

# Reversible Heart Failure and Rhabdomyolysis Caused by Primary Hypoparathyroidism during Lactation

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Hypocalcemia can be complicated, on rare occasions, by congestive heart failure and may also be associated with labor and lactation in some cases. Herein, we report a 30-year-old woman with hypocalcemia-induced heart failure secondary to primary idiopathic hypoparathyroidism precipitated by lactation. The patient presented with chest pain and paresthesia in both arms and legs during breast-feeding after her second delivery. She had severe hypocalcemia and low parathyroid hormone levels. Hypocalcemia-induced rhabdomyolysis further aggravated her hypocalcemia symptoms. The echocardiogram showed global hypokinesia with an ejection fraction of 47%. After calcium and vitamin D replacement, her symptoms and ventricular function improved. Hypocalcemia needs to be considered in patients with heart failure, because it is readily reversible. To the best of our knowledge, this is the first report of a patient with heart failure and rhabdomyolysis induced by primary hypoparathyroidism during lactation. (*Endocrinol Metab* 26:268-271, 2011)

**Key Words:** Heart failure, Hypocalcemia, Hypoparathyroidism

## INTRODUCTION

Extracellular calcium concentrations are important for the normal function of nerves and muscles. The classic symptoms of hypocalcemia are neuromuscular excitability from mild forms of muscle cramping, spasms, tingling, and numbness to life threatening laryngospasm, bronchospasm, and even seizures [1]. Cardiac function may also be affected, manifested by a prolonged QT interval, cardiac dysarrhythmia, and in rare cases, heart failure [2]. The demand for calcium in milk production to supply the rapidly mineralizing neonatal skeleton places significant stress on maternal calcium homeostasis [3]. Hypocalcemia associated with lactation is a rare condition reported previously in patients with vitamin D deficiency [4]. We report a 30-year-old woman with hypocalcemia-induced heart failure secondary to primary idiopathic hypoparathyroidism during lactation.

## CASE REPORT

A 30-year-old woman presented to the emergency room with

chest pain, dyspnea, and paresthesia in both arms and legs. Nine months ago, she was in labor with her second baby and lactated until 2 days ago. Recently she was under significant psychotic stress and began to experience intermittent dyspepsia, chest pain, and tingling sensations in her arms and legs for one week. She had no past history of cardiac, renal, or thyroid disease. In addition, there was no history suggestive of malabsorption, alcohol abuse, previous neck surgery or family history of similar illnesses. Also, her children did not exhibit neonatal tetany. Physical examination showed her blood pressure was 110/70 mmHg and pulse rate was 90 beats/min. Her breathing was shallow and labored with respiratory rate of 38 breaths/min. Lung auscultation revealed bronchoalveolar breathing sounds without crackles or wheezing. Cardiac examination revealed a regular heart beat without murmurs and there were no signs of peripheral edema or hepatosplenomegaly.

The electrocardiogram showed sinus rhythm, T wave inversion in leads V1-6, II, III, and aVF, and a prolonged QT interval of 0.397 seconds (Fig. 1). Chest X-ray showed mild pulmonary congestion but no evidence of cardiomegaly. First readings of myocardial enzyme revealed creatine phosphokinase (CPK) 2605 U/L (26-174);

