Hypocalcemia is a less-recognized but reversible cause of heart failure. We report a 56-year-old gentleman with chronic kidney disease, coronary artery disease and hypertension, presenting with exertional dyspnea, orthopnea, and bilateral lower legs edema for one week. His jugular venous pulses were elevated. Cardiac examination revealed regular heart beat and an S3 gallop without murmurs. Pertinent laboratory data revealed plasma creatinine 4.2 mg/dL and elevated creatinine kinase (585 IU/L). Electrocardiography showed normal sinus rhythm with nonspecific ST-T changes and a corrected QT (QTc) interval of 0.7 seconds (normal 0.36-0.43 seconds). Echocardiography demonstrated generalized hypokinesia of the left ventricle with ejection fraction of 20-25%. Aggressive therapy with carvedilol, spironolactone, intravenous nitroglycerin and furosemide failed to ameliorate the patient’s clinical symptoms. Later, marked hypocalcemia (plasma total calcium 4.28 mg/dL) was noted, and a normalization of serum calcium concentration improved the heart failure dramatically. Early recognition of hypocalcemia as a precipitating factor of congestive heart failure will promote the rapid initiation of effective therapy.

Key Words: Hypocalcemia • Congestive heart failure • Hypoparathyroidism

INTRODUCTION

Clinical manifestations of hypocalcemia vary from very mild and asymptomatic biochemical abnormality to severe life-threatening disorders, such as laryngeal spasm, tetany, and seizures. In addition to neuromuscular disorders, cardiovascular manifestations, such as prolonged QT interval, ventricular arrhythmia, and heart failure, can also occur in hypocalcemia. Many clinicians may be unaware of hypocalcemia associated with heart failure, since it is often ignored or only briefly mentioned in standard internal medicine. Furthermore, in the presence of coexisting factors leading to heart failure, such as coronary artery disease with ischemic cardiomyopathy, the hidden cause of heart failure due to hypocalcemia may be easily overlooked. We describe a patient featuring refractory heart failure due to unrecognized hypocalcemia. The decompensated heart failure was rapidly reversed by aggressive calcium supplementation. The previously reported cases of hypocalcemic heart failure (HHF) are also reviewed.

CASE REPORT

A 56-year-old man presented with exertional dyspnea, orthopnea, and bilateral lower leg edema for one week. He had a history of hypertension and type 2 diabetes under medication for 20 years, and more recently, he had been receiving carvedilol, doxazocin, and insulin injection to control hypertension and diabetes. One year prior to this hospitalization, he was admitted because of congestive heart failure with left ventricle (LV) ejection...
fraction (EF) of 30-35%. Coronary artery disease (CAD) with triple-vessel disease was diagnosed, and percutaneous coronary intervention (PCI) was performed. Hypocalcemia (plasma total calcium level 7.3 mg/dL) was noted during that hospitalization. The heart failure got improvement, with LV EF increased to 40-45% after PCI and medication with intravenous nitrate and furosemide. The plasma calcium level returned to normal (8.6 mg/dL) after calcium supplementation. The patient was discharged with the diagnosis of CAD with congestive heart failure and received regular outpatient follow-up. Additionally, the patient also suffered from psoriasis vulgaris.

On this most recent admission, his blood pressure was 140/80 mmHg, heart rate 96 beats/min, respiratory rate 22/min, body temperature 36.8°C, and oxygen saturation 94% on room air. Cardiac examination revealed regular heart beat and an S3 gallop without murmurs. Bilateral basilar moist crackles were heard on chest auscultation. There were jugular venous distention, mild hepatomegaly, and edema of his legs & scrotum. Chvostek’s and Trousseau’s signs were negative. Psoriasis vulgaris was noted as multiple sharply-demarcated and erythematous plaques with silvery scales over his trunk, arms, buttocks and abdomen.

Pertinent laboratory studies showed renal failure, with blood urea nitrogen 92 mg/dL (8-25 mg/dL), creatinine 4.2 mg/dL (0.7-1.2 mg/dL), and normal plasma magnesium level (2.1 mEq/L) (Table 1). Elevated creatinine kinase (585 IU/L) with normal creatinine kinase-MB (23 IU/L) level was also noticed. Chest radiography revealed cardiomegaly with pulmonary congestion. The patient’s electrocardiography (ECG) showed normal sinus rhythm, intraventricular conduction delay, and a corrected QT (QTc) interval of 0.7 seconds (normal 0.36-0.43 seconds) (Figure 1A). Echocardiography demonstrated generalized hypokinesia of LV with EF of 20-25% (Figure 2A). CAD with congestive heart failure was tentatively diagnosed.

Standard medications for heart failure including carvedilol 12.5 mg daily, spironolactone 25 mg daily, intravenous furosemide 80 mg every 8 hours, nitroglycerin 10 µg/min, and oxygen supplement failed to ameliorate his cardiac symptoms. The plasma biochemistry data showed profound hypocalcemia (plasma total calcium level 4.28 mg/dL). Intravenous 10% calcium gluconate was started at a dosage of 1 gram every 6 hours. The patient became normocalcemic (8.28 mg/dL) after calcium supplementation for 6 days, and electrocardiographic QTc interval returned to normal limit (0.43 seconds) (Figure 1B). The LV EF increased to 45-50% (Figure 2B). The cardiac symptoms, skin lesions, and renal function much improved in three weeks. Both extreme hypocalcemia and a low concentration of parathyroid hormone (PTH, 7.9 pg/mL) indicated primary hypoparathyroidism. The patient was discharged under stable condition and received oral calcitriol 0.5 µg daily, and calcium citrate 950 mg three times daily. He did well, and repeated electrocardiography showed no prolongation of QTc during two years’ follow-up.

**DISCUSSION**

Calcium ions play a crucial role in contraction of cardiac myocytes. Depolarization of the sarcolemma results in calcium influx and release of calcium ions from the sarcoplasmic reticulum. Interaction of calcium ions with troponin C results in initiation of cross-bridging between actin and myosin. The increase in cross-bridging is proportional to the increase in intracellular calcium concentration. Calcium is subsequently rapidly taken up by the sarcoplasmic reticulum, leading to the relaxation of cardiac myocytes until the arrival of another depolar-
This patient with previous CAD, chronic renal failure, and hypertension developed recurrent heart failure with prolonged QT interval. The echocardiographic evidence of generalized left ventricular hypokinesia and documented hypocalcemia achieved a diagnosis of HHF, further supported by improved heart function with calcium and oral calcitriol supplements because the heart failure was refractory to standard medication. Primary hypoparathyroidism, which caused hypocalcemia in this patient, was confirmed by low plasma parathyroid hormone level. A total of 27 cases of HHF, including our patient, have been reported in the literature. There were 17 females and 10 males. The etiologies of HHF include idiopathic hypoparathyroidism (13/27, 48%), status post subtotal thyroidectomy (22%) and parathyroidectomy (18%) with hypoparathyroidism, chronic renal failure (3%), and nutritional osteomalacia (3%). The HHF can be precipitated by coexisting hypomagnesemia and underlying organic heart disease. Plasma total calcium level at the onset of HHF is extremely low, with range of 4-6 mg/dL after correction for plasma albumin. Patients with HHF can also present with variable neurological...
symptoms, such as extremity paresthesia, muscle cramp, carpopedal spasm, weakness and seizure, although some patients manifest with HHF alone. After aggressive calcium supplementation, the HHF can be recovered completely within 3-4 weeks.

Elevation of plasma creatinine kinase (CK), electrocardiographic evidence of ST-T wave changes, and echocardiographic evidence of myocardial dysfunction, which mimics acute myocardial infarction in emergency setting, can also develop in hypocalcemic patients with normal coronary anatomy. Hypocalcemia lowers cell membrane potentials, resulting in increased cell membrane permeability and leakage of cytoplasmic proteins from muscle cells, causing elevation of plasma CK level. With persistent normal MB fraction, the plasma CK level returned to normal during calcium supplementation, and there was a significant improvement of left ventricular function after correction of this metabolic disorder. Hypocalcaemia, rather than coronary artery disease, was likely responsible for the cardiac myopathic feature in our patient.

Generalized psoriasis precipitated by various factors could be associated with hypocalcemia. Hypocalcemia in these patients is usually caused by malabsorption, surgical or idiopathic hypoparathyroidism. It was suggested that hypocalcemia might damage cell adhesion molecules, such as cadherins, which depend on calcium. Mineral metabolism abnormalities and reduced levels of vitamin D metabolites in hypocalcemia had been also postulated. Correcting the hypocalcemia with calcium and vitamin D could completely cure such skin lesions.

Furosemide should be cautiously used in heart failure patients with hypocalcemia. Since furosemide may induce hypocalcemia by increasing urine calcium wasting, the usual therapeutic measures for heart failure without calcium replenishment may not achieve satisfactory response. In this case, severe hypocalcemia might have been induced by furosemide during initial heart failure treatment, resulting in worsening clinical signs and hemodynamics.

This case report reminds clinicians to be aware of hypocalcemia as a possible cause of decompensated heart failure. Once hypocalcemia is recognized, it should be treated and the possible cause of hypocalcemia should be sought and treated as well. This will ultimately improve the patient’s outcome.

REFERENCES

