Case Report

http://dx.doi.org/10.4070/kcj.2013.43.8.573
Print ISSN 1738-5520 • On-line ISSN 1738-5555

kcj
Korean Circulation Journal

Takotsubo Cardiomyopathy Associated with Severe Hypocalcemia Secondary to Idiopathic Hypoparathyroidism

Ho sung Rhee, MD, Se-Whan Lee, MD, Young Kyu Jung, MD, Ung Jeon, MD,
Sang-Ho Park, MD, Seung-Jin Lee, MD, Won-Yong Sin, MD, and Dong-Kyu Jin, MD

Department of Internal Medicine, School of Medicine, Soonchunhyang University, Cheonan Hospital, Cheonan, Korea

The etiology and pathophysiology of takotsubo cardiomyopathy have not yet been fully clarified. We report a case of takotsubo cardiomyopathy associated with severe hypocalcemia secondary to hypoparathyroidism. A 69-year-old woman presented with acute pulmonary edema caused by severe left ventricular dysfunction with apical ballooning compatible with takotsubo cardiomyopathy. Laboratory tests revealed severe hypocalcemia secondary to idiopathic hypoparathyroidism. Coronary angiography showed normal coronary artery function. Her symptoms and signs of heart failure improved dramatically with the correction of hypocalcemia through calcium and calcitriol replacement. **(Korean Circ J 2013;43:573-577)**

KEY WORDS: Takotsubo cardiomyopathy; Hypocalcemia; Hypoparathyroidism.

Introduction

Takotsubo cardiomyopathy or left ventricular (LV) apical ballooning syndrome is an acquired disorder typically characterized by transient LV dysfunction with marked apical akinesia and ballooning.[1)2)] Hypocalcemia is an uncommon but reversible cause of congestive heart failure. However, most cases of hypocalcemia-induced cardiomyopathy present with diffuse LV hypokinesia with a trend toward dilated cardiomyopathy, rather than LV apical ballooning.[3-6)] Herein we report what we believe to be the first case of takotsubo cardiomyopathy associated with severe hypocalcemia secondary to idiopathic primary hypoparathyroidism. The clinical signs and symptoms of congestive heart failure and the objective parameters of LV systolic function rapidly improved after correction of the hypocalcemia.

Received: December 8, 2012
Revision Received: January 21, 2013
Accepted: January 31, 2013
Correspondence: Se-Whan Lee, MD, Department of Internal Medicine, School of Medicine, Soonchunhyang University, Cheonan Hospital, 31 Suncheonhyang 6-gil, Dongnam-gu, Cheonan 330-721, Korea
Tel: 82-41-570-3677, Fax: 82-41-574-5762
E-mail: lovelee93@hanmail.net

• The authors have no financial conflicts of interest.

Case

A 69-year-old woman presented to the emergency department of our institution with a three-day history of exertional dyspnea and chest discomfort that had progressed to dyspnea at rest. She complained of a six-year history of numbness in both hands and leg cramps. She was diagnosed as having hypocalcemia secondary to idiopathic primary hypoparathyroidism and was treated with calcium lactate and calcitriol. One year earlier, she had suffered from intermittent cognitive dysfunction with memory loss and was diagnosed with senile dementia. Thereafter, she was irregularly given medication to treat hypoparathyroidism. One month before the present admission, calcium lactate and calcitriol had been discontinued. On arrival, physical examination revealed low blood pressure (90/60 mm Hg), tachycardia with a heart rate of approximately 102 beats per minute, and tachypnea with a respiration rate of 25 per minute. Her body temperature was 36.4°C and oxygen saturation on room air was 90%. Chest auscultation revealed rales in the bilateral lung field without murmur. Spasm and cramps of both extremities were noted but the remainder of the physical and neurological examination yielded no remarkable results. Initial electrocardiogram showed sinus tachycardia, negative T waves in leads V 1-4 and a slightly prolonged QT interval (corrected QT interval=490 msec). Chest X-ray showed cardiac enlargement with pulmonary congestion and

