

## Cardiac failure secondary to idiopathic hypoparathyroidism: A case report

İdiyopatik hipoparatiroidiye bağlı gelişen kalp yetersizliği: Olgu sunumu

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Hypocalcemic cardiomyopathy due to hypoparathyroidism is a very rare condition. Ensuing heart failure due to hypocalcemia is refractory to conventional treatment. We reported a 41-year-old man who developed cardiac failure due to hypocalcemia secondary to idiopathic hypoparathyroidism. Echocardiography showed biventricular low ejection fraction, dilated heart chambers, pulmonary hypertension, and valvular regurgitations. Serum calcium and parathyroid hormone levels were low. After treatment of heart failure and calcium-vitamin D supplementation, signs and symptoms of heart failure improved rapidly. At 6 months, biventricular systolic and diastolic functions returned to normal. Serum calcium level should be monitored in every patient with cardiac failure, and hypocalcemia should be considered in patients with refractory heart failure.

**Key words:** Cardiomyopathy, dilated/etiology; heart failure/etiology; hypocalcemia/complications; hypoparathyroidism/complications.

Calcium plays a key role in the contraction of heart muscle and the regulation of metabolism.<sup>[1]</sup> Plasma ionized calcium level is vital, since intracellular sarcoplasmic reticulum cannot provide maintenance of adequate calcium level to initiate myocardial contraction.<sup>[2]</sup> Hypocalcemia results in reduced myocardial contraction, left ventricular systolic dysfunction, and as a result, systolic heart failure.<sup>[3]</sup> There are heart failure case reports which develop due to hypocalcemia caused by various factors.

In this article, a case with heart failure due to hypocalcemia secondary to idiopathic hypoparathyroidism and refractory to conventional treatment was reported.

Hipoparatiroidizme bağlı gelişen hipokalsemik kardiyomiyopati oldukça nadir görülen bir durumdur. Hipokalsemiye bağlı gelişen kalp yetersizliği konvansiyonel kalp yetersizliği tedavisine dirençlidir. Bu yazıda, idiyopatik hipoparatiroidiye bağlı hipokalsemi sonucu kalp yetersizliği gelişen 41 yaşında bir erkek hasta sunuldu. Ekokardiyografisinde her iki ventrikülde düşük ejeksiyon fraksiyonu, dilate kalp boşlukları, pulmoner hipertansiyon ve kapak yetersizlikleri izlenen hastada serum kalsiyum ve paratiroid hormon düzeyleri çok düşük bulundu. Kalp yetersizliği tedavisine ek olarak kalsiyum ve D3 vitamini desteği ile hastanın kalp yetersizliğine ait semptom ve bulguları geriledi. Altıncı ay kontrolünde her iki ventrikülün sistolik ve diastolik fonksiyonu normale dönmüştü. Serum kalsiyum düzeyi kalp yetersizliği olan her hastada bakılmalı, tedaviye dirençli kalp yetersizliğinde hipokalsemi akla gelmelidir.

**Anahtar sözcükler:** Anahtar sözcükler: Kardiyomiyopati, dilate/ etyoloji; kalp yetersizliği/ etyoloji; hipokalsemi/ komplikasyon; hipoparatiroidizm/komplikasyon.

### CASE REPORT

A 41-year old male patient visited the district state hospital with increasing complaints of dyspnea (NYHA class III), cough, and fatigue for the past 15 days. The patient was diagnosed with upper respiratory tract infection and treated accordingly. As the complaints continued, a chest X-ray was performed and pleural effusion was detected. The patient was then referred to the Chest Medicine Department of our university hospital. The pleural puncture fluid was found to be consistent with transudate and any finding of pulmonary embolism was not observed in the computed tomography angiography of the thorax. A cardiology evaluation was requested following increased dyspnea and findings suggesting pulmonary congestion in the physical examination of the patient. Following echocardiography and diagnosis of left

