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SEVERE HYPERCALCEMIA MIMICKING ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

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Abstract

The identification of ST-segment elevation on the electrocardiogram is an integral part of decision making in patients who present with suspected ischemia. Unfortunately, ST-segment elevation is nonspecific and may be caused by noncardiac causes such as electrolyte abnormalities. We present a case of ST-segment elevation secondary to hypercalcemia in a patient with metastatic cancer.

Introduction

Whenever there is a suspicion of myocardial ischemia, the identification of ST-segment elevation is critical as emergent angiography is indicated for patients with ST-segment elevation myocardial infarction (STEMI).[1] Unfortunately, the finding of ST-segment elevation is nonspecific, and approximately 80% of patients who present with chest pain and ST-segment elevation are found to have a coronary lesion with a TIMI Grade Flow of 0 to 1 at angiography.[2,3] Additionally, approximately 3% of patients with suspected STEMI are found to have angiographically normal coronary arteries.[4] Electrolyte abnormalities including hyperkalemia[5-7] and hypercalcemia[7-11] may present with ST-segment elevation and a pseudo-infarction pattern on the electrocardiogram (ECG). In patients presenting with suspected STEMI, the decision to proceed with invasive angiography must often be made before laboratory results are available. In patients at risk for electrolyte abnormalities, clinicians must be aware of the common ECG changes associated with electrolyte abnormalities to avoid unnecessary procedural risks in a potentially unstable patient. The following reviews a patient with metastatic cancer who presented with severe hypercalcemia and ST-segment elevation.

Case Presentation

A 65-year-old female presented to the emergency department complaining of nausea, vomiting, and fatigue for the past week and an episode of near syncope. She had a remote history of left breast cancer status post lumpectomy and radiotherapy 19 years prior. Approximately 5 months prior to admission, she was found to have a new 6.2 x 5.5 cm mass in the left breast and underwent a biopsy consistent with high-grade carcinoma of the breast (estrogen receptor negative, progesterone receptor negative, and human epidermal growth factor 2 negative). During evaluation, she was also found to have a 2.8 cm lung mass. She underwent biopsy that was consistent with bronchoalveolar adenocarcinoma. In addition, she had an 11.0 x 8.0 cm mass in the lower abdomen, and biopsy was consistent with poorly differentiated carcinoma. She had been treated with cisplatin chemotherapy and radiation in the months prior to admission, with the most recent dose 1 month prior.

In the emergency department, she had altered mental status and was responsive to pain only. An ECG (Figure 1) demonstrated new ST-segment elevation in V1 through V3 concerning for STEMI. Since her symptoms were not suggestive of myocardial infarction but her ECG findings were, an emergent bedside transthoracic echocardiogram was done, demonstrating an ejection fraction of 60% to 65% without any segmental wall motion abnormalities, and there was normal motion of the anterior wall. Given her clinical history combined with the echocardiographic findings, she did not undergo coronary angiography as STEMI was felt to be unlikely. Her laboratory results are shown in Table 1. Most significantly, her troponin was measured at arrival, 3 hours, and 12 hours after admission, and all levels were < 0.10 ng/mL, which excluded myocardial infarction as the cause of her electrocardiographic changes. Her serum calcium was elevated at > 14.0 mg/dL and her ionized calcium was 2.52 mmol/L (upper limit of normal 1.32 mmol/L). Her parathyroid hormone was in the low end of the normal range and her parathyroid hormone-related peptide was significantly elevated, confirming the diagnosis of humoral hypercalcemia of malignancy.[12] Interestingly, she had no history of hypercalcemia, and 8 days prior to admission she had a metabolic profile measured with a normal total serum calcium of 9.3 mg/dL. She underwent brain computed tomography followed by magnetic resonance imaging that did not show any evidence of intracranial hemorrhage, stroke, or metastatic disease. She was treated for hypercalcemia with the aggressive administration of 0.9% normal saline, intravenous pamidronate, calcitonin, and furosemide. An ECG demonstrated resolving ST-segment elevation with normalization of the serum calcium level (Figure 2).

