ST-elevation myocardial infarction due to coronary thrombus in the context of diabetic ketoacidosis in a young patient with a new diagnosis of type-2 diabetes

Keywords

Acute coronary syndrome, percutaneous coronary intervention, intracoronary imaging, diabetes mellitus, case report

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Short title

Thrombotic STEMI as first presentation of diabetes

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Summary

The association between cardiovascular disease and diabetes is increasingly understood and shared therapeutic targets are emerging. We describe the presentation and successful management of STEMI secondary to coronary thrombus in a young patient with a new diagnosis of type 2 diabetes and diabetic ketoacidosis (DKA).

Background

This case emphasises the importance of considering aetiology of myocardial infarction other than coronary atherosclerotic plaque rupture, particularly in young patients presenting with acute coronary syndrome. The cardiovascular sequelae of severe metabolic derangement can be life threatening and DKA should be considered in the context of acute illness with metabolic acidosis.

Case presentation

A 24-year-old male was admitted as an emergency via the ambulance service to our regional cardiology centre with a view to percutaneous coronary intervention (PCI). He presented with chest pain on a background of schizophrenia, intermittent alcohol excess, cigarette smoking, obesity (BMI 32kg/m2) and a family history of premature cardiovascular disease, his mother having died of an acute myocardial infarction in her 40's. The patient denied Illicit drug use and there was no documented history of this. Regular prescribed medication were olanzapine 15mg once daily and fluoxetine 80mg once daily and had been established for over a year.

Symptoms included a 24-hour history of vomiting and diarrhoea following excess alcohol consumption and a six-hour history of severe central chest pain radiating to his left arm with associated autonomic symptoms. There was no polyuria or excessive thirst and weight had been stable.

On arrival the patient was in discomfort, diaphoretic and tachycardic with a heart rate of 110bpm. Initial blood pressure was 134/86mmHg and there was no subsequent haemodynamic compromise. On physical examination, lungs were clear to auscultation and heart sounds were normal with no cardiac murmur or gallop. Jugular venous pressure was not elevated and there was no peripheral oedema. The abdomen was soft and non-tender to palpation throughout with no organomegaly.

12-lead electrocardiogram (ECG) demonstrated ST-segment elevation in leads II, III and AVF with reciprocal ST-segment depression in lead I and AVL (*Figure 1*). Emergency coronary angiography performed 12-minutes following the ECG in *Figure 1* demonstrated preserved

flow (TIMI – "Thrombolysis in Myocardial Infarction" Grade III) in the right coronary artery (RCA) but occlusion of the distal posterior left ventricular (PLV) branch. Coronary intravascular ultrasound (IVUS) identified thrombus burden throughout the RCA but did *not* demonstrate atherosclerotic plaque rupture (*Figure 2*). The left coronary system was normal in appearance. Following coronary intervention chest pain resolved. However, the patient remained tachycardic and diaphoretic.

Investigations and differential diagnosis

Routine laboratory investigations revealed hyperglycaemia (blood glucose 20.4mmol/L), a raised anion gap metabolic acidosis (lactate 10.9mmol/L, bicarbonate 15mmol/L) and ketonuria (3+) in keeping with DKA. Liver enzymes were mildly elevated in the context of recent alcohol excess. White blood cell count was elevated at 25.9 (109/l) with neutrophilia and C-reactive protein (CRP) was normal. High sensitivity troponin T was elevated at 1212 ng/L and total serum cholesterol was 6.2mmol/L with LDL 3.9mmol/L. Prothrombin time and partial thromboplastin time were normal. Thrombophilia screen was not undertaken as results would be influenced by acute thrombosis and anticoagulant therapy. Complete admission laboratory results are presented in *Table 1.*

Transthoracic echocardiography demonstrated impaired left ventricular systolic function (estimated left ventricular ejection fraction 49%) with inferior wall hypokinesis. There was no evidence of atrial or ventricular septal defect, and no evidence of intracardiac thrombus. The primary diagnosis was inferior STEMI in the context of a new diagnosis of diabetes complicated by DKA. Significant lactataemia contributed to a mixed acidosis picture secondary to tissue hypoperfusion in the setting of acute cardiac ischaemia and catecholamine surge. Clinical examination and investigations did not support systemic infection or sepsis syndrome. Specifically, chest radiograph was normal, CRP <1mg/L and nasopharyngeal swab polymerase chain reaction testing for SARS-CoV-2 was negative. Further investigations were undertaken to clarify the underlying metabolic diagnosis. Glycosylated haemoglobin (HBA1c) was 64mmol/mol. C-peptide level was elevated at 996pmol/L with concomitant random serum glucose of 12.6 mmol/L suggesting significant endogenous insulin production and insulin resistance. Both glutamic acid decarboxylase antibodies (Anti-GAD) and islet antigen 2 antibodies (Anti- IA2) were undetectable. Consensus opinion on the underlying metabolic diagnosis considering the patient's body habitus and absence of autoimmunity is type 2 diabetes. Ketoacidosis in the setting of type 2 diabetes is uncommon and recent alcohol excess

is likely to have led to an enhanced state of physiological stress and contributed to metabolic decompensation [1].

Haematology	
White Blood Cells	25.9 (10^9/l)
Red Blood Cells	4.7 (10^{12}/l)
Haemoglobin	158 g/L
Haematocrit	0.4 l/l
Mean Cell Volume	92.9 fl
Platelets	352 (10^9/l)
Neutrophils	22.4 (10^9/l)
Renal function and electrolytes	
Sodium	134 mmol/L
Potassium	3.2 mmol/L
Chloride	94 mmol/L
Bicarbonate	15 mmol/L
Urea	1.2 mmol/L
Creatinine	76 umol/L
Estimated Glomerular Filtration Rate	>60 ml/min
Liver function	
Bilirubin	9 umol/L
Aspartate Aminotransferase	74 IU/L
Alanine Aminotransferase	152 IU/L
Gamma-Glutamyl Transferase	145 IU/L
Bone profile	
Adjusted Calcium	2.2 mmol/L
Phosphate	1.2 mmol/L
Magnesium	0.59 mmol/L
Albumin	43 g/L
Alkaline Phosphatase	99 IU/L
Lipid profile	
Cholesterol	6.2 mmol/L
Triglyceride	3.1 mmol/L
High-Density Lipoprotein	0.9 mmol/L
Low-Density Lipoprotein	3.9 mmol/L
Cholesterol/HDL	7
Other	
Lactate	10.9 mmol/L
High Sensitivity Troponin T	1212 ng/L
Serum Osmolality	290 mOsm/kg

Table 1 **– Admission laboratory test results**

Treatment

Acute coronary syndrome was treated with oral antiplatelet agents and intravenous unfractionated heparin and morphine in a pre-hospital setting. This was followed by emergency primary PCI using low pressure balloon angioplasty to the occluded PLV branch, then aspiration thrombectomy yielding large amounts of macroscopic red thrombus from the RCA. Persisting intracoronary thrombus was confirmed on IVUS following coronary intervention and intravenous glycoprotein IIb/IIIa inhibitor was subsequently administered. Secondary

prevention medications including ACE-inhibitor, beta-blocker and statin were initiated. Previous case reports have highlighted recurrent STEMI in the setting of type 2 diabetes, DKA and coronary artery thrombus and we advised a three-month treatment period with dual antiplatelet therapy [2].

DKA was treated with intravenous fluids, variable rate intravenous insulin infusion and electrolyte replacement. Metabolic disturbance resolved quickly; within six hours of presentation blood glucose had reduced to 10mmol/L and lactate to 3.1mmol/L. By 15 hours, acid base status had normalised, ketonuria resolved and minimal doses (0-0.5 units/hr) of intravenous insulin were needed to maintain blood glucose levels within normal range. Insulin was discontinued after 24-hours. Following specialist review, metformin and dapagliflozin were initiated as oral hypoglycaemic agents.

