Case Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
48(7) 1–8

DOI: 10.1177/0300060520942115
journals.sagepub.com/home/imr
SAGE

Hypocalcemic cardiomyopathy after parathyroidectomy in a patient with uremia: A case report and literature review

Wei Zhang[1], Feng Xue[2], Quandong Bu[1] and Xuemei Liu[1]

Abstract

Hypocalcemia is a rare, but reversible, cause of dilated cardiomyopathy. Although cardiomyopathy may cause severe heart failure, calcium supplementation can reverse heart failure. We report here a patient with uremia and secondary hyperparathyroidism, who was complicated by persistent hypocalcemia and refractory heart failure. The cardiac failure was refractory to treatment with digitalis and diuretics, but dramatically responded to calcium therapy and restoration of normocalcemia. As a result, the patient was eventually diagnosed with hypocalcemic cardiomyopathy. To the best of our knowledge, this is the first case of this disease to be reported in a patient with uremia. Findings from our case may help clinicians to better understand hypocalcemic cardiomyopathy. Our case might also provide new insight into long-term cardiac complications and prognoses of patients undergoing parathyroidectomy due to secondary hyperparathyroidism.

Keywords

Calcium, hypocalcemic cardiomyopathy, hypoparathyroidism, uremia, hypotension, heart failure, secondary hyperparathyroidism

Date received: 12 December 2019; accepted: 23 June 2020

Introduction

Hypocalcemia, irrespective of its etiology, can lead to severe impairment of left ventricular contractility, which manifests as

[1]Department of Nephrology, The Affiliated Hospital of Qingdao University, Qingdao, China
[2]Department of Anesthesiology, The Affiliated Hospital of Qingdao University, Qingdao, China

Corresponding author:
Xuemei Liu, Department of Nephrology, The Affiliated Hospital of Qingdao University, 16 Jiangsu Road, Qingdao 266003, China.
Email: liuxuemei201718@163.com

dilated cardiomyopathy, and is usually defined as hypocalcemic cardiomyopathy.[1] This type of cardiomyopathy may lead to a rarely diagnosed type of heart failure that is refractory to standard therapy, but may be completely reversible when treated properly with calcium and vitamin D. In 1980, Bashour et al.[2] described two patients with hypocalcemia, which was secondary to hypoparathyroidism, who also showed heart dilatation and congestive heart failure. The cardiac failure was refractory to treatment with digitalis and diuretics, but responded to restoration of normocalcemia through calcium therapy. These authors called this condition "hypocalcemic cardiomyopathy." We report a patient with uremia and secondary hyperparathyroidism (SHPT) who was complicated by reversible hypocalcemic cardiomyopathy. To the best of our knowledge, such a case has not been previously reported, and this case may provide clinicians with added insight for treatment of patients with hypocalcemic cardiomyopathy.

Case report

A 62-year-old man was admitted to our department on 12 February 2018 with a longer than 3-month history of progressive dyspnea. Five years earlier, the patient was diagnosed with chronic glomerulonephritis and uremia and had started regular hemodialysis. At the time of that diagnosis, his blood pressure (BP) had been well controlled with medication, and he did not show other symptoms, such as recurrent shortness of breath or dyspnea. He had greatly reduced activity tolerance and experienced obvious wheezing after climbing two flights of stairs. However, he did not have any obvious restriction to walking on a flat surface and did not have nocturnal dyspnea.

During the 3 months before the current presentation, the patient had experienced persistent hypotension, even after discontinuing his antihypertensive drug therapy. Moreover, his BP during hemodialysis was often as low as 80 to 90/50 to 60 mmHg, and ultrafiltration could often not be completed because of his low BP. The patient had also undergone parathyroidectomy and partial parathyroid intramuscular transplantation because of SHPT 5 months before the current presentation (Table 1). Thereafter, he experienced postoperative hypocalcemia, with serum calcium concentrations as low as 1.2 mmol/L. Despite the hypocalcemia, he did not show any obvious finger twitching or numbness of the skin or extremities. The hypocalcemia improved after calcium supplement therapy and he was discharged (Table 1). The patient started regular hemodialysis, with intermittent blood calcium monitoring or calcium supplementation therapy. He denied any history of hypertension, diabetes mellitus, or coronary atherosclerotic heart disease. He did not have an otherwise abnormal personal or family medical history. The patient did not have a history of drinking or genetic disease.