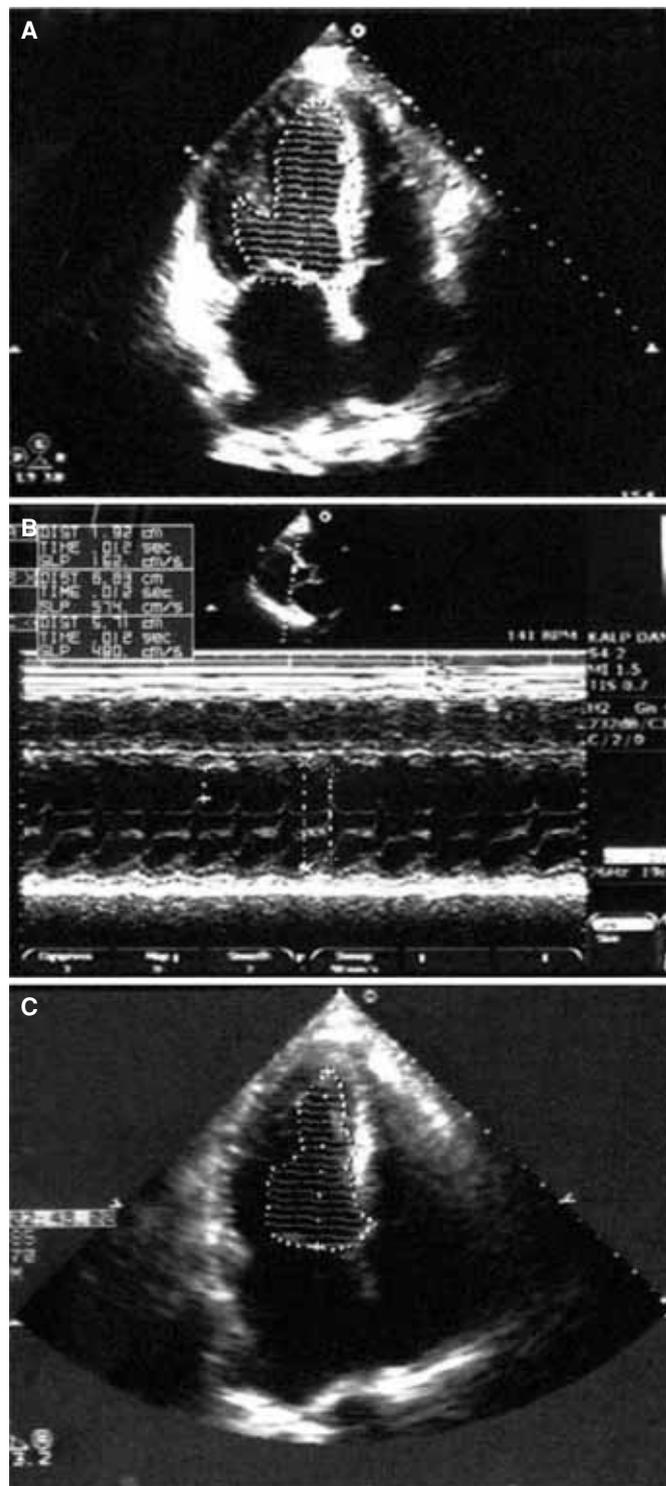
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ventricular failure, ACE inhibitor, aspirin and emergency furosemide treatment was initiated due to the decompensated status of the patient. However, he was hospitalized in the cardiology clinic for further evaluation and treatment, since no regression was observed in his symptoms.