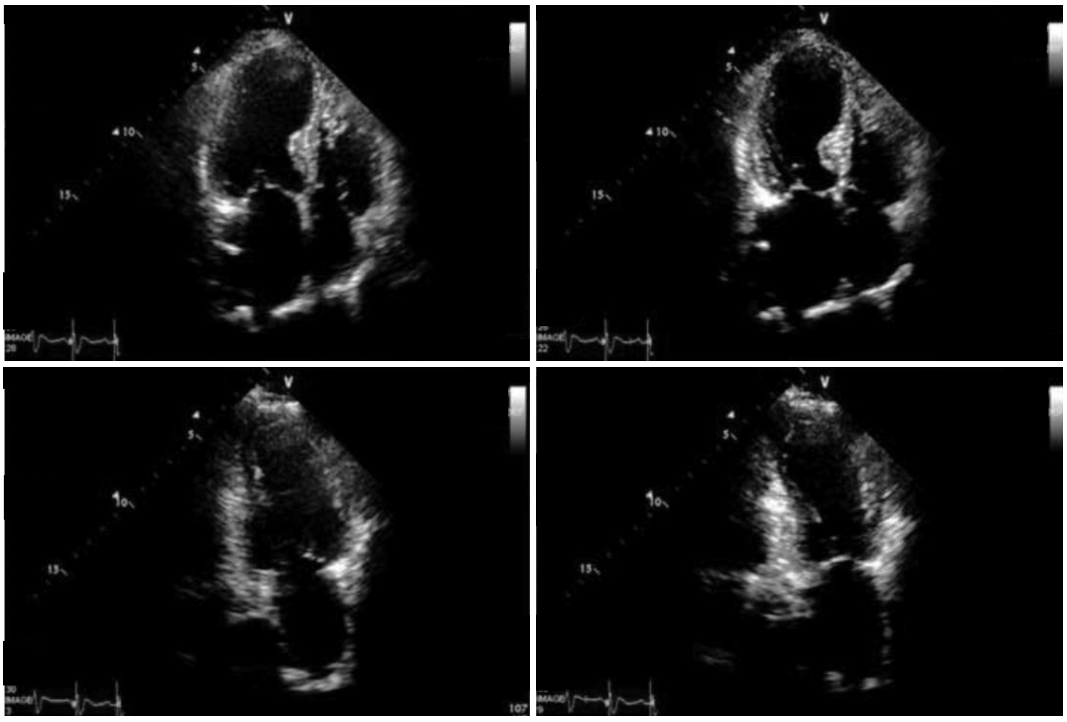

Fig. 1. Echocardiography (left; diastolic phase, right; systolic phase) prior to treatment, showing enlarged left ventricle with apical ballooning and severe mid-segment hypokinesia during systole, sparing basal segment.

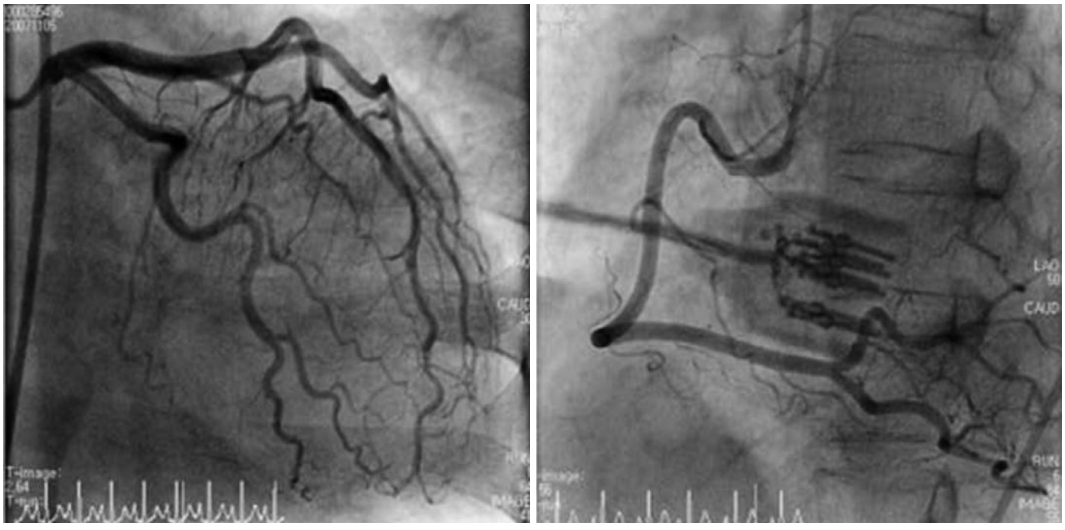

Fig. 2. Coronary angiography showing nearly normal coronary artery.