Discussion

This patient presented with hypercalcemia and a pseudoinfarction pattern on the ECG. Fortunately this pattern was recognized before proceeding with invasive angiography,

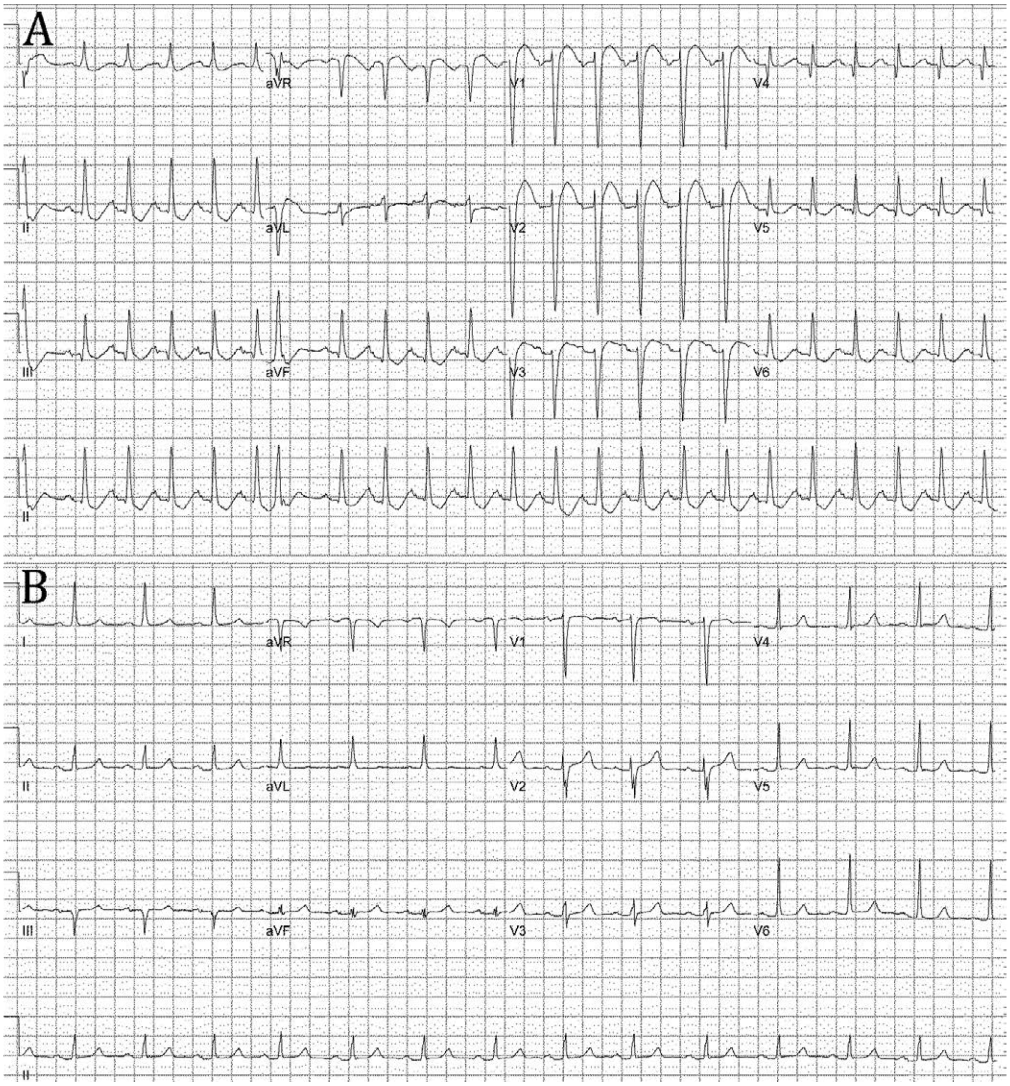

Figure 1. Presenting electrocardiogram (A) demonstrating new ST-segment elevation in V1-V3 compared with prior ECG (B) obtained 4 months prior.

Test	Result	Reference Range
Sodium	143 mEq/L	135-148 mEq/L
Potassium	3.4 mEq/L	3.5-5.0 mEq/L
Chloride	102 mEq/L	99-109 mEq/L
CO_2	29 mEq/L	24-31 mEq/L
BUN	17 mg/dL	8-24 mg/dL
Creatinine	1.1 mg/dL	0.5-1.5 mg/dL
Glucose	106 mg/dL	65-99 mg/dL
Albumin	3.9 g/dL	3.4-5.4 g / dL
Calcium	> 14.0 mg/dL	8.6-10.6 mg/dL
Ionized calcium	2.54	1.11-1.32 mmol/L
Parathyroid hormone	13 pg/mL	13-65 pg / mL
Parathyroid hormone-related peptide	13 pmol /L	< 2.0 pmol/L
Troponin T	< 0.10 serially measured x 3	<0.11 ng/mL

Table 1. Laboratory evaluation on admission.