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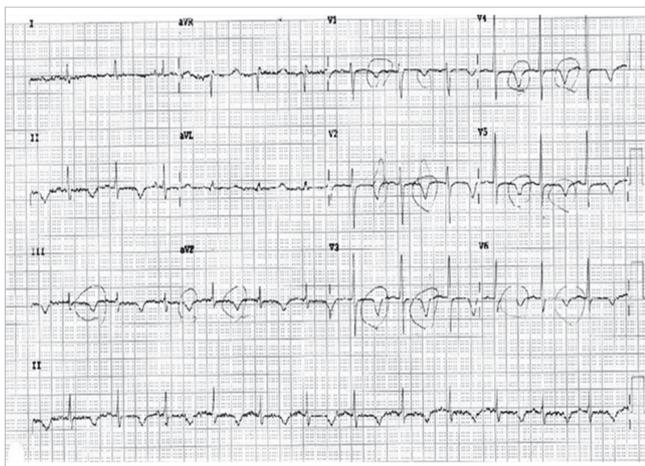
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lactate dehydrogenase (LDH) 916 U/L (240-480); MB fractionation of CPK (CPK-MB) 7.76 ng/mL (0-3); troponin-I 0.02 ng/mL (0-0.05); troponin-T 0.010 ng/mL (0.01-0.1); and aspartate aminotransferase (AST) 45 IU/L (4-37). The patient was managed with heparin and nitroglycerin infusion. An echocardiogram showed mild mitral valve regurgitation and hypokinesia of inferoseptum, midanterolateral, midinferolateral, inferoapex, and anteroapex, and impaired left ventricular function (ejection fraction 47%). Coronary angiography was performed to exclude acute coronary syndrome. There was no stenotic lesion in her epicardial coronary arteries, so we stopped heparin and nitroglycerin treatment.

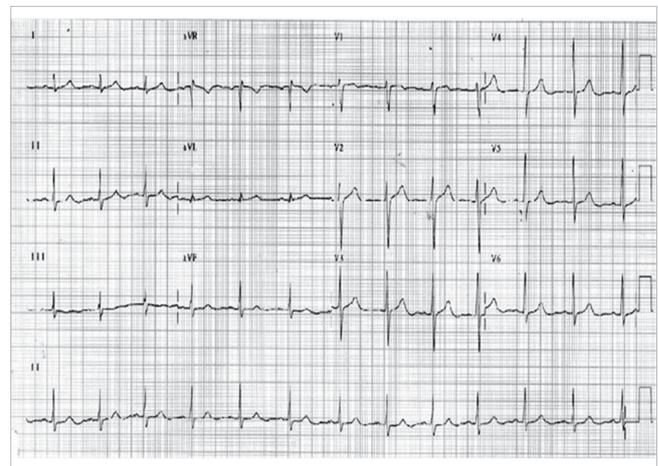
Serum concentrations of calcium were 4.4 mg/dL; ionized calcium 0.44 mmol/L (1.13-1.32); phosphorus 5.6 mg/dL; magnesium 0.9 mg/dL (1.3-2.1); total protein 6.0 g/dL; albumin 3.8 g/dL; alanine aminotransferase (ALT) 23 IU/L; alkaline phosphatase (ALP) 77 IU/L (35-104); total bilirubin 0.51 mg/dL; urea 8.8 mg/dL; creatinine 0.50 mg/dL; glucose 103 mg/dL; Na 141 mEq/L; K 3.3 mEq/L; and Cl 102 mEq/L. Arterial blood gas analysis showed respiratory and

metabolic alkalosis as follows: pH 7.455; PaCO<sub>2</sub> 37.2 mmHg; PaO<sub>2</sub> 113 mmHg; HCO<sub>3</sub> 25.7 mM/L; and SaO<sub>2</sub> 99.4%. The patient was also treated with intravenous infusion of calcium gluconate and magnesium sulfate. Saline hydration was performed to prevent rhabdomyolysis-induced acute renal failure. Further hormonal screening for hypocalcemia showed intact parathyroid hormone (PTH) 2 pg/mL (10-65); calcitonin 1.0 pg/mL (0-10); 25-hydroxyvitamin D [25(OH)D] 6.40 ng/mL (7.6-75); and 1,25-dihydroxyvitamin D [1,25(OH)<sub>2</sub>D] 48.70 pg/mL (20.1-46.2). Thyroid function tests and screening for autoimmune antibodies were normal. The extreme hypocalcemia and low PTH concentration were consistent with diagnosis of primary hypoparathyroidism.