Upon the most recent admission, a physical examination showed a BP of 95/64 mmHg and a pulse of 80 beats/minute. There was no distension of the bilateral jugular veins. His lungs were bilaterally clear to auscultation, without rales, and his heart rate was regular, without murmurs, gallops, or rubs. The patient's abdomen was soft, without tenderness or rebound pain. His liver and spleen were not palpable. There was no evidence of shifting dullness, his lower limbs were not edematous, and Trousseau's and Chvostek's signs were negative. The patient's laboratory examination results showed a hematocrit of 32.3%, a low serum calcium level, and elevated levels of troponin I and normal creatine kinase-MB (Table 1). The patient's liver and thyroid function was, normal but his corrected QT interval was 0.51 s (normal $\leq$0.44 s, Figure 1). Thoracic computed

Table 1. Clinical indicators and medications used during the two hospitalizations.

		Prior hospitalization		Current hospitalization	
		Before parathyroidectomy	After parathyroidectomy	Upon admission	At discharge
Hemoglobin, g/L (normal, 130–175)		94	93	114	99
iPTH, pg/L (normal, 15–65)		2370.0	19.0	65.59	58.12
Serum calcium, mmol/L (normal, 2.11–2.52)		2.27	1.67	1.58	2.18
Serum phosphorus, mmol/L (normal, 0.85–1.51)		3.28	1.37	1.21	1.17
Serum magnesium, mmol/L (normal, 0.75–1.02)		1.12	0.92	0.98	0.96
Blood pressure, mmHg		107/70 (with antihypertensive drugs)	114/72 (without antihypertensive drugs)	95/64 (without antihypertensive drugs)	112/71 (without antihypertensive drugs)
Dialysis dry weight, kg		73	73	69	69
BNP, pg/L (normal, 0–100)		12.40	107.6	6859.0	1966.0
CK-MB, μg/L (normal, <6.73)				1.26	1.13
hs-cTnI, ng/mL (normal, 0–0.0342)		0.031		0.041	0.032
Myoglobin, μg/L (normal, 28–72)				68	65
Cardiac ultrasound (Figure 1)	LA anteroposterior diameter (cm)	3.7	–	3.9	3.7
	LVDd (cm)	5.2	–	6.4	6.3
	LVDs (cm)	4.1	–	5.5	4.7
	LVEF %	65%	–	27%	48%
Medication		Lanthanum carbonate 750 mg, 3 times/day	Calcium, administered intravenously and accumulated to 8–10 g daily High calcium dialysis (dialysate calcium concentration, 1.75 mmol/L) Calcium was gradually	Vitamin D_3 (0.25 μg, daily) Calcium carbonate and vitamin D3 tablets (1 tablet, daily) (this was a reduction after surgery by the patient)	Calcium, administered intravenously to accumulate (6–8 g, daily while in hospital) High calcium dialysis (dialysate calcium concentration, 1.75 mmol/L) in hospital

(continued)

Table 1. Continued

	Prior hospitalization		Current hospitalization	
	Before parathyroidectomy	After parathyroidectomy	Upon admission	At discharge
		changed to oral vitamin D_3 (0.5 μg, 3 times/day, post-discharge) Calcium carbonate and vitamin D3 tablets (1 tablet, 3 times/day, post-discharge)		Vitamin D_3 (0.25 μg, 2 times/day) Calcium carbonate and vitamin D3 tablets (1 tablet, 3 times/day)

iPTH, intact parathyroid hormone; BNP, brain natriuretic peptide; CK-MB, creatine kinase-MB; hs-cTnI, high-sensitivity troponin I; LA, left atrium; LVDd, left ventricular end-diastolic diameter; LVDs, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction. Calcium carbonate and vitamin D_3 tablets contained 1.5 g calcium carbonate and 125 IU of vitamin D_3.

