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A reversible hypocalcemia dilated cardiomyopathy caused by primary hypoparathyroidism

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ABSTRACT

Dilated cardiomyopathy (DCM) is characterized by dilation and impaired contraction of one or both ventricles. Affected patients have impaired systolic function and may or may not develop overt heart failure (HF). Prognosis is generally poor without heart transplantation. We experienced a case of a 10-year-old child with dilated cardiomyopathy (DCM) accompanied by undiagnosed primary hypoparathyroidism. In our case, aggressive management of hypoparathyroidism significantly improved the manifestations of DCM. The case presentation highlights the importance of considering hypoparathyroidism as a cause of reversible myocardial dysfunction.

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INTRODUCTION

Cardiomyopathy is a rare but life-threatening condition in children with a reported incidence of 1.1/100 000 children. [1]Dilated cardiomyopathy (DCM) is the most common type of cardiomyopathy.The causes include myocarditis, toxins, metabolic disturbances, genetic factors and other unknown reasons. The presenting manifestations can include heart failure,atrial and/or ventricular arrhythmias, and sudden death can occur at any stage of the disease. The congestive heart failure is irreversible in most conditions but except the courses including alcohol drinking, pregnancy, chronic uncontrolled tachycardia, hypothyroidism, hyperthyroidism, drug use and other endocrine dysfunctions.

Hypoparathyroidism (HPT) is characterized by anabnormally low level of secretion of the parathyroid hormone(PTH), a hormonal factor that is very important in calciumbalance and homeostasis. Theconsequence of PTH deficiency is hypocalcaemia. Within the cardiovascular system, hypocalcaemia is known to both impair myocardial contractility and prolong the QT interval, which predisposing to ventricular arrhythmias.

We present a 10-year-old patient of DCM with hypoparathyroidism. The patient kept healthy status and had normalization of the left ventricular ejection fraction with mini-field left ventricular size as well as shortened QTc during normalization of calcium within a 2-year-follow-up.

CASE REPORT

A 10-year-old female was brought to the emergency room with severe dyspnea. She had suffered progressive dyspnea for 2months and developed 5 days before admission. On physical examination, the vital signs were shown such as blood pressure 100/70 mmHg, pulse rate 120 beats per minute, respiratory rate 26 breaths per minute and O_2 saturation 96% in room air. In addition, the patient had pale and dry skin. Heart rate was regular and a second

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grade systolic murmur was heard at the apex. Breath sounds were decreased with no rales on both sides of the lung field. Liver was palpable two fingers and neck vein distension was observed.The patient also had bilateral presence of non-pitting edema of the foot and ankle. On physical examination, neurological system was intact. Chest x-ray revealed prominent cardiomegaly with pulmonary congestion. After one hour of admission, she presents a syncope after admission, electrocardiography showed Torsades de pointes (TdP) (Figure 1) and laboratory studiesrevealed reduced total serum calcium of 1.01 mmol/dL (reference range 2.23 to 2.80).TdPwas eliminatedafter administration of calcium and magnesium sulfate delivered and external cardiac massage.

Later electrocardiography (ECG) (Figure 2) showed a prolongation of QT interval (560ms) at the expense of the ST segment and inverted T wave in v_1-v_6. Echocardiogram (ECHO) (Figure 3)revealed normalanatomic relations between heart chambers and great vessels. Severely dilated left atrium and left ventricle with in walls andpoor contractility were noted. The shortening fraction (SF) was 12% (normal range 28–40%) andejection fraction (EF) was 28% (normal range 55–65%). The diastolic and systolic dimensions of the LV were 60 and 53 mm, respectively. Moderate mitraland tricuspid valvular regurgitation were identified. Based on her symptoms and the results of the accessory examinations,we could make a diagnosis of congestive heart failure.

Additional studies were performed to determine the etiology of congestive heart failure. Laboratory studies revealed reduced total serum calcium of 0.88 mmol/dL (reference-range, 2.10 to 2.90), magnesium of 0.69 mg/dL (reference-range, 0.8 to 1.0). The phosphorus and creatinine levels were 2.4mmol/dL (reference range, 1.29 to 2.26) and 1.5 mg/dL (reference range, 0.6 to 1.2). Serum levels of creatine kinase-MB and troponin-I were within the respective normal ranges.Hormone analysis was performed and showed free T_4 and thyroid stimulating hormone to bewithin the respective normal ranges, while intact parathyroidhormone (PTH-intact, terminal) level was lower than 3 pg/mL (reference range, 10 to 69). The serum levers of liver function test were within the respective normal ranges. On complete blood counts, the patient had white blood cell counts 5460/mm^3 with 42% neutrophils, hemoglobin 11.8 g/dL and platelets 119000/mm^3. Serum electrolytes showed [Na^+] = 137.7mmol/L,and [K^+] = 3.95meq/L. Fluorescentantinuclear antibody test were also assessed to ruleout autoimmune disease in which their serum levels were withinthe respective normal ranges.Alkaline phosphataseof 239 units/L (normal age appropriate range 150–420 units/L). Brain computerized tomography (CT) showed bilateral and symmetrical

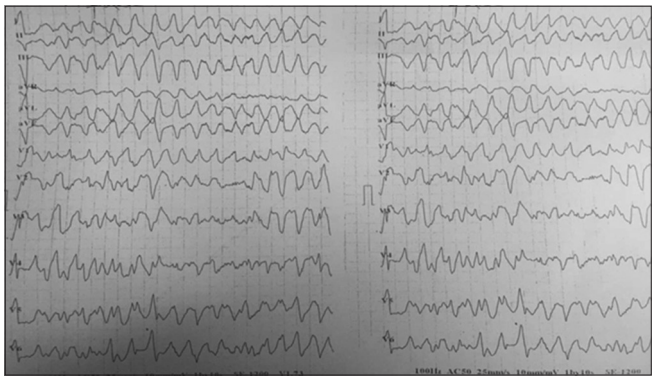

Figure 1: Electrocardiography showed Torsades de pointes(TdP) when syncope happened after admission

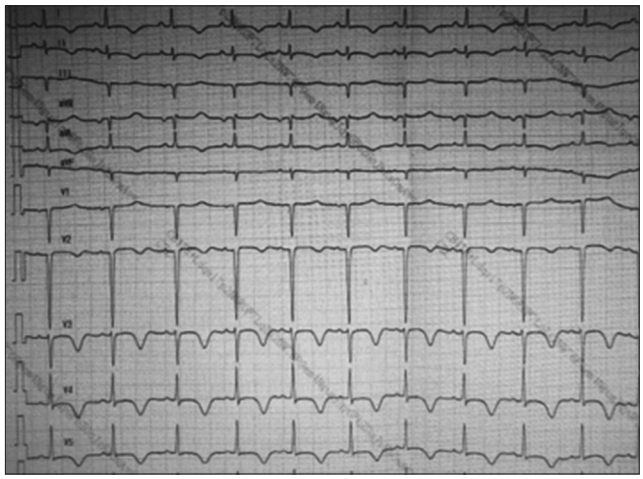

Figure 2: Electrocardiography (ECG) showed a prolongation ofQT,adverse T wave

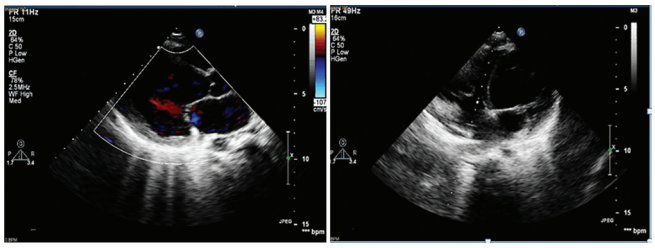

Figure 3: Echocardiogram (ECHO) revealed normalanatomic relations between heart chambers and great vessels but severely dilated left atrium and left ventricle with in walls

calcification of basal ganglia. Cardiac magnetic resonance imaging (MRI) (Figure4) showed dilated left atrium and left ventricle with no morphological or functional alterations in delayed enhancement sequences. The patient had no history of congenital heart disease, rheumatic carditis,viralmyocarditis,hypertension, Kawasaki disease, diabetes mellitus, alcohol drinking or smoking. In addition, she complained of a three-year history of tetany in both hands and legcramps. Two year earlier, she had suffered from convulsion nearly one time a monthand then was diagnosed of epilepsy which was treated with antiepileptic drugs.

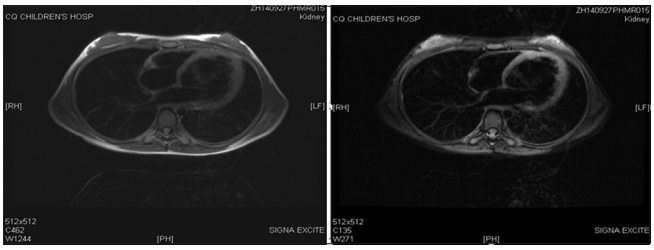

Figure 4: MRI showed dilated left atrium and left ventricle with no morphological or functional alterations in delayed enhancement sequences

In addition, she has no history of neck surgery and no evidence of auto immune disease. Based on these findings, the diagnosis of idiopathic hypo-parathyroidismhypocalcemia-cardiomyopathy was made.

Therapy

Treatment was started with dobutamine and calcium chloride infusion which were graduallytapered and switched to oral anti-failure medications (captopril, digoxin, furosemide, hydrochlorothiazide andspironolactone) and oral calciumand calcitriol.The patient got a remarkable improvement of dyspnea in 5 days. Chest X-ray showed a reduction of cardiomegalywith clearance of pulmonary edema. The initialtotal calcium level was 0.88 mmol/L, and increased to 2.09 mmol/L after several days of calcium supplementation. She was discharged after 10-day-stay and ECHO showed a drastic improvement in SF and EF to 19% and 38% respectively. The LV diastolic and systolic dimensions were decreasedto 60 and 48 mm. The prolonged QT interval was also reduced from 560 ms to 508 ms. The discharge medications included oral calcium, calcitriol, and congestive heart failure medications. Since discharge, the patient has been followed up on a regular basis. After 5 weeks of discharge, the ECHO showed the LV ejection fraction was increased from 38% when discharged to 52%. The LV diastolic and systolic dimensions were decreased to 53 and 37 mm the prolonged QT interval was also reduced to 494ms. Digoxin, hydrochlorothiazide andspironolactone were stopped, metoprolol was added for 1-year further therapy with calcium and calcitriol treatments which were maintained for 2 years until now. Throughout 2-year-follow-up, his serumcalcium has been on the lower side (1.92–2.32 mmol/dL) with normalized phosphorus. The patient remained well without tetany and convulsion, had a gradual increased in left ventricular systolic functions. LV systolic function becomes nearly normal to 53% at six months and 59% at one year after discharge. He also had a gradual decrease in the enlarged left ventricular chamber and reached nearly normal size at 2 years after discharge which was longer than that of the time needed to recovery the heart function. Furthermore the prolonged QT interval wasn't shortened to normal range until recent follow-up which showed 413 ms although the inverse T wave was up-right at one year after discharge.

DISCUSSION

Endocrine system diseases often involving the cardiovascular system. Sometimes the cardiovascular system symptom was the main or only symptoms at first which makes misdiagnosis or missed diagnosis. Early diagnosis and timely treatment of the primary disease is very important for reverse the damage of cardiovascular system.

Idiopathichypoparathyroidism is an infrequent condition of unknown etiology. Accepted criteria for its diagnosis are (a) low serum calcium, (b) high serum phosphates and (c) exclusion of renal insufficiency, steatorrhea, chronic diarrhea, alkalosis and rickets and osteomalacia. It always manifestswith signs of hypocalcemia such astetany, epileptic seizures, hypotension (in acute hypocalcaemia), but the heart is rