CASE REPORT

Not all ST-segment changes are myocardial injury: hypercalcaemia-induced ST-segment elevation

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SUMMARY

ST-segment elevation myocardial infarction is an important, life-threatening diagnosis that requires quick diagnosis and management. We describe the case of an 83-year-old man with coronary artery disease, ischaemic cardiomyopathy with left ventricular ejection fraction of 15%, newly diagnosed multiple myeloma that had an initial ECG showing ST-segment elevation in anterior leads V1–3 and ST-segment depression in lateral leads concerning for an ST-segment elevation myocardial infarction. Troponins were negative and his calcium was 3.55 mmol/L. It was thought that the ECG changes were not indicative of cardiac ischaemia but, rather, hypercalcaemia. He was treated with fluids, diuretics and zolendronic acid, with subsequent resolution of ST-segment changes. This case demonstrates that one must consider disease other than myocardial ischaemia as the culprit of ST-segment changes if physical examination and history do not point towards myocardial injury, as unnecessary invasive revascularisation procedures have inherent risks.

BACKGROUND

ST-segment elevation myocardial infarctions (STEMIs) are frequently encountered in hospital visitations and admissions. There are, however, several known mimickers of STEMI that are well documented, but hypercalcaemia is not one of them. Consequently, hypercalcaemia leading to ECG changes consistent with an STEMI is considered not only very unique but also rare. As noted in this paper, it may not be as rare as believed, but only under-reported with a lack of common association. By recognising this, clinicians can be made aware of this mimicker and prevent adverse outcomes that could easily be avoided.

CASE PRESENTATION

An 83-year-old man with a history of severe ischaemic cardiomyopathy, left ventricular ejection fraction of 15%, coronary artery disease (CAD), status postcoronary artery bypass grafting and recently diagnosed multiple myeloma, was referred to our medical centre, for further management. On admission, he reported progressive shortness of breath and increasing leg swelling. These symptoms were worse with exertion and had associated light-headedness, but no chest pain or pressure. He had recently gained 4.54 kg. His vitals and physical examination were consistent with compensated chronic congestive heart failure with no change from baseline. His heart failure was managed with a chronic low-dose dobutamine drip.

On admission to the intensive care unit, the patient's blood pressure was 99/66 mm Hg and heart rate 74 bpm, and he had an oxygen saturation of 94% on 2 L nasal cannula. Pertinent positive physical findings included mild jugular venous distention, mild bilateral inspiratory rales and crackles at the lung bases as well as bilateral 2+ pitting oedema in the lower extremities. He was not sweaty or clammy, and in no apparent distress. He was not in acute decompensated congestive heart failure since there was no acute deteriorating or worsening of his symptoms.

INVESTIGATIONS

The patient's ECG on admission showed normal sinus rhythm and normal axis, and met Sokolow-Lyon voltage criteria for left ventricular hypertrophy. QT and QTc intervals were 371 and 418, respectively. In addition, there was 2–3 mm ST-segment elevation in anterior leads V1–V3 and ST-segment depression in the lateral lead requiring an emergent cardiology consult (figure 1). Comparison with previous ECGs showed inconsistent ST-segment changes with occasional ST-segment elevation. Serial cardiac enzymes on admission were negative while other laboratory studies showed anaemia (haemoglobin of 75 g/L), acute renal insufficiency, hyperkalaemia and marked hypercalcaemia with serum calcium level of 3.55 mmol/L. A bedside echocardiogram showed no new wall motion abnormalities, but did show baseline reduced left ventricular ejection fraction and severe global hypokinesis.

DIFFERENTIAL DIAGNOSIS

The patient was well known to the cardiology service. The differential diagnosis was initially quite narrow at acute myocardial infarction (AMI) given how the ST-segment elevation was confined to only a handful of leads. Several risk factors made the diagnosis of an STEMI likely: history of proven CAD, status postcoronary artery bypass grafting and an ejection fraction of 15%. However, other clinical data were inconsistent with a diagnosis of an STEMI: no chest pain, haemodynamic stability and a negative troponin. A cardiac catheterisation was not performed due to the patient's renal insufficiency and anaemia, which led to a bedside echo that did not indicate any new wall motion abnormalities. While a bedside echo cannot rule out any new ischaemic changes in a patient with diffuse hypokinesis, the results were, nevertheless, reassuring. Given the low clinical suspicion for an STEMI and the relative contraindication to a

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Figure 1 ST-segment elevation in V2, V3 and V4 with serum calcium level of 3.55 mmol/L.

catheterisation, time was available to explore other potential causes. On examination of the available literature, the ECG findings were attributed to acute hypercalcaemia secondary to the patient's multiple myeloma. Prior to this literature search, hypercalcaemia was not on the differential.

TREATMENT

The patient was subsequently medically managed with intravenous normal saline, furosemide and zoledronic acid. Other medical therapy included aspirin, carvedilol and atorvastatin. Lisinopril was held due to renal insufficiency.

OUTCOME AND FOLLOW-UP

The patient's ST-segment changes progressively resolved as his calcium improved over several days (figures 2 and 3). He continued to deny any chest pain or pressure during his admission and did not deteriorate clinically. In addition, subsequent troponins

were negative, which, along with the overall prognosis, led to deferral of cardiac catheterisation. Several months later, our patient peacefully passed away at home, of what was determined by the coroner to be heart failure.

DISCUSSION

Centers for Disease Control and Prevention data shows that, in 2011, AMI led to approximately 120 000 deaths while diseases of the heart as a whole led to nearly 600 000.¹ In 2012, several organisations jointly published the third universal definition of AMI (box 1).²

The standard of care for patients with STEMI is either fibrinolysis or primary percutaneous intervention (PCI).³ The earlier the reperfusion therapy is initiated, the greater the benefit.⁴ The American Cardiology Association/American Heart Association (ACA/AHA) guidelines state that "appropriate and timely use of some form of reperfusion therapy is likely more important than

Figure 2 Prior ECG showing up-sloping ST-segment elevation in the same leads with serum calcium level of 2.5 mmol/L.

Figure 3 Resolution of ST-segment changes with serum calcium level of 2.1 mmol/L showing baseline left ventricular hypertrophy.

the choice of therapy.”³ However, PCI became the preferred reperfusion strategy for most patients with STEMI, as randomised trials have consistently shown lower rates of mortality, recurrent ischaemia and major complications such as intracranial haemorrhage.^{5 6} In the event of a true STEMI, current ACA/AHA guidelines state that door-to-needle time for fibrinolysis should be 30 min while door to balloon time for PCI-capable hospitals should be 90 min.^{5 7} However, these lifesaving measures are not without risk. Noto *et al*⁸ found a 1.7% risk of major complications based on 59 792 cardiac catheterisation and coronary angiography patients (table 1). Additionally, fibrinolysis is also not without its own set of complications. Analysis from the GUSTO-I trial showed a 1.8% risk of severe bleeding and an 11.4% risk of moderate bleeding.⁹ Further, FASTRAK II found a 1.2% risk of stroke and a 0.7% risk of intracranial haemorrhage when fibrinolysis is utilised.¹⁰ In addition, a small portion of patients suspected of having STEMI do not have

signs of CAD. Analysis of the PRAGUE studies found that 2.6% of patients suspected with STEMI had normal coronary arteries.¹¹

The causes of ST-segment changes other than myocardial injury are well documented and observed in clinical practice.¹² One study found that 91% of men 16–58 years of age had ST-segment elevation of 1–3 mm in one or more precordial leads.¹³ Myocarditis and pericarditis have cardiac origins but do not affect the coronary arteries.¹⁴ Aortic dissection and pulmonary embolism have a non-cardiac vascular origin,^{15 16} while electrolyte abnormalities and cholecystitis have a non-cardiac source.^{17 18} Among electrolyte abnormalities, hyperkalaemia is the most common.¹⁴ Levine *et al*,¹⁸ in 1956, coined the term dialysable currents of injury after noticing ST-segment elevation in dialysis patients with hyperkalaemia.

Although much more uncommon, our case illustrates another electrolyte abnormality causing ECG changes. Acute ST-segment elevation changes caused by hypercalcaemia and mimicking a myocardial infarction have occasionally been documented in the literature, although many speculate it may be more common.^{19 20} Littmann *et al*,¹⁹ over 14 years, identified 16 cases of hypercalcaemia leading to ST-segment elevation mimicking AMI, in a tertiary care facility in North Carolina. In their

Box 1 Third universal definition of myocardial infarction (MI)²

Criteria for acute MI

Rise or fall of cardiac biomarkers above the upper limit of normal with one or more of the following

- ▶ Symptoms of ischaemia
- ▶ New or presumed new significant ST-segment T wave changes or new left bundle branch block (LBBB)
- ▶ Development of pathological Q waves
- ▶ Imaging evidence of new loss of viable myocardium or new regional wall motion abnormalities.
- ▶ Identification of an intracoronary thrombus by angiography or autopsy

Cardiac death with symptoms suggestive of MI and new ischaemic ECG changes or LBBB but with cell death occurring before cardiac biomarker values increased or biomarkers were obtained.

Table 1 Risk of cardiac catheterisation and coronary angiography⁸

Cardiac catheterisation and coronary angiography risks	Per cent
Vascular complications	0.43
Arrhythmia	0.38
Contrast reaction	0.37
Perforation of heart chamber	0.28
Other complications	0.28
Haemodynamic complications	0.26
Death	0.11
Cerebrovascular accident	0.07
Myocardial infarction	0.05

study, the most common diagnosis for hypercalcaemia was malignancy with age ranging from 35 to 72 years. They concluded that hypercalcaemia as the cause of ECG changes should be considered in the absence of a clinical suggestion of AMI or digitalis toxicity, a scooped ST-segment without abnormal Q waves or T wave inversions.