tomography suggested enlargement of the cardiac shadow and mild coronary artery calcification. Further, echocardiography showed an enlarged anteroposterior diameter of the left atrium, as well as enlarged left ventricular end-diastolic and end-systolic diameters. The left ventricular wall diameter was normal (Table 1). Additionally, the overall magnitude of ventricular wall motion was decreased and the left ventricular ejection fraction was 27%, which suggested left atrial and ventricular enlargement, reduced left ventricular systolic and diastolic function, and mild mitral and tricuspid regurgitation (Figure 2). An abdominal ultrasound did not indicate abnormalities of the liver, suprahepatic veins, gallbladder, pancreas, or spleen, but both kidneys were atrophic.

The reason for the cardiomyopathy in our patient was not apparent. While searching for the cause of cardiomyopathy, we administered calcium supplementation therapy to restore normocalcemia. Digoxin was also used and regular hemodialysis treatment was continuously performed to attempt to improve cardiac function through enhanced ultrafiltration and control of dry weight. However, the patient continued to show poor cardiac function and low BP during the first few days of hospitalization. One week after admission to the hospital (where he underwent four hemodialysis sessions, with a dialysate calcium concentration of 1.75 mmol/L), his dry weight was stabilized at approximately 69 kg. After 1 week of treatment, including calcium supplementation, the patient's heart failure symptoms were greatly attenuated, his BP was stabilized to 110 to 120/65 to 75 mmHg, and he gradually tolerated ultrafiltration during hemodialysis. These results were inconsistent with current traditional therapeutic measures for improving cardiac function. Cardiac color ultrasound was repeated by the same physician, and it showed an improved ventricular