On the third day at the hospital, intravenous calcium was replaced by oral elemental calcium at 1.2 g and calcitriol at 0.25 µg, daily. Total serum calcium increased to 7.0 mg/dL, serum phosphorus decreased to 4.4 mg/dL, and CPK decreased to 390 IU/L. 24 hour urine levels of calcium and creatinine were 63.7 mg/d (100-300) and 0.47 g/d (0.74-1.57), respectively. Serum magnesium level was nor-



**Fig. 1.** Baseline electrocardiogram showed sinus rhythm, T wave inversion in leads V1-6, II, III, and aVF, and a prolonged QT interval of 0.397 seconds.



**Fig. 2.** Follow-up electrocardiogram at 2 months after treatment showed that T wave inversion as seen on Figure 1 disappeared and QT intervals normalized.

**Table 1.** Biochemical studies and medications in the patient

	Reference	Day 1	Day 7	2 months	4 months
Total calcium (mg/dL)	8.4-10.4	4.4	7.0	7.9	8.7
Phosphorus (mg/dL)	2.7-4.5	5.6	4.4	4.6	3.3
Albumin (g/dL)	3.4-4.8	3.8	4.6	4.5	4.4
Magnesium (mg/dL)	1.3-2.1	0.9	1.3		
Creatine phosphokinase (U/L)	26-174	2605	390		
25-hydroxyvitamin D (ng/mL)	4.8-52.8	6.4		19.6	22.8
Parathyroid hormone (pg/mL)	10-65	2		3.6	2.3
Elemental calcium (mg/day)		1800	1800	1800	
Calcitriol (µg/day)			0.5	1	1

mal but intact PTH level consistently remained low (Table 1). The patient's carpopedal spasms and chest pain improved gradually and eventually subsided. She was discharged on the seventh day at the hospital, receiving oral elemental calcium at 1.8 g and calcitriol at 0.5 µg, daily. In subsequent follow-up, she remained asymptomatic and a normal electrocardiogram with corrected calcium level of about 7.5 mg/dL (Fig. 2). Four months after discharge, the replacement with oral elemental calcium (1.8 g) and calcitriol (1 µg) daily was maintained to obtain a serum corrected calcium level of 8.0-8.5 mg/dL (Table 1). A follow-up echocardiogram showed normal function of the left ventricle with improved regional wall motion abnormality and normal ejection fraction. The patient did well with oral calcium and calcitriol without requiring cardiac medications.

## DISCUSSION

Calcium plays an important role in myocardial contraction. Intracellular calcium in the sarcoplasmic reticulum initiates myocardial contraction when it binds to the troponin-tropomyosin complex, permitting cross-linkage between actin and myosin [5]. The strength of the contraction is influenced by the magnitude of extracellular calcium influx. At the renal level, a rise in cytosolic free calcium in the renal tubular cells promotes natriuresis. Thus, sodium retention during hypocalcemia may be a factor in the pathogenesis of cardiac failure [6].

At least 27 cases of congestive heart failure caused by severe hypocalcemia have been reported [7]. Although a causal relationship has not yet been established, the resolution of congestive cardiac failure associated with hypocalcemia after the correction of metabolic abnormalities strongly supports the potential causal relationship between hypocalcemia and heart failure. Lin et al. [7] reported that the etiologies of hypocalcemic heart failure include idiopathic hypoparathyroidism (48%), status post subtotal thyroidectomy (22%) parathyroidectomy (18%) with hypoparathyroidism, chronic renal failure (3%), and nutritional osteomalacia (3%). Total plasma calcium levels at the onset of hypocalcemic heart failure are extremely low, with a range of 4-6 mg/dL after correction for plasma albumin. After aggressive calcium supplementation, hypocalcemic heart failure can be recovered completely within a few weeks to a few months [5,7].

