Hypercalcemia Due to Vitamin D Intoxication with Clinical Features Mimicking Acute Myocardial Infarction

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Abstract

We report a case of hypercalcemia in an elderly patient due to vitamin D intoxication with clinical features and electrocardiogram (ECG) findings mimicking acute myocardial infarction. A 78-year-old man was referred to our department with symptoms of general fatigue, anorexia and chest pain. The ECG demonstrated ST elevation in leads V1 to V3 and diffuse T wave flattening, resulting in myocardial infarction being suspected. However, his symptoms, including chest pain, gradually improved and the ECG returned to normal in accordance with a fall in his serum calcium level. We introduce the use of QaTc interval shortening in differentiating ST-T changes of hypercalcemia from those of true myocardial ischemia.


Key words: electrocardiogram (ECG), QaTc interval, hypercalcemia, vitamin D intoxication, acute myocardial infarction

Introduction

Iatrogenic vitamin D intoxication is a fairly common and well-recognized cause of hypercalcemia, which can be associated with morbidity and even mortality if left untreated (1–3). Electrocadioographic changes associated with hypercalcemia include a shortened QT interval, mainly the ST segment portion. Decreased T wave amplitude and T wave notching or inversion are also observed in severe hypercalcemia, with increasing hypercalcemia sometimes producing a high takeoff of the ST segment in leads V1 and V2. Thus electrocardiographic findings in this condition can simulate those of acute myocardial ischemia (4). We report a case of hypercalcemia due to vitamin D intoxication in which symptoms and electrocardiographic findings mimicked those seen in acute myocardial infarction.

Case Report

A 78-year-old man was referred to our hospital on November 17, 2000 with a suspected acute myocardial infarction. No significant family history was obtained, except for paternal hypertension and a cerebrovascular accident. The past medical history included pulmonary tuberculosis at the age of 13 and cholecystolithiasis for which he underwent a partial cholecystectomy at the age of 62. After having been diagnosed with osteoporosis in July 1995, he was treated with 1α-OH-D3 (alfacalcidol) 1.0 µg/day and also made every effort to maximize his calcium intake by drinking milk and mineral water. In January 1996, his family doctor subsequently prescribed an angiotensin converting enzyme (ACE) inhibitor (imidapril hydrochloride, 5 mg/day) for gradually rising blood pressure. In addition, lower back pain secondary to the severe osteoporosis was treated with a nonsteroidal anti-inflammatory drug (NSAID) (proglumetacin maleate, 270 mg/day). On March 28, 2000, the patient was admitted to the family physician’s hospital with general fatigue and anorexia. Laboratory studies showed renal dysfunction accompanied by anemia and urinary tract infection (hemoglobin, 8.8 g/dl; urea nitrogen, 78.0 mg/dl; creatinine, 7.9 mg/dl; white blood cells, 11,500/mm³; C-reactive protein, 1.26 mg/dl; and pyuria). The imidapril hydrochloride and proglumetacin were discontinued because the concomitant use of an ACE inhibitor and a NSAID were thought to have exacerbated his renal impairment. He was subsequently rehydrated with intravenous saline and his renal function normalized in three weeks (urea nitrogen, 18.9 mg/dl; creatinine, 1.1 mg/dl). Around seven months after this occasion...
sode, the patient developed a further episode of fatigue and anorexia, this time accompanied by nausea. Over the next ten days he developed increasing lethargy and weakness, and on the day of admission he complained of severe chest pain which was not relieved by nitrate given by buccal spray.

Physical examination on admission revealed a slender male (height, 164 cm; body weight, 47 kg) who was lethargic but alert. He had moderately high blood pressure (156/84 mmHg) and tachycardia of 108 per minute. His neck was supple with no jugular venous distension or lymphadenopathy. Examination of his heart, lungs and abdomen was unremarkable except for crepitations heard bilaterally in the lower lobes.

