We report a case of hypocalcemic heart failure without underlying myocardial disease. Two-dimensional and Doppler echocardiography revealed dilatation and impaired contraction of the left ventricle, but did not show any valvular dysfunction. Cardiac catheterization showed a normal coronary artery, and cardiac muscle biopsy showed morphological changes in mitochondria and endoplasmic reticulum, which may be due to metabolic changes. This patient was asymptomatic after the serum calcium concentration was normalized.

Key words: Hypoparathyroidism, Heart failure

Calcium plays a key role in cardiac muscle contraction and metabolism. In 1943, Rose suggested the possibility of a relationship between chronic parathyroid insufficiency and myocardial damage (1). However, as we found only a few reports of hypocalcemic heart failure (2–7), the hypocalcemic state seems to be a relatively uncommon cause of congestive heart failure.

We report herein a case of hypocalcemic heart failure without underlying myocardial disease, and show the findings of cardiac muscle biopsy. Two-dimensional and Doppler echocardiography showed dilatation and impaired contraction of the left ventricle, but did not show any valvular dysfunction. Cardiac catheterization showed a normal coronary artery. Cardiac muscle biopsy presented morphological changes in mitochondria and endoplasmic reticulum, which may be due to metabolic changes. This is the first report of cardiac muscle change during hypocalcemia, and the first case which has followed the ejection fraction in echocardiography during the hypocalcemic state.

CASE REPORT

A 65-year-old Japanese woman presented with unexplained myalgia in both hands and legs in January 1989. Because of severe pain, she was admitted to our hospital on March 1, 1990. On admission, she was alert and complained of easy fatigability and numbness in both hands. The axillary temperature was 38.1°C. The blood pressure was 146/90 mmHg, and the pulse rate was 80/min and regular. No rales and no murmurs were audible. The liver was not enlarged and there was no pitting edema. Neither Chvostek's sign or Trousseau's sign were present. There were no contributory factors in her family or in her past history. Complete blood count and urine analysis were normal. The erythrocyte sedimentation rate (ESR) was 127 mm/h; C-reactive protein (CRP) was 8.5 mg/dl. Biochemical findings were as follows: total protein 6.7 g/dl; albumin, 2.9 mg/dl; sodium, 140 mEq/l; potassium, 3.2 mEq/l; chlorine, 99 mEq/l; calcium, 4.8 mg/dl; phosphate, 4.7 mg/dl; magnesium, 2.3 mEq/l; serum glutamic oxaloacetic transaminase (SGOT), 31 IU/dl; serum glutamic pyruvic transaminase (SGPT), 8 IU/dl; lactate dehydrogenase (LDH), 467 IU/dl; blood urea nitrogen (BUN), 11 mg/dl; creatinine (Cr), 1.1 mg/dl; uric acid, 4.9 mg/dl; total bilirubin, 1.1 mg/dl;
mg/dl; fasting blood sugar, 89 mg/dl; and 24-h Cr clearance was 97.1 l/day. Immunological examination showed rheumatoid factor (RA test), positive; rheumatoid factor, (RAHA), 320; anti-nuclear antibody, 80; direct Coombs, positive; indirect Coombs, negative; anti-adrenal antibody; negative; anti-pituitary antibody, positive.

The thyroid function was normal and anti-thyroid microsome antibody (MCPA) and anti-thyroglobulin antibody (TGPA) were negative. Intact parathyroid hormone assay revealed a level of 11 pg/ml (normal range, 23–73 pg/ml), and other hormonal data were in the normal ranges. The Ellsworth-Howard test was performed. The intravenous injection of 100 IU hPTH caused an approximate 23-fold increase in urinary cAMP excretion, and urine excretion of phosphate was 36.4 mg/2h. The chest radiograph presented a normal appearance and an electrocardiogram (ECG) disclosed only a slightly prolonged QT interval. No abnormalities were observed on the electromyograph. All these findings suggested that this patient had some undefined collagen disease with hypoparathyroidism. The oral administration of glucocorticoid (prednisolone 30 mg/day) was begun.