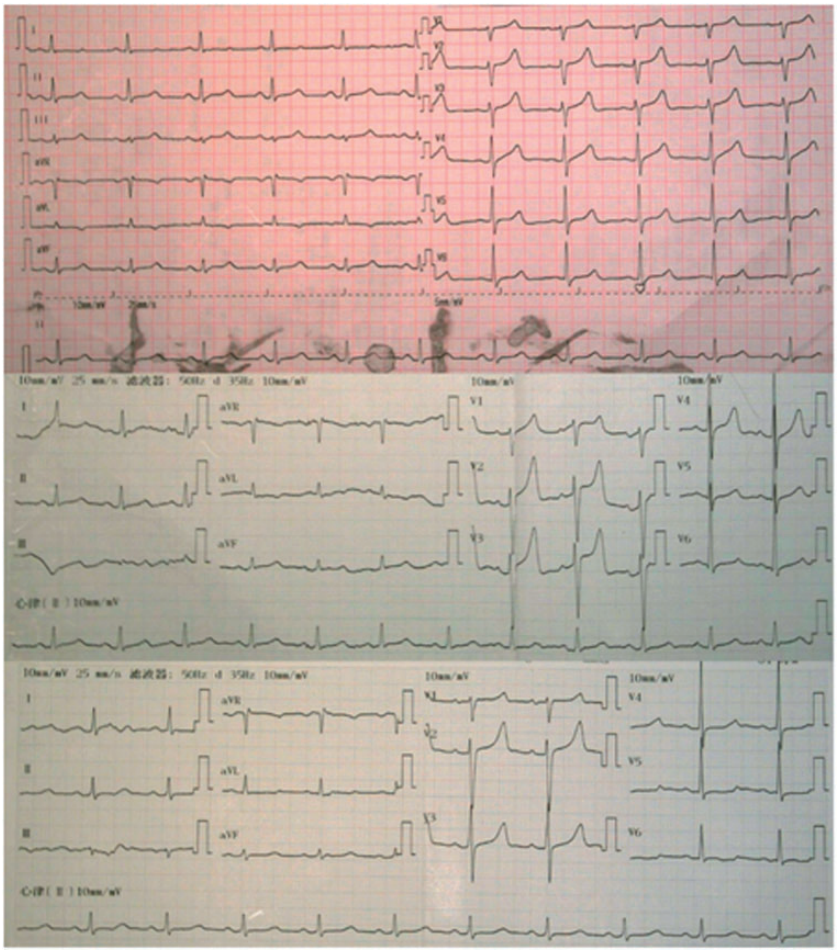

Figure 1. The patient's electrocardiogram in hospital. The electrocardiogram shows a long corrected QT interval (0.48–0.52 s)

anteroposterior diameter and improved left ventricular end-diastolic and end-systolic diameters (Table 1). Further, the patient's left ventricular ejection fraction was 48% and left ventricular function was stronger and greatly improved (Figure 1). Therefore, the final diagnosis was determined to be hypocalcemic cardiomyopathy. The patient was followed for 3 months, during which time his symptoms subsided, his BP remained stable, and his dry weight remained steady at 70 kg. After discharge, the patient was treated with twice daily oral vitamin D_3 (0.25 μg), and calcium carbonate and vitamin D3 (1.5 g of calcium carbonate and 125 IU of vitamin D_3 per tablet) with one tablet, three times/day. Post-discharge, the patient's serum calcium (2.26 mmol/L), phosphorus (1.45 mmol/L), and parathyroid hormone (PTH) (97.71 pg/mL) levels were normal.

As required by our institutional ethics committee, the patient provided informed consent for his treatment and for publication of this anonymized case report. A formal approval number was provided by

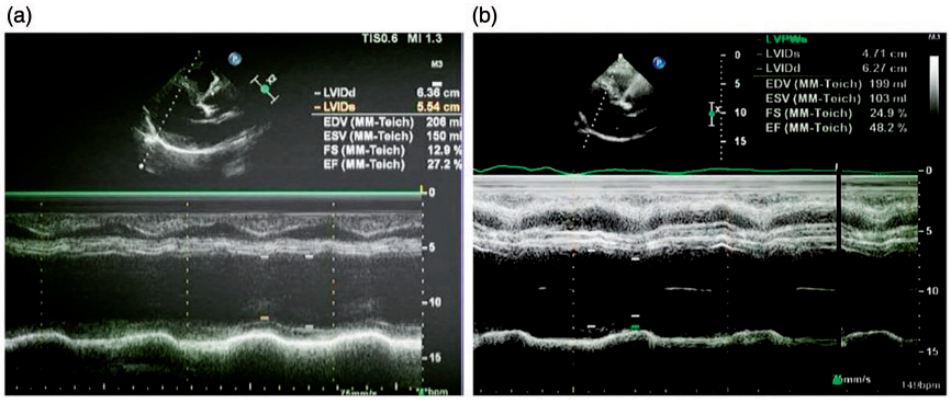

Figure 2. Cardiac ultrasound results. (a) Results obtained upon admission to the hospital for the most recent admission; (b) results obtained following treatment before discharge.

the ethics committee of the Affiliated Hospital of Qingdao University (No: QYFYWZLL25641).

Discussion

Patients with uremia often experience cardiovascular damage because of excessive PTH levels. In some patients, parathyroidectomy or kidney transplantation may improve cardiac function because of decreased PTH levels.[3] However, our patient showed heart failure symptoms after parathyroidectomy, and therefore, the cause of the heart disease needed to be determined. The patient was on maintenance hemodialysis and did not have any infections, or a history of genetic disease or prior cardiovascular disease. Multiple electrocardiograms and myocardial injury marker examinations failed to indicate any apparent changes. Therefore, the diagnosis of acute coronary syndrome or Takotsubo syndrome[4] was not supported. Our patient showed a recent and steady loss of dry weight in the absence of apparent capacity overload. Therefore, his heart failure was suspected to be associated with cardiomyopathy. After diagnostic calcium supplementation, his cardiac function improved and enlargement of his heart decreased in a short time, which was inconsistent with heart failure caused by uremic cardiomyopathy. Therefore, we believe that the patient experienced reversible cardiomyopathy caused by hypocalcemia, leading to a final diagnosis of hypocalcemic cardiomyopathy. To the best of our knowledge, this is the first case of a patient with uremia who was complicated by hypocalcemic cardiomyopathy after undergoing parathyroidectomy.