Our patient was initially misdiagnosed as acute coronary syndrome based mainly on chest pain, elevated cardiac enzymes, T wave inversion in V1-6, II, III, and aVF leads on electrocardiogram, as well as hypokinesia and left ventricular dysfunction on an echo-

cardiogram, similar to a case reported by Rallidis et al. [8]. However, the demonstration of normal coronary arteries and the restoration of left ventricular dysfunction after the correction of hypocalcemia made the link between myocardial dysfunction and hypocalcemia highly possible. Primary hypoparathyroidism was confirmed by marked hypocalcemia and low intact PTH levels after the correction of hypomagnesemia and stopping lactation. The patient had no history of previous neck surgery or radiation therapy on her head and neck, or family history of similar illness, and there was no evidence of congenital anomaly, autoimmune disease, and malabsorption. Although we did not check her intracranial calcifications and cataract which were evidences of chronic hypocalcemia, we think she had been hypocalcemic, presumably for a long time. A long time is required to develop heart failure, and she remembered later that she had intermittently experienced tingling sensations since 2003. Her hypocalcemic symptoms disappeared immediately after her corrected calcium levels were higher than 6.0 mg/dL with the replacement of calcium. She may have adapted to low serum calcium levels, but lactation, vitamin D deficiency, hypomagnesemia, and alkalosis aggravated hypocalcemia further, and she was presented with heart failure mimicking acute coronary syndrome and rhabdomyolysis as the first manifestation of idiopathic primary hypoparathyroidism. Hypocalcemia-induced rhabdomyolysis also worsened the hypocalcemia and vice versa.

The large output of calcium into milk subjects lactating women to a negative calcium balance, placing considerable stress on maternal calcium homeostasis [3]. Therefore, it is expected that lactation might uncover subclinical hypoparathyroidism in undiagnosed women. Although intake or intestinal absorption of calcium is increased and renal excretion of calcium is very low during lactation, the most important mechanism to meet this calcium demand is the rapid and transient demineralization of maternal skeleton which is mainly mediated by elevated parathyroid hormone-related protein (PTHrP) during estrogen deficiency [3]. Levels of calcium and calcitropic hormones during lactation have been associated with the following: total calcium is normal to mildly elevated; ionized calcium is slightly elevated; PTH is slightly low; 1,25(OH)<sub>2</sub>D is normal; calcitonin is elevated; and PTHrP is elevated by the mammary gland [3]. In the non-lactating state, the parathyroid gland is the central regulator of calcium homeostasis, but during lactation, the mammary gland becomes an accessory parathyroid gland, secreting PTHrP instead of PTH [9]. While the level and activity of PTH does not change, increased PTHrP levels seem to contribute to a

state of maternal functional hyperparathyroidism, and the requirement for calcitriol treatment may be alleviated in hypoparathyroid patients during lactation [3,4]. Our patient had stopped breast feeding two days prior to admission and decreased PTHrP may have unmasked subclinical hypoparathyroidism, although we did not check PTHrP levels.

In conclusion, we present a case that was initially presented with hypocalcemia-induced heart failure mimicking acute coronary syndrome and rhabdomyolysis secondary to idiopathic primary hypoparathyroidism shortly after stopping lactation and to the best of our knowledge, this is the first report to show this. The physiological calcium demand during lactation strained the maternal resources to a state that unmasks subclinical pathologies. Because severe hypocalcemia can cause myocardial dysfunction that is potentially reversible with the correction of metabolic abnormality, hypocalcemia should be considered in patients with heart failure, especially those with symptoms such as paresthesias. In addition, our knowledge about the changes of calciotropic hormones during lactation will help the understanding of maternal calcium homeostasis.

### SUMMARY

Hypocalcemia can rarely be complicated by congestive heart failure and be unusually associated with labor and lactation. We report

a 30-year-old woman with hypocalcemia-induced heart failure secondary to primary idiopathic hypoparathyroidism precipitated by lactation. To the best of our knowledge, this is the first report of a patient with heart failure and rhabdomyolysis caused by primary hypoparathyroidism during lactation.

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