Outcome and follow-up

ST-segment changes persisted for approximately 24 hours following PCI, likely related to distal thrombus embolization. 12-lead ECG three days following initial presentation demonstrated inferior Q waves and T- wave inversion (*Figure 3*). Blood glucose levels remained within normal range on oral hypoglycaemic agents without ketonuria. The patient was discharged from hospital after four days. Through lifestyle measures he has achieved 6kg of weight loss and HBA1c has reduced to 51mmol/mol. There is outpatient follow-up in place with cardiology, cardiac rehabilitation including smoking cessation counselling and specialist diabetes clinical teams.

Discussion

The association between diabetes and cardiovascular disease is well recognised. Underpinning pathophysiological processes include vascular endothelial dysfunction, accelerated atherosclerosis, increased platelet activation and impaired fibrinolysis leading to a prothrombotic state [3,4]. In a large population-based cohort study in patients with STEMI, diabetes was associated with a 72% excess risk of death [5]. DKA further promotes a prothrombotic state with increased von Willebrand factor and decreased free protein S and protein C activity [6]. Arterial thrombosis in this setting has been recognised for over 50 years [7].

Symptom chronology in this case suggests that metabolic disturbance was followed by myocardial ischaemia. Combined with evidence of *thrombotic* coronary occlusion in otherwise normal coronary arteries in a 24-year-old patient we believe that DKA was responsible for the

acute coronary syndrome (ACS). Myocardial infarction due to a primary coronary atherosclerotic event can also precipitate DKA and our patient had multiple risk factors for atherosclerosis including a family history of premature cardiovascular disease, cigarette smoking, obesity, dyslipidaemia, and type-2 diabetes of uncertain duration. However, intracoronary imaging did not identify plaque rupture and metabolic decompensation following a cardiac event typically occurs in individuals with established type-1 diabetes. A temporal illustration of the possible underlying physiological mechanisms in this case is presented in *Figure 4*.

Shared therapeutic pathways between diabetes and cardiovascular disease continue to emerge. Dapagliflozin is a potent and reversible, selective sodium-glucose cotransporter-2 inhibitor (SGLT2i) which reduced the rate of hospitalization for heart failure and cardiovascular death relative to placebo in patients with multiple risk factors for cardiovascular disease. SGLT2 inhibitors whilst designed as oral hypoglycaemic agents, are advantageous in cardiovascular secondary prevention therapy, reducing major adverse cardiovascular events, heart failure admissions and progression of renal disease [8].

Learning points/take home messages

- Aetiology of myocardial infarction other than coronary atherosclerotic plaque rupture should be considered in young patient groups presenting with acute coronary syndrome.
- Cardiovascular sequelae of severe metabolic derangement can be life threatening.
- Acute coronary syndrome and other physiological stressors such as excess alcohol consumption can lead to metabolic decompensation in susceptible individuals. Recognition of cardiac risk factors in these patients is important.
- DKA should be a differential diagnosis in the context of acute illness with metabolic acidosis regardless of previously established endocrine pathology.
- Emerging shared therapeutic pathways in cardiovascular and endocrine disease provide the opportunity for individualised treatment approaches, and underline the benefits of collaborative, cross-speciality care.

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Figures

Figure 1 - 12-lead ECG at presentation demonstrating inferior STEMI
Figure 2 - A) Angiographic appearance of thrombus in proximal RCA and reduced flow in PLV branch. B) Coronary thrombosis confirmed on IVUS in proximal RCA
Figure 3 - 12-lead ECG three-days following presentation demonstrating inferior Q-waves and T-wave inversion
Figure 4 - Temporal illustration of possible mechanisms of myocardial infarction and DKA

Patient's perspective

"I phoned an ambulance because I had chest pain. I was told by the ambulance crew that I was having a heart attack, so I was rushed to hospital where I had an emergency procedure. After that I was taken to the ward and started on tablets and drip medications. It was explained that I had diabetes and would need some new medications. After a couple of days, I started to feel better."

