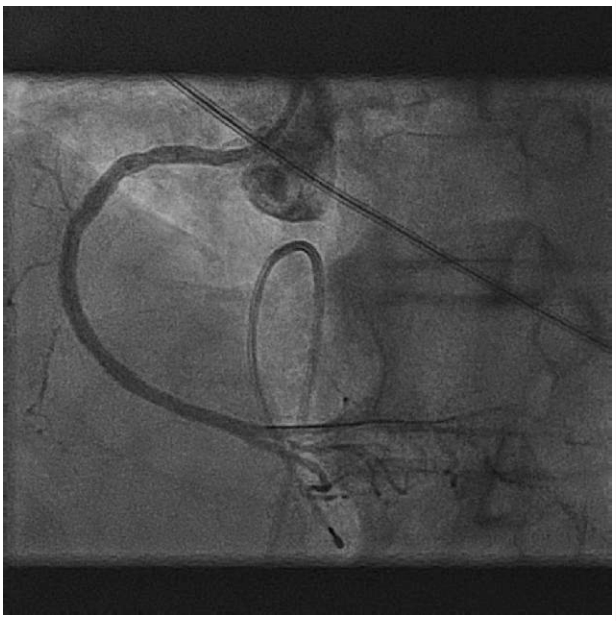


Figure 5 Left anterior oblique projection of the right coronary artery after implantation of one drug-eluting stent.

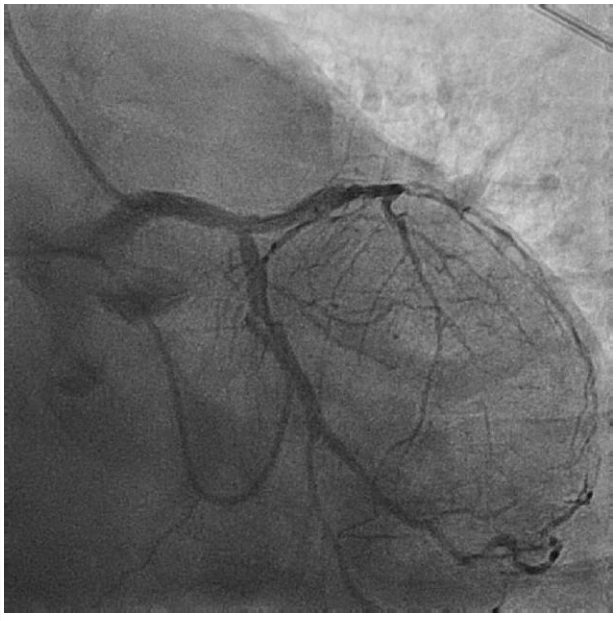


Figure 4 Posteroanterior caudal projection of the left coronary artery showing no significant stenosis.

and inferior ST-elevation after isoprenaline administration. In both cases, the patient's symptoms and ECG improved after sublingual nitroglycerine administration, and subsequent coronary angiography showed no obstructive coronary artery disease, raising the likelihood that these presentations were due to coronary spasm.

Conclusion

We report a case of myocardial infarction precipitated by the therapeutic use of isoprenaline in a patient with high-grade AV block, who had occult incidental coronary artery disease. This was treated successfully with percutaneous coronary intervention to the RCA. Our case highlights the important educational point that isoprenaline can potentially precipitate myocardial ischaemia. Thus, it should be used with caution in patients with known or suspected coronary artery disease. Chest pain in a patient treated with isoprenaline may represent myocardial ischaemia and warrants urgent assessment and investigation.

Lead author biography

Dr Ashwin Radhakrishnan is a final year interventional cardiology trainee in Birmingham, UK. He underwent training in the West Midlands Deanery and completed a research MD investigating coronary microvascular dysfunction in chronic kidney disease at the University of Birmingham. He has an interest in cardiorenal medicine and complex PCI.

Supplementary material

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

Consent: The patient voluntarily agreed to participate in this case report and has provided written consent for the publication of information in accordance with COPE guidelines.

Conflict of interest: None declared.

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Data availability

The data underlying this article will be shared upon reasonable request to the corresponding author.

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