both pleural effusion. Laboratory testing indicated the following results: total serum calcium concentration, 5.0 mg/dL (reference range: 8.0-10.5 mg/dL), with free ionized calcium, 2.8 mg/dL (reference range: 4.0-4.5 mg/dL); serum phosphorous, 6.1 mg/dL; albumin, 3.7 g/dL; creatinine, 0.9 mg/dL; magnesium, 1.9 mg/dL; PTH, 170 pg/mL (reference range: 180-560 pg/mL); intact PTH, 10.7 pg/mL (reference range: 6.2-29.0 pg/mL) and 25-OH vitamin D, 9.3 ng/mL (reference range: 6.9-69.5 ng/mL). N-terminal pro-B-type natriuretic peptide was 12968 pg/mL; creatine phosphokinase, 1029 IU/L; Myoglobin, 91.78 ng/mL; Troponin-T, 0.234 ng/mL, and thyroid function was within the normal range. Initial echocardiography demonstrated a contractile pattern with preserved basal segment, akinesia of the apical segment and severe hypokinesia of the middle segment of the LV, compatible with takotsubo cardiomyopathy (Fig. 1). The ejection fraction was estimated to be 32%. Initial treatment with administration of furosemide, spironolactone, angiotensin II receptor blocker and intravenous calcium gluconate with close monitoring of serum free ionized calcium levels was started. On the fourth day of admission, we performed coronary angiography and a left ventriculogram. The former revealed normal coronary arteries (Fig. 2)

and the latter showed markedly improved LV contractility excluding residual localized akinesia of the mid to apical antero-septal wall, demonstrating the resolving course of the takotsubo cardiomyopathy (Fig. 3). The clinical symptoms and signs of congestive heart failure and the objective parameters of LV systolic function obtained by serial echocardiography improved rapidly after correc-

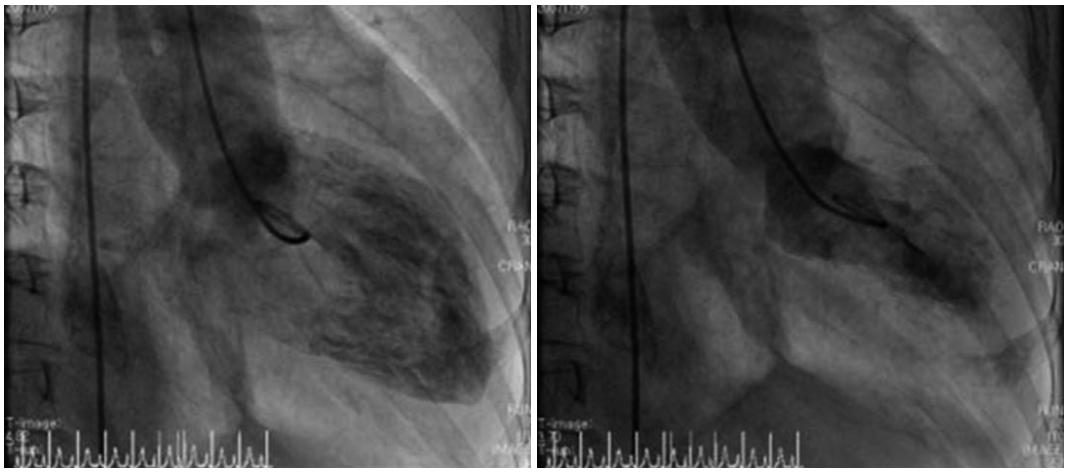

Fig. 3. Left ventriculogram during systole (left) and diastole (right), performed on the fourth day of admission. Note the markedly improved left ventricular contractility and apical ballooning with focal residual wall motion abnormality on the mid to apical antero-septal wall.

Table 1. Serial change of calcium concentration and left ventricular ejection fraction during therapy

Admission day	Ionized calcium (mg/dL)	Total calcium (mg/dL)	Ejection fraction (%)
On admission	2.8	5.0	32 (by echocardiography)
Day 4	3.2	6.4	52 (by ventriculogram)
Day 8	3.8	8.5	58 (by echocardiography)
Day 12	3.9	8.0	65 (by echocardiography)