It was revealed that the patient had no previous cardiac complaint and that his complaints started within the last two to three weeks. The patient had a history of 15 pack years of cigarette smoking. He also underwent bilateral cataract surgeries twice, 10 years and 4 years ago. He had no thyroid related problem. His father was diagnosed with coronary artery disease in his early ages. According to the physical examination results, his general condition was moderate, he had mild dyspnea, blood pressure was 110/70 mmHg, pulse 128/min arrhythmic, respiratory rate 18/min, and fever 36°C. The heart sound was arrhythmic, tachycardic, and irregular; a 2/6 degree pansystolic murmur was heard at the apex. Fine inspiratory rales were heard in both lungs. No hepatomegaly, pretibial edema, jugular venous pressure was observed. There was not particular Chvostek's and Trousseau's signs in the physical examination, due to the known hypocalcemia (evaluated at the Chest Medicine Unit). Electrocardiography showed atrial fibrillation with rapid ventricular response (heart rate 144/min), prolongation of the QT interval vs heart rate (Qt<sub>c</sub>: 548 ms), R loss in V2-3. The telecardiography showed an increase in cardiothoracic rate and pulmonary hilar congestion. The laboratory tests demonstrated serum calcium 6.3 mg/dl (N: 8.2-10.4 mg/dl), ionized calcium 6.4 mg/dl, phosphorus 6.3 mg/dl (N: 2.4-5 mg/dl), urea 65 mg/dl (N: 10-50 mg/dl), creatinine 1.26 mg/dl (N: 0.7-1.3 mg/dl), magnesium 1.87 mg/dl (N: 1.5-2.6 mg/dl), protein 6.7 g/dl (N: 6-8.5 g/dl), albumin 4 g/dl (N: 3.5-5 g/dl), and parathyroid hormone 2 pg/ml (N: 15-65 pg/ml). Phosphorus in the spot urine was 0.35 mg/dl. All other biochemical tests, thyroid function tests, immunological markers were found within reference range. The transthoracic echocardiography performed during hospitalization demonstrated global hypokinesia in both ventricles (left ventricular EF 20%; right ventricular EF 35%). Left atrial dilatation was 4.7 cm and dilatation in both ventricles (left ventricle end-diastolic diameter 6.3 cm and end-systolic diameter 5.4 cm; right ventricle end-diastolic diameter 3.2 cm), moderate mitral and tricuspid valve insufficiency were found, and systolic pulmonary artery pressure was 50 mmHg (Figure 1a, b). The bone densitometry result was normal. The patient was diagnosed with idiopathic hypoparathyroidism following endocrinologic examination. Treatment with peroral calcitriol 1.5 µg/day and ionized calcium 2 g/day was initiated. For cardiac treatment, peroral furosemide, carvedilol (low dose initiated and then titrated), perindopril, aspirin and SC enoxaparine were given. The patient whose heart rate decreased but who still had atrial

fibrillation was orally digitalized after his general condition was normal. The patient also underwent coronary angiography and simultaneous endomyocardial biopsy to exclude myocarditis, one of the causes of



**Figure 1 (A-B).** Measurement of left ventricular ejection fraction and size with modified Simpson and M-mode echocardiography before calcium treatment. **(C)** Measurement of left ventricular ejection fraction with modified Simpson method at 6 months after treatment.

**Table 1. Serum calcium and phosphorus levels and transthoracic echocardiography data before treatment, at discharge and at 6 months**

	Before treatment	At discharge	At 6 months follow-up
Calcium (mg/dl)	6.3	8.8	9.3
Phosphorus (mg/dl)	6.3	3.9	3.1
Left ventricular end-systolic diameter (cm)	5.4	4.3	3.1
Left ventricular end-diastolic diameter (cm)	6.3	5.7	4.9
Right ventricular end-diastolic diameter (cm)	3.2	2.6	2.5
Left atrium (cm)	4.7	4.1	4.1
Left ventricle ejection fraction (%)	20	40	62
Right ventricle ejection fraction (%)	35	60	65
Mitral valve insufficiency	2	1	1
Tricuspid valve insufficiency	2	1	Mild
Systolic pulmonary artery pressure (mmHg)	50	Normal	Normal

reversible heart failure. The results showed that the coronary arteries were normal and the LVEF was 25%. A mild mitral valve insufficiency was also observed. The pathology report of biopsy material demonstrated a focal minimal myocardial hypertrophy and minimal pericellular fibrosis. Upon continuation of atrial fibrillation, the patient was given warfarin to obtain INR 2.0-3.0 and the calcitriol dose was increased from 1.5 µg/day to 2.5 µg/day. Approximately three weeks later, the serum calcium level increased to 8.8 mg/dl, the phosphorus level decreased to 3.9 mg/dl, and the patient reverted to normal sinus rhythm. The patient's general condition rapidly improved and his complaints disappeared. The echocardiography was reperformed during the discharge and it was demonstrated that the left atrial, left ventricular and right ventricular diameters were found to be decreased; RVEF returned to normal, LVEF increased to 40%, the valve insufficiencies regressed and pulmonary artery systolic pressure reverted to normal. The patient was discharged with the prescription of oral calcitriol (1.5 µg/day), ionized calcium (2 g/day), carvedilol (50 mg/day), perindopril (4 mg/day), warfarin (5 mg/day) and aspirin (100 mg/day). At 6 months follow-up visit no complaint was reported by the patient and he was still at normal sinus rhythm and echocardiographic exam showed that the diameters of cardiac spaces and LVEF returned to normal (Figure 1c). The serum calcium and phosphorus levels and echocardiographic parameters during follow-up period are shown in Table 1.