191 *Figure 1* - 12-lead ECG at presentation demonstrating inferior STEMI

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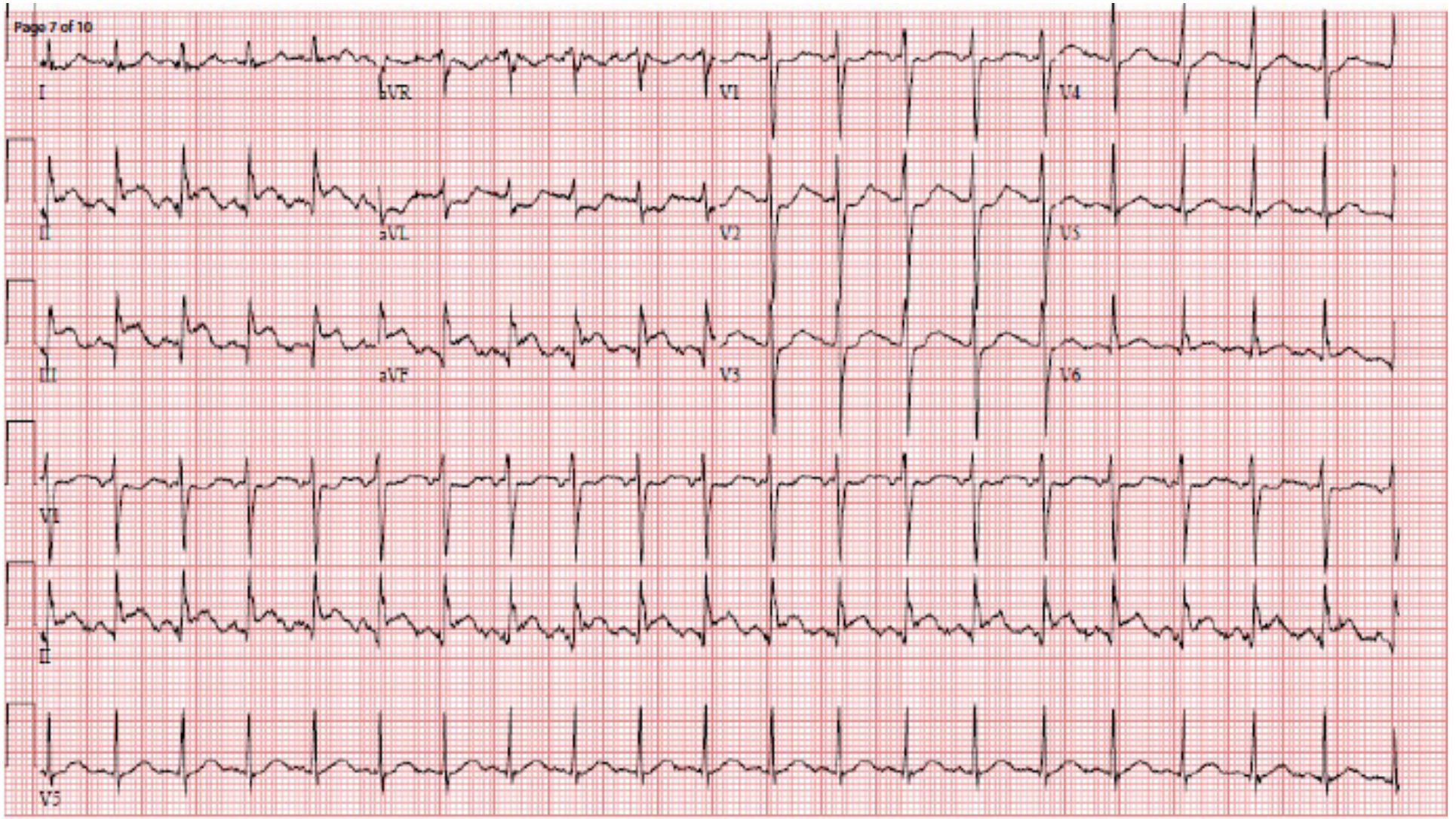
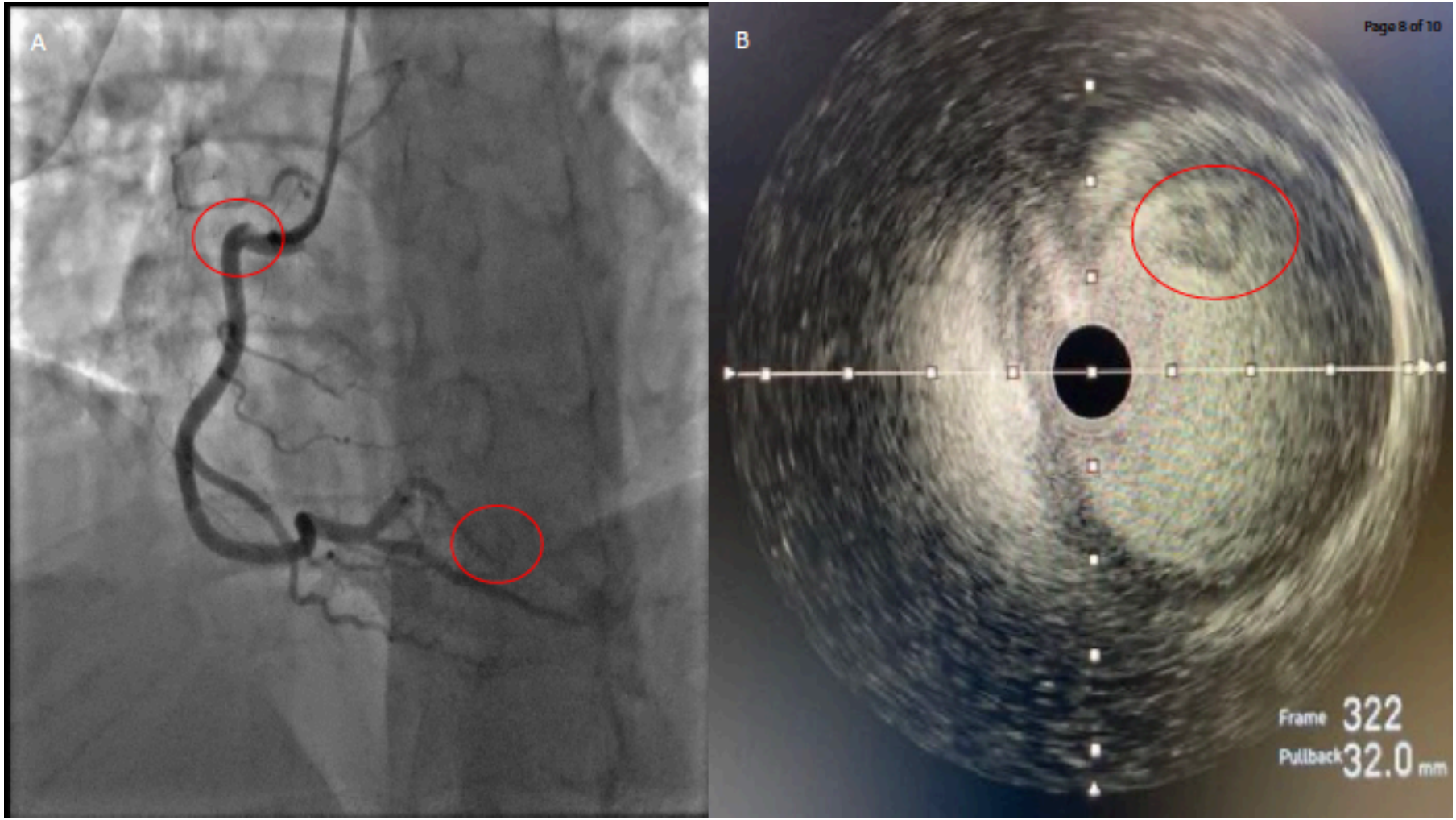
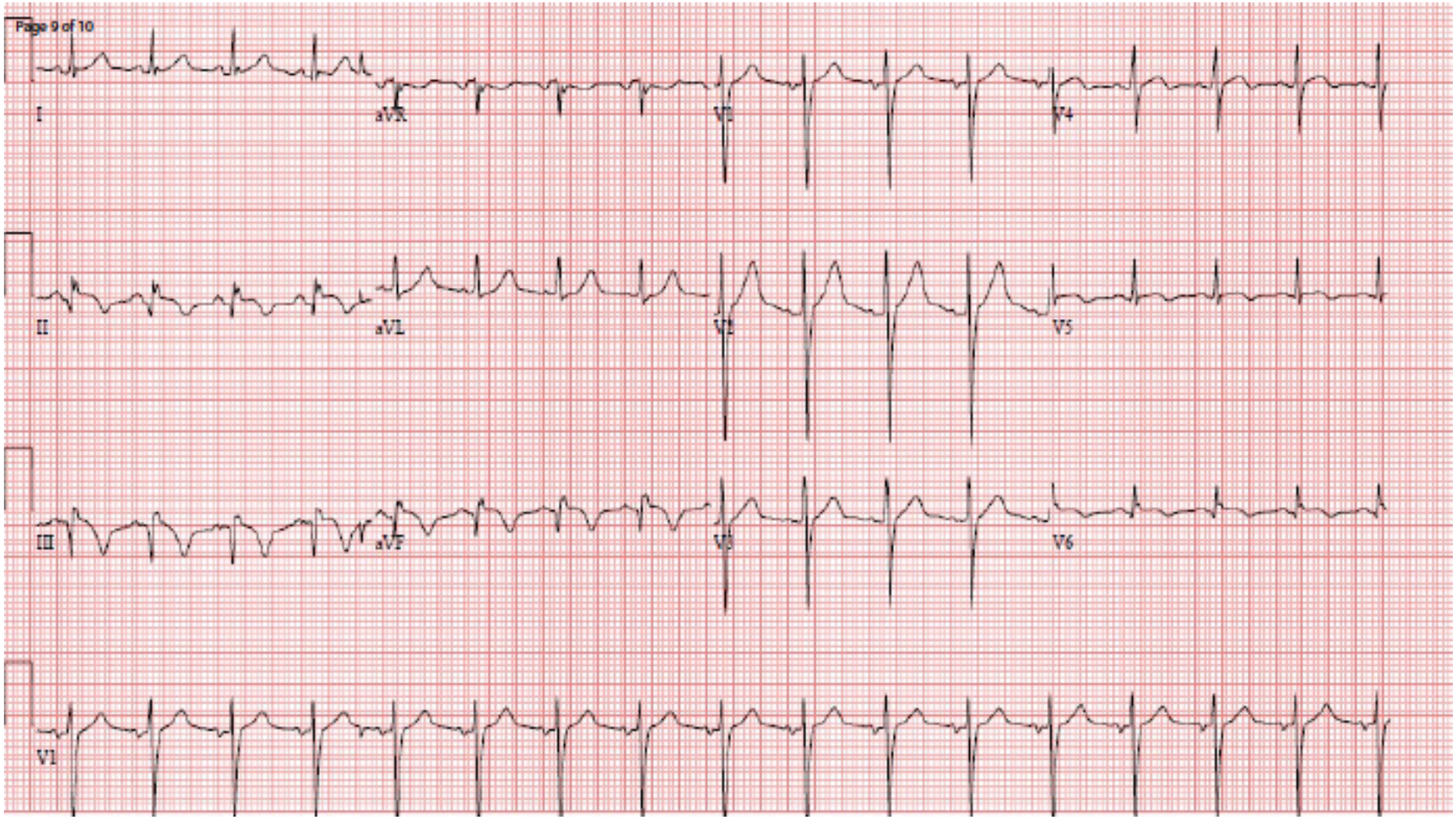


Figure 2 - A) Angiographic appearance of thrombus in proximal RCA and reduced flow in PLV branch. B) Coronary thrombosis confirmed on IVUS in proximal RCA



195 *Figure 3* - 12-lead ECG three-days following presentation demonstrating inferior Q-waves and T-wave



196 *Figure 4* - Temporal illustration of possible mechanisms of myocardial infarction and DKA

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