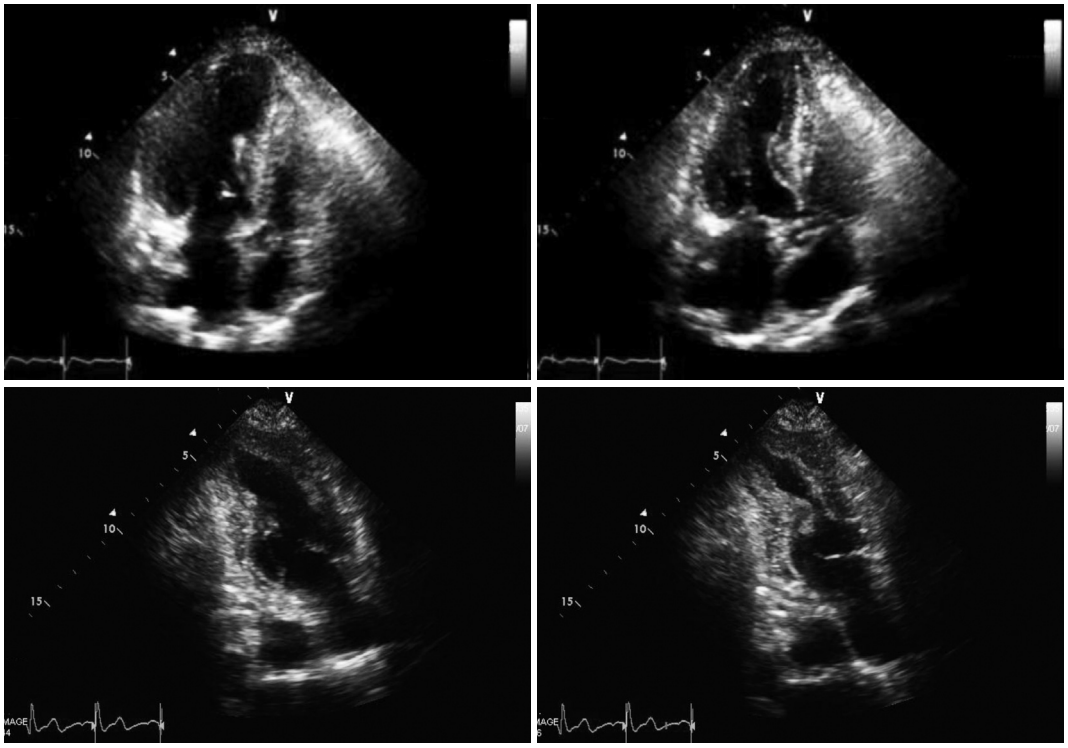

Fig. 4. Echocardiography (left; diastolic phase, right; systolic phase) after treatment, showing complete improvement of the dimension and contractility of the left ventricle.

http://dx.doi.org/10.4070/kcj.2013.43.8.573

tion of the hypocalcemia (Table 1). On the twelfth day of admission, the echocardiographic findings showed complete resolution of the regional wall motion abnormalities of the LV with an ejection fraction of 65% (Fig. 4) and the patient was discharged with no symptoms and signs of either heart failure or hypocalcemia. During the ensuing 18 month follow-up period, repeated echocardiograms showed normal ventricular contractility and there were no further episode of heart failure with the maintenance of daily alfacalcidol and calcium carbonate.

Discussion

Calcium ions play a vital role in the sequence of excitation-contraction and relaxation of the cardiac muscle fibers.[8] Profound and prolonged reduction of serum calcium may result in contractile dysfunction of the myocardium and hypocalcemia is an uncommon but well-known reversible cause of heart failure.[3-5] However, most cases of hypocalcemia-induced cardiomyopathy present with diffuse LV hypokinesia rather than LV apical ballooning.[3-7] As calcium is essentially required for myocardial contractile function, the parathyroid hormone also has a positive inotropic action on the myocardium. This effect probably occurs because the parathyroid hormone increases both the entry of calcium into myocardial cells and the release of endogenous myocardial norepinephrine.[9] There have been several case reports of reversible congestive heart failure associated with hypocalcemia caused by hypoparathyroidism, all of which presented with diffuse LV hypokinesia rather than apical ballooning.[10][11] We herein report a unique case of reversible cardiomyopathy associated with hypocalcemia secondary to untreated hypoparathyroidism presenting with transient LV apical ballooning rather than diffuse LV hypokinesia. Takotsubo cardiomyopathy is an increasingly well-known cardiac syndrome that mimics myocardial infarction. It is characterized by transient wall motion abnormalities involving the apical and mid-portions of the LV that resemble the shape of a traditional Japanese octopus trap, and which occur in the absence of significant obstructive coronary disease.[11][12] Although exaggerated sympathetic stimulation is thought to be the possible mechanism of this syndrome, the current evidence supporting any of the proposed underlying pathophysiological mechanisms is not compelling. Several mechanisms have been proposed to explain the unusual features of this syndrome, such as multi-vessel coronary vasospasm, coronary microvascular dysfunction, and catecholamine-mediated cardiotoxicity.[12-14] Diverse preceding emotional or physical stressors have been identified as the trigger event in most patients with takotsubo cardiomyopathy.[14] However, the precise etiologic and pathophysiologic basis of this syndrome has not been fully clarified. Our case demonstrates the occurrence of takotsubo cardiomyopathy secondary to hypocalcemia, the cause of which was previously diagnosed primary hypoparathyroidism with inadequate replacement of vitamin D due to newly-developed cognitive dysfunction. The attributing factor of hypocalcemia-induced takotsubo cardiomyopathy in our case is justified by the following: 1) no other cause was found in the patient's medical history and examination; 2) coronary angiography showed no coronary artery lesions, and 3) improvement of apical ballooning was achievable after calcium replacement that correlated well with the rising serum calcium level. For the treatment of hypocalcemia-induced cardiomyopathy, calcium replacement is crucial: clinical and hemodynamic improvement could not have been achieved with standard heart failure therapy if the serum calcium deficiency had not been corrected. Initial intravenous calcium infusion consists of 100 to 200 mg of elemental calcium (1 to 2 grams of calcium gluconate) over a period of ten minutes due to the risk of serious cardiac arrhythmias. Slow intravenous calcium infusion should be continued with frequent measurement of the serum ionized calcium level until the symptoms and signs of hypocalcemia and heart failure are controlled and safe and stable ionized calcium levels are achieved. We believe that our case is the first case of takotsubo cardiomyopathy associated with severe hypocalcemia. The clinical signs and symptoms of heart failure and the objective parameters of LV systolic function rapidly improved after correction of the hypocalcemia. Although the precise mechanism of hypocalcemia-induced takotsubo cardiomyopathy remains to be elaborated, and there is no clear relationship between hypocalcemia and the proposed mechanisms of takotsubo cardiomyopathy such as multi-vessel spasm, microvascular dysfunction and catecholamine-mediated cardiotoxicity, we suggest that hypocalcemia should be included as a possible cause of takotsubo cardiomyopathy and physicians should check the calcium level of patients with this syndrome.

References

1. Tsuchihashi K, Ueshima K, Uchida T, et al. Transient left ventricular apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction. Angina Pectoris-Myocardial Infarction Investigations in Japan. *J Am Coll Cardiol* 2001;38:11-8.
2. Kurisu S, Sato H, Kawagoe T, et al. Tako-tsubo-like left ventricular dysfunction with ST-segment elevation: a novel cardiac syndrome mimicking acute myocardial infarction. *Am Heart J* 2002;143:448-55.
3. Bashour T, Basha HS, Cheng TO. Hypocalcemic cardiomyopathy. *Chest* 1980;78:663-5.
4. Chraibi S, Drighl A, Nafidi S, Zahraoui M, Tahiri A, Chraibi N. [Hypocalcemic dilated cardiomyopathy: rare cause of heart failure]. *Ann Med Interne (Paris)* 2001;152:483-5.
5. Levine SN, Rheams CN. Hypocalcemic heart failure. *Am J Med* 1985;

78(6 Pt 1):1033-5.
6. Suzuki T, Ikeda U, Fujikawa H, Saito K, Shimada K. Hypocalcemic heart failure: a reversible form of heart muscle disease. *Clin Cardiol* 1998;21:227-8.
7. Rallidis LS, Gregoropoulos PP, Papasteriadis EG. A case of severe hypocalcaemia mimicking myocardial infarction. *Int J Cardiol* 1997;61:89-91.
8. Opie LH. *Mechanism of cardiac contraction and relaxation.* In: Braunwald E, Zipes D, Libby P, editors. *Heart Disease*. 8th ed. Philadelphia (PA): Saudersi ELSEVIER;2007. p.509-38.
9. Bogin E, Massry SG, Harary I. Effect of parathyroid hormone on rat heart cells. *J Clin Invest* 1981;67:1215-27.
10. Csanády M, Forster T, Julesz J. Reversible impairment of myocardial function in hypoparathyroidism causing hypocalcaemia. *Br Heart J* 1990;63:58-60.
11. Huddle KR. Cardiac dysfunction in primary hypoparathyroidism. A report of 3 cases. *S Afr Med J* 1988;73:242-4.
12. Abe Y, Kondo M, Matsuoka R, Araki M, Dohyama K, Tanio H. Assessment of clinical features in transient left ventricular apical ballooning. *J Am Coll Cardiol* 2003;41:737-42.
13. Wittstein IS, Thiemann DR, Lima JA, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med* 2005;352:539-48.
14. Pilgrim TM, Wyss TR. Takotsubo cardiomyopathy or transient left ventricular apical ballooning syndrome: a systematic review. *Int J Cardiol* 2008;124:283-92.

http://dx.doi.org/10.4070/kcj.2013.43.8.573