## DISCUSSION

Calcium is important for myocardial contraction. The intracellular sarcoplasmic reticulum serves as a calcium reservoir and binds to the calcium-troponin-tropomyosin complex released in the cytoplasm. Actin and myosin are then activated and myocardial contraction is initiated. Contraction is maintained by extracellular calcium influx into the cell. The less problematic the influx is, the more

potent the contraction will be. Myocardial contraction is weak in hypocalcemia.<sup>[1,2]</sup> In addition, calcium impacts renal sodium excretion. In hypocalcemia, renal sodium excretion is reduced and water retention is increased.<sup>[4]</sup> Parathyroid hormone has a positive inotropic effect; it increases calcium influx into the myocardial cells and also increases endogenous myocardial norepinephrine release.<sup>[5]</sup>

Cases with heart failure due to hypocalcemia have been reported in the literature. These are cases who initially received conventional heart failure treatment, but when no response was obtained with treatment, extensive evaluation has been performed and these cases were diagnosed with hypocalcemia. Most of the cases were diagnosed with heart failure clinically and myocardial dilatation and low systolic performance in single or both ventricles were observed in the echocardiography, radionuclide angiography, and cardiac catheterization.<sup>[1,6]</sup> The myocardial performance of our case was assessed by echocardiography. Hypocalcemia may be seen with hypomagnesemia. Although calcium level may return to normal, adequate response to treatment may not be obtained unless hypomagnesemia is corrected.<sup>[2]</sup> Serum magnesium level was normal in our case. Findings suggesting paresthesia and tetany may also be seen in severe hypocalcemia. Lack of such complaints and findings in our case can be explained by not so low serum calcium level.

There are various factors leading to hypocalcemia. These include removal or damage to the parathyroid glands as a complication following thyroid surgeries,<sup>[3,7-9]</sup> end stage renal failure,<sup>[10,11]</sup> hypoalbuminemia and sepsis where frequent blood transfusions are required,<sup>[10]</sup> thalassemia (parathyroid gland hemosiderosis),<sup>[12]</sup> clinical presentation of hypoparathyroidism with facial and cardiac malformations such as Di George's syndrome,<sup>[6]</sup> neonatal hypocalcemic dilated cardiomyopathy due to 22q11

microdeletion,<sup>[13]</sup> intensive use of *loop* diuretics<sup>[3]</sup> or idiopathic hypoparathyroidism<sup>[2,14]</sup> characterized by hypocalcemia, hyperphosphatemia and low parathyroid hormone levels, which suggests no etiology measured by coronary angiography, cardiac catheterization, endomyocardial biopsy to investigate common causes of dilated cardiomyopathy (as seen in our case).

Hypocalcemia is one of the reversible causes of heart failure. In the presence of such conditions, the underlying etiology should be evaluated and the patient should be given calcium and vitamin D<sub>3</sub> supplements. As in our case, clinical and laboratory findings of heart failure improve immediately with this therapeutic support. In our case left ventricular function improved in 20 days and normal function was achieved in 6 months (Table 1).

Myocarditis, one of the common causes of reversible heart failure usually recovers at a 90% rate. However, the rest 10% reverts to fulminant myocarditis.<sup>[15]</sup> This was eliminated in our case by obtaining biopsy for myocarditis.

In conclusion, hypocalcemia is one of the causes of reversible heart failure. Serum calcium levels should be measured in all patients with heart failure and the etiology of hypocalcemia should be investigated. In addition to conventional treatment of heart failure, calcium and vitamin D<sub>3</sub> supplements should be administered. When serum calcium levels return to normal limits, clinical and laboratory improvement is achieved.

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