On the fourth treatment day, the patient suddenly felt dyspnea. Her blood pressure was 124/86 mmHg and the pulse was 95/min. Moist rales were heard bilaterally. The jugular vein was distended and the liver was enlarged, and there was pitting edema on the lower extremities. A chest radiograph showed cardiac enlargement and evidence of pulmonary edema (Fig. 1). The ECG demonstrated T wave inversion in leads V1–V5. Echocardiography indicated slightly enlarged left cardiac chambers with a lowered ejection fraction of 54%. No valvular dysfunction was identified by Doppler technique. The serum calcium was 4.8 mg/dl; albumin, 3.4 mg/dl; CRP, 1.2 mg/dl; and ESR, 44 mm/h. Intravenous administration of calcium carbonate 17 mEq/day, and oral administration of furosemide 40 mg/day were begun. On the 11th day, the serum calcium increased to 6.4 mg/dl and all symptoms and signs of heart failure disappeared. The T wave inversion was improved in the ECG. The chest radiograph showed no cardiac enlargement nor pulmonary edema. Echocardiogram confirmed no abnormalities, and the ejection fraction increased to

Fig. 1. Chest X-ray showing pulmonary edema when congestive heart failure occurred.

Fig. 2. Light micrograph of the cardiac muscle showing normal findings (hematoxylin and eosin stain, original magnification ×400).

Fig. 3. Electron micrograph of the cardiac muscle showing dilated sarcoplasmic reticulum, electron-dense granules in the sarcoplasm, and size variability in the mitochondria (original magnification ×8,500).
80%. Cardiac left ventriculogram revealed normal wall motion with an ejection fraction of 72%, and coronary arteriogram was normal. At the time of catheterization, three specimens of cardiac muscle tissue were obtained by biopsy (Figs. 2, 3). The cardiac muscle was normal by light microscopic observation, but electron microscopy disclosed dilated sarcoplasmic reticulum and electron-dense granules, and size variability in the mitochondria. During the rest of the days in hospital, her serum calcium was maintained at a level of 6.5 mg/dl or more, and she never showed any of the signs or symptoms of congestive heart failure without furosemide. She was discharged in an asymptomatic state, receiving calcitriol (1.0 μg/day) and prednisolone (10 mg/day).

**DISCUSSION**

As first demonstrated by Ringer's work in 1883 (8), calcium plays an important role in myocardial function. Extracellular calcium is needed for myocardial function, because the influx of extracellular calcium initiates muscle contraction, and the magnitude of influx has a direct effect on the strength of the contraction (9). Calcium also influences the renal excretion of sodium, and sodium retention influences the occurrence of congestive heart failure (10-12). Hypoparathyroidism causes chronic hypocalcemia, and it is reasonable to assume that hypoparathyroidism is likely to induce congestive heart failure. In fact, however, it does not occur frequently, and the reason is unknown.

High-dose glucocorticoid causes calciuresis and worsens hypocalcemia. In the present case, however, serum and urine calcium did not show a significant change. Glucocorticoid also causes sodium retention. Though the serum sodium concentration did not change significantly, glucocorticoid administration might have an influence on the occurrence of heart failure.

It is well known that underlying hypertensive and atherosclerotic disease causes impaired cardiac function. In the present case, however, the coronary vessels were normal, and no sign of collagen disease, sarcoidosis, amyloidosis, or myocarditis was found in the cardiac muscle obtained during the hypocalcemic state. These facts strongly suggest that hypocalcemia causes congestive heart failure.

We did not find any apparent cardiac lesions, so we performed cardiac biopsy to confirm the exact mechanism of transient cardiac deterioration. Light microscopic observation showed normal muscle. But electron microscopic observation showed dilated sarcoplasmic reticulum, electron-dense granules in the sarcoplasm and size variability in mitochondria. The sarcoplasmic reticulum is the area of calcium translocation, so we suspect that hypocalcemia might cause dilated sarcoplasmic reticulum. And mitochondria is the area of energy production. These facts suggest that the changes were due to metabolic abnormalities, but probably were not specific for hypocalcemia.

Hypocalcemia as a cause of cardiac dysfunction is often overlooked, but in the hypocalcemic state, it must be noted that not only metabolic but also morphological changes occur in cardiac muscle. Many reports suggest that heart failure due to hypocalcemia is reversible (4-7), but no report has shown the relationship between the serum calcium concentration and cardiac contraction. In the present case, the ejection fraction was low when the serum calcium level was decreased, and it improved as the serum calcium level increased. This is direct evidence that serum calcium is necessary for cardiac muscle contraction. Once hypocalcemic heart failure occurs, the hypocalcemia must be corrected immediately.

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