Findings in this case indicate that clinicians should monitor hypocalcemia after parathyroidectomies, and monitor pre- and postoperative cardiac function in patients with uremia. This is because hypocalcemia is an independent predictor of all-cause mortality in heart failure and chronic kidney disease.[5] Particular attention should be paid to the effects of low PTH levels on cardiovascular disease and survival in these patients. Currently available data on the effects of hypocalcemia and low PTH levels in cardiovascular disease and survival in patients with uremia are clearly insufficient. Therefore, our data may serve as a unique entry point for additional cardiorenal syndrome research.

The current literature indicates that hypocalcemia, hypovitaminosis, and

hypoparathyroidism can lead to reversible cardiomyopathy.[3,6–13] In the present case, there was considerable hypocalcemia and hypoparathyroidism. However, because vitamin D concentrations were not monitored, we are unable to determine if hypovitaminosis was involved in hypocalcemic cardiomyopathy. Hypocalcemia-induced cardiomyopathy is usually reversible when normocalcemia is restored,[6] with normal cardiac function returning within 3 to 12 months. Some case reports have shown that normal cardiac function may be restored within a week of restoring normocalcemia.[7,12,13]

The mechanisms underlying development of dilated cardiomyopathy induced by chronic hypocalcemia remain unclear, despite the pivotal role of calcium in the cardiovascular system being well known. Calcium acts as a messenger via changes in intracellular calcium levels through the actions of calcium channels, exchangers, pumps, and the calcium-sensing receptor.[8,14] Experimental results have indicated that reduced myocardial contractility, in the presence of hypocalcemia, generally presents as reduced left ventricular function and cardiac indicators.[15] Calcium supplementation can increase myocardial contractility and cardiac output. Hypocalcemia can result in reduced calcium-sensing receptor activation, reduced myocardial contractility,[16] and prolongation of the corrected QT interval, potentially leading to life-threating arrhythmias.[16] Our patient had a long history of presumed hypocalcemia, but his cardiac function improved after the hypocalcemia was corrected. This led to the diagnosis of hypocalcemic cardiomyopathy. The role of hypocalcemia in precipitating cardiomyopathy is evident. However, among the many effects of hypocalcemia, cardiomyopathy only rarely develops. This may be due to differences in the calcium ion cycle during the contraction and diastolic phases of cardiomyocytes and skeletal muscle cells. Persistent severe hypocalcemia induces cardiac inhibition without affecting skeletal muscle function, which means that cardiac dysfunction caused by hypocalcemia is easily overlooked.[9] However, cardiomyopathy may also be related to genetic susceptibility or other factors that have not yet been determined.

PTH plays a vital role in the cardiovascular system, although its primary function is maintenance of calcium homeostasis. When normal PTH levels are disrupted, PTH might affect pathological and physiological function of the heart. Hypoparathyroid cardiomyopathy is a rare heart disease that can present as reduced myocardial tension, cardiac cavity enlargement, arrhythmia, and congestive heart failure.[17] Development of hypoparathyroid-associated cardiomyopathy is primarily associated with hypoparathyroidism-induced hypocalcemia, hypomagnesemia, and hypoparathyroidism. In the present case, whether the sudden changes in blood calcium and PTH levels affected the cardiovascular system remain unclear.

Uremia-related cardiovascular disease, which is the leading cause of death in patients with uremia, is presently an active research topic among cardiorenal syndrome researchers. However, insufficient attention is currently being paid to changes in cardiac function and BP, as well as to factors that affect these cardiac variables, in patients with uremia before and after surgery for SHPT. We should monitor serum calcium levels in all patients undergoing hemodialysis, especially in those with parathyroidectomy, and pay close attention to the relationship between hypocalcemia and cardiac function. Additionally, questions regarding whether persistently low postoperative PTH levels benefit patients with uremia or cause higher mortality require in-depth exploration and discussion.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

ORCID iD

Wei Zhang https://orcid.org/0000-0001-7233-6062

References

1. Chavan CB, Sharada K, Rao HB, et al. Hypocalcemia as a cause of reversible cardiomyopathy with ventricular tachycardia. *Ann Intern Med* 2007; 146: 541–542.
2. Bashour T, Basha HS and Cheng TO. Hypocalcemic cardiomyopathy. *Chest* 1980; 78: 663–665.
3. Zand L and Kumar R. Serum parathyroid hormone concentrations and clinical outcomes in ESRD: a call for targeted clinical trials. *Semin Dial* 2016; 29: 184–188.
4. Andreozzi F, Cuminetti G, Karmali R, et al. Electrolyte disorders as triggers for Takotsubo cardiomyopathy. *Eur J Case Rep Intern Med* 2018; 5: 000760.
5. Miura S, Yoshihisa A, Takiguchi M, et al. Association of hypocalcemia with mortality in hospitalized patients with heart failure and chronic kidney disease. *J Card Fail* 2015; 21: 621–627.
6. Avsar A, Dogan A and Tavli T. A rare cause of reversible dilated cardiomyopathy: hypocalcemia. *Echocardiography* 2004; 21: 609–612.
7. Yilmaz O, Kilic O, Ciftel M, et al. Rapid response to treatment of heart failure resulting from hypocalcemic cardiomyopathy. *Pediatr Emerg Care* 2014; 30: 822–823.
8. Bansal B, Bansal M, Bajpai P, et al. Hypocalcemic cardiomyopathy-different mechanisms in adult and pediatric cases. *J Clin Endocrinol Metab* 2014; 99: 2627–2632.
9. Jung YJ, Kim SE, Hong JY, et al. Reversible dilated cardiomyopathy caused by idiopathic hypoparathyroidism. *Korean J Intern Med* 2013; 28: 605–608.
10. De Oliveira Martins Duarte J, Pestana Pereira PML, Sobral ASG, et al. A rare and reversible case of heart failure-hypocalcemia due to hypoparathyroidism. *Clin Case Rep* 2019; 7: 1932–1934.
11. Saini N, Mishra S, Banerjee S, et al. Hypocalcemic cardiomyopathy: a rare presenting manifestation of hypoparathyroidism. *BMJ Case Rep* 2019; 12: e229822.
12. Batra CM and Agarwal R. Hypocalcemic cardiomyopathy and pseudohypoparathyroidism due to severe vitamin D deficiency. *J Assoc Physicians India* 2016; 64: 74–76.
13. Elikowski W, Malek-Elikowska M and Lachowska-Kotowska P. Severe reversible hypocalcemic cardiomyopathy diagnosed 36 years after subtotal thyroidectomy - a case report. *Pol Merkur Lekarski* 2017; 43: 26–31.
14. Szent-Györgyi AG. Calcium regulation of muscle contraction. *Biophys J* 1975; 15: 707–723.
15. Lamb GD. Excitation-contraction coupling in skeletal muscle: comparisons with cardiac muscle. *Clin Exp Pharmacol Physiol* 2000; 27: 216–224.
16. Tfelt-Hansen J, Hansen JL, Smajilovic S, et al. Calcium receptor is functionally expressed in rat neonatal ventricular cardiomyocytes. *Am J Physiol Heart Circ Physiol* 2006; 290: H1165–H1171.
17. Schlüter KD and Piper HM. Cardiovascular actions of parathyroid hormone and parathyroid hormone-related peptide. *Cardiovasc Res* 1998; 37: 34–41.