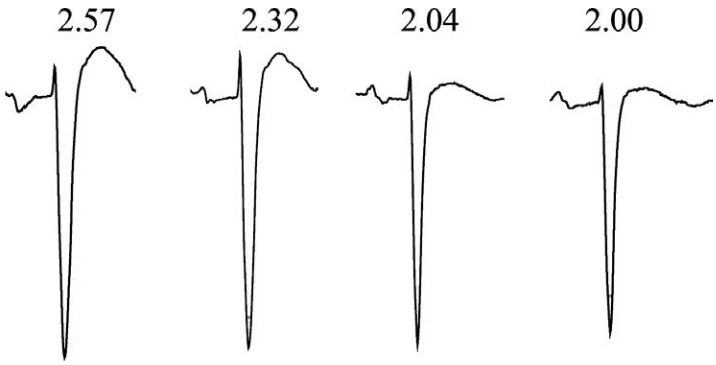

Figure 2. Lead V1 morphology by ionized calcium level demonstrating resolving elevation of the ST segment and reduction in voltage with improvement in the plasma ionized calcium level.

and appropriate treatment for hypercalcemia was initiated once laboratory results returned. The electrocardiographic changes associated with hypercalcemia are summarized in Table 2. The most commonly recognized manifestations of hypercalcemia on the ECG are shortening of QT interval with upsloping of the T wave.[13] This phenomena of QT interval shortening is primarily due to changes in the phase 2 (plateau phase) of the cardiac action potential, which is a balance between inward calcium flow through the L-type calcium channel coupled with outward potassium flow through the delayed rectifier potassium channel and is affected by the presence of excess serum calcium.[14] On the ECG, the lower limits for the duration of QTc is not well defined but it is reasonable to consider a normal QTc interval as between 360 ms and 450 ms in males and 370 ms to 470 ms in females.[15,16] Interestingly, when this patient's ionized calcium was elevated at 2.54 mmol/L, her QTc was actually normal at 420 ms.[17] Prior studies have demonstrated that in patients with hypercalcemia, the interval between the start of the Q wave and the apex of the T (QaTc) interval is a more reliable indicator of hypercalcemia on the ECG than the traditional QT interval (measured from the beginning of the Q wave to the end of the T wave), with a QaTc duration of less than 0.27 being 90% specific for the presence of hypercalcemia in patients at risk for hypercalcemia.[13,18] The QaTc in this patient was shorted at 240 ms during the period of time when her serum calcium was significantly elevated at 2.54 mmol/L, consistent

Shortening of QT interval
Abrupt upslope of the T wave
PR prolongation
Increase in the amplitude of QRS
ST-segment elevation

Table 2. Electrocardiographic changes with hypercalcemia.

Author; Date	Age/ Sex	Clinical Diagnosis	Serum Ca^{2+} (mg/dL)	QTc (ms)	Leads with ST segment elevation
Hajsadeghi et al.; 2011[26]	60/M	Hyperparathyroid crisis	20.5	310	aVL (V1-V6) not shown
Fang et al.; 2010 [10]	52/M	Squamous cell lung cancer with bone metastases	16[a]	–	V1-V3
Donovan J, Jackson SM; 2010[20]	39/M	Hypercalcemia due to calcium carbonate overdose	23[a,b]	–	Abnormal morphology in leads II, aVF, V2-V3
Wesson et al.; 2009 [8]	69/F	Primary thyroid malignancy	20.36[a,b]	–	V1-V5
Littmann et al.; 2007[22]	62/M	Squamous cell lung cancer with bone metastases	16.5	258	V3-V4
	52/M	Myeloma multiplex	15.8	402	V2-V3
	49/M	Non-Hodgkin's lymphoma	17	420	I, aVL, V2-V5
	39/M	Sepsis; hyperalimentation	12.9	415	I, II, V2-V6
	23/M	Post-rhabdomyolysis hypercalcemia	14.7	418	V2-V6
	44/M	Squamous cell lung cancer with bone metastases	18.5	383	V2
	72/M	Plasmacytoma	15.1	336	II, III, aVF, V2-V3
	70/F	Endometrial cancer	14.8	399	I, aVL, V2
	45/F	Hyperparathyroidism	20.2	326	V1-V3
	48/M	Multisystem organ failure, hyperalimentation	10.9	360	I, aVL, V2-V5
	35/M	Hyperparathyroidism	13.3	408	V1-V2
	43/M	Hyperparathyroidism	11.4	382	V2-V4
	50/M	Chronic pancreatitis	11.1	393	V2-V4
	48/F	Esophageal cancer with bone metastases	15.0	418	V2—V5
	86/M	Hyperparathyroidism	11.4	400	V2-V4
	36/F	Squamous cell vulvar cancer	10.5	352	V1-V4
Nishi et al.; 2006[9]	31/M	Hyperparathyroidism	17.8	415	V1-V5
Ashizawa et al.; 2003[11]	78/M	Hypercalcemia due to vitamin D intoxication	16.2	234 (QaTc) 345 (QTc)	V1-V3; mild depression in II, III, aVF
Topsakal et al.; 2003[27]	67/F	Hyperparathyroidism aggravated by use of a thiazide diuretic	18.5	–	II, III, aVF, V4-V6; depression in I, aVL

[a]Converted from mmol/L
[b]Denotes corrected Ca^{2+}

Table 3. Summary of hypercalcemia-associated ST-elevation case reports.

Brugada syndrome [28]
Early repolarization syndrome [29]
Hyperkalemia [30]
Left ventricular hypertrophy [31]
Left bundle branch block [31]
Pericarditis [32] and myocarditis [33]
Prinzmetal angina [34]
Takotsubo cardiomyopathy [35]
Ventricular aneurysm [36]

Table 4. Important causes of ST elevation that are not related to acute coronary syndrome.

with severe hypercalcemia. On the ECG prior to development of hypercalcemia, her QTc was 440 ms and baseline QaTc was 350 ms (serum 9.0 mg/dL). This case emphasizes that it is not necessarily the shortening of the QT interval that is specific for hypercalcemia but rather the shortening of the initial portion of the QT interval from changes in the phase 2 action potential that are specific for hypercalcemia. Other less-common findings seen in hypercalcemia include PR prolongation and a diffuse increase in the amplitude of the QRS complex. In this case, the PR segment was normal at 140 ms (normal = 120 ms to 200 ms), however amplitude of the QRS decreased as the ionized calcium level decreased (Figure 2).[19]

One of the more rarely described electrocardiographic changes with hypercalcemia is ST segment elevation. Prior reports of hypercalcemia presenting with ST-segment elevation have been described in the setting of vitamin D intoxication,[11] milk-alkali syndrome,[20] hyperparathyroidism,[9,21] and malignancy.[8,10,22] In plasma, approximately 40% of the calcium exists in a biologically active ionized form and the remainder is protein bound (40%, primarily bound to albumin) or complexed (10%) with phosphate or citrate.[23] To our knowledge, this is the first case report that describes the relationship between the ST-segment elevation and plasma ionized calcium level. As was typical of this case, hypercalcemia of malignancy often presents with profoundly elevated levels of serum calcium. Values greater than 14 mg/dL is associated with a 50% increase in the risk of death within 30 days.[24] The largest published case series of ST-segment elevation in hypercalcemia documented 16 cases over 14 years with serum calcium levels ranging from 10.5 mg/dL to 20.2 mg/dL and approximately 50% of these cases were secondary to underlying malignancy.[22] The majority of the electrocardiographic changes are found in the precordial leads. One proposed explanation for the ECG changes in hypercalcemia is that the shortening of the QaTc allows for a high take-off of the ST segment, mimicking an acute MI.[11] This would fit well with the findings in our patient, who had a markedly shortened QaTc on the ECG in the setting of a significantly elevated ST segment. It is important to note that hypercalcemia may cause other electrocardiographic abnormalities that can mimic myocardial ischemia including inverted, biphasic, notched, or flattened T waves.[11,25] Figure 2 demonstrates a characteristic flattened T-wave as the elevation of the ST segment resolved. In addition to hypercalcemia there are other important causes of ST segment elevation (Table 4).

Conclusions

ST-segment elevation is a known consequence of severe hypercalcemia, and clinicians should be aware that high calcium levels may be associated with a pseudo-infarct pattern on the ECG. In patients with a history of malignancy who may be especially prone to hypercalcemia, the possibility of electrolyte-induced ECG changes should be considered when evaluating the ECG for signs of ischemia.

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