Our literature review found 26 other documented cases of ST-segment elevation in the setting of hypercalcaemia.^{19–29} Recently, Schutt *et al*²⁰ outlined nearly all of these cases (including his own). The cause of hypercalcaemia ranged from malignancy to hyperparathyroidism to vitamin D intoxication. Some patients were exposed to a coronary intervention that revealed normal coronary angiography. Given these reports, hypercalcaemia leading to ST-segment changes may be more common than previously thought, with identification and diagnosis lacking. Since coronary angiography in patients with hypercalcaemic nephropathy can lead to further renal function impairment, clinicians should be cautious about proceeding with vascular intervention.^{30 31}

While not present in our patient, hypercalcaemia can cause chest pain, making the diagnosis of hypercalcaemia-induced ST-segment elevation even more challenging. Several mechanisms have been proposed for why chest pain may develop, ranging from calcium deposition in the coronary arteries, fibrous skeleton of the heart and valvular cusps, to accelerated coronary atherosclerosis in hypercalcaemia secondary to hyperparathyroidism.^{32 33}

Positive ECG findings most frequently occur in patients with serum calcium over 4 mmol/L but may appear with calcium as low as 2.5 mmol/L.¹⁹ ECG features of hypercalcaemia include increased amplitude of QRS, ST-segment elevation and PR prolongation, with shortening of the QT interval and associated up-sloping of the T wave, the latter feature being the most common.³⁴ Myocardial cells rely on a host of ions for proper contractility and function. If these ions are not in the proper equilibrium, the myocyte membrane potential may be affected, leading to physiological and ECG changes.³⁵ In general, with hypercalcaemia, myocardial contractility and irritability increase. The manifestation of ST-segment elevation with hypercalcaemia appears most localised to the anterior leads, V1–V3. The exact mechanism is not fully understood, although several have been proposed. Ashizawa *et al*²¹ described how shortening of the Q wave apex (QaTc) leads to a high take-off of the ST-segment, which can appear to be an AMI. Consequently, the T wave is closer to the end of the QRS complex, making it appear elevated.¹⁹ Kukla *et al*²² also reported this phenomenon in two cases. The equilibrium of the outward K flow through the delayed rectifier potassium channel and the inward calcium flow through the L-type calcium channels are the likely aetiology.³⁶ Another possible mechanism noted by Ashizawa *et al* involves how hypercalcaemia can lead to a biphasic or flattened T wave appearing as ST-segment elevation.^{37 38} The aetiology of these specific ECG changes is due to hypercalcaemia's effect on action potential repolarisation or its effect on other cations that transfer across the myocardial cell membrane.^{37 38}

While most patients present with clinical and laboratory evidence suggestive of a particular diagnosis, others have a more enigmatic presentation. Even in less clear cases, the best clinical option would be to send the patient for cardiac catheterisation. However, in our patient, renal insufficiency and anaemia allowed additional time for diagnostic work up prior to intervention. In patients who are less likely to have acute coronary syndrome, other causes should be explored in a timely manner prior to further intervention. Clinicians must weigh the urgency

(and risks) of intervention against the benefits of waiting for more laboratory results. A study of 11 hospital emergency rooms showed that the turn-around time (time between when the laboratory received the order and when the laboratory values were verified) for a metabolic panel was between 13 and 29 min.³⁹ This same study found the turnaround time for non-point-of-care cardiac enzymes to be longer, at 28–41 min. These findings suggest that the clinician might best wait for basic laboratories, such as a chemistry panel, before making a decision on intervention. However, given the variability in lab equipment, it is difficult to establish a general statement about whether to wait for lab results or to proceed with cardiac catheterisation. Complicating the decision, some laboratories return troponin results before chemistry panels. The decision rests with the clinician based on individual circumstances. Nevertheless, if clinical discrepancies make the probability of an STEMI low, it is reasonable to wait for basic laboratories before any type of intervention is pursued. Physicians should always treat the patient first and use ECG results to support a broader differential.

Learning points

- ▶ In the absence of concerning symptoms and initial low probability, ECG changes that look like an ST-segment elevation myocardial infarction (STEMI) should be worked up for potential mimickers.
- ▶ Hypercalcaemia should be included in the differential diagnosis for the cause of ST-segment elevation on ECG.
- ▶ The aetiology of hypercalcaemia causing the appearance of an STEMI on ECG is unknown but may be related to high take-off of the ST-segment or flattening of the T wave.
- ▶ In the appropriate situation, it may be prudent to wait for further laboratories and imaging before rushing patients to procedures/tests that could cause unnecessary harm.
- ▶ Remember that diagnostic test results should be carefully integrated into the total care of the patient.

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