The electrocardiogram (ECG) demonstrated sinus tachycardia, ST elevation in V1 to V3, mild ST depression in II, III, and aVF, and generalized flattening of the T waves (Fig. 1). As acute myocardial infarction or vasospastic angina could not be excluded, emergency coronary angiography (CAG) was performed; showing no significant stenoses in the RCA or the LCA (Fig. 2). However, when the results of his laboratory tests became available and hypercalcemia was recognized, left ventriculography was not completed. Hematologic tests showed a hemoglobin of 10.8 g/dl, hematocrit of 31.9%, platelet count of 263,000/mm³, and white blood cell count of 11,500/mm³. Analysis of blood chemistry was as follows: total protein, 7.8 g/dl; albumin, 4.9 g/dl; sodium, 141 mEq/l; potassium, 4.1 mEq/l; chloride, 98 mEq/l; calcium, 16.2 mg/dl; inorganic phosphorus, 6.1 mg/dl; urea nitrogen, 51 mg/dl; creatinine, 5.1 mg/dl; aspartate aminotransferase (AST), 11 IU/l; alanine aminotransferase (ALT), 10

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**Figure 1.** Electrocardiogram on admission showed ST elevation in V1 to V3, mild ST depression in II, III and aVF, and generalized flattening of the T waves.

**Figure 2.** Coronary angiography on admission showing no significant stenoses in RCA (A) and LCA (B).
Figure 3. Serial electrocardiograms demonstrated ST elevation in V₁ to V₃, generalized T wave flattening and shortened QaTc interval to gradually normalize in accordance with falling serum calcium level.

Discussion

In addition to primary hyperparathyroidism, malignancy associated with hypercalcemia (MAHC), and familial hypercalciuric hypercalcemia, vitamin D intoxication is one of the main causes of hypercalcemia. However, although even low-dose daily vitamin D supplementation for prophylactic treatment of osteoporosis has been reported to cause severe hypercalcemia in the elderly (3), some clinicians still continue to prescribe vitamin D inappropriately or without adequate monitoring. In the present case, the serum concentration of total 1,25-(OH)₂D was within the normal range. Several studies report normal or only marginally elevated total 1,25-(OH)₂D levels among vitamin D intoxicity patients (5-7), and Pettifor et al have proposed that the increased free 1,25-(OH)₂D levels might contribute to the pathogenesis of hypercalcemia related to vitamin D toxicity (7). 1α-OH-D₃ is thought to suppress PTH either directly, or indirectly by increasing serum calcium. Although the value of HS-PTH, which is influenced by renal dysfunction, was above the normal range, the level of intact-PTH was at the lower limit of normal in this case, suggesting that the hypercalcemia was caused by a non-PTH-mediated mechanism, probably vitamin D intoxication.
Chest pain is rarely seen in patients with hypercalcemia; however, there are several reported mechanisms by which chest pain can develop, including increased deposition of calcium in the fibrous skeleton of the heart and valvular cusps as well as in coronary arteries (8, 9), in addition to accelerated coronary atherosclerosis (10) in hypercalcemia from primary hyperparathyroidism. Slavich et al reported a case of primary hyperparathyroidism and angina pectoris with a normal coronary arteriogram in which surgical removal of the parathyroid adenoma relieved the chest pain (11). A further mechanism of chest pain in hypercalcemia other than coronary atherosclerosis or aortic stenosis occurs with cardiac muscle hypercontractility and left ventricular hypertrophy, leading to increased oxygen demand and relative myocardial ischemia (12, 13). Similarly, the chest pain resolved in this patient after calcium levels and blood pressure had been normalized, indicating a possible relative myocardial ischemia.

The CAG and laboratory data made a diagnosis of myocardial infarction unlikely in the present case. However, the ECG changes of severe hypercalcemia (>14 mg/dl) can mimic acute myocardial infarction in two ways: First, calcium shortens phase 2 of the cardiac muscle action potential, leading to shortening of the ST segment. As the ST segment is difficult to measure however, QT intervals have been used to evaluate the ECG effects of hypercalcemia. The QT interval can be divided into QoT, QaT, and QeT intervals, which are measured from the beginning of the QRS complex to the origin (O), apex (A), and the end (E) of the T wave, respectively. QT intervals were corrected for heart rate by Bazett's formula (14). The shortening of QaTc seen in hypercalcemia produces a high takeoff of the ST segment simulating acute myocardial ischemia (Fig. 4). The corrected QT intervals (QTC), particularly the QaTc interval, are reliable indicators of clinical hypercalcemia (15, 16), with abnormal QaTc (<0.30 second) being observed in moderate to severe hypercalcemia (15). Secondly, flattened or biphasic T waves are prominent in moderate to severe hypercalcemia, mimicking those seen in myocardial ischemia (17, 18).

In summary, we report a case of hypercalcemia with chest pain, in which ECG changes mimicked myocardial ischemia. In a situation in which emergency calcium assays are not available, the ability to diagnose hypercalcemia from the ECG is valuable, and a QaTc interval of 0.27 second or less is a reliable indicator (16) in differentiating hypercalcemia from true myocardial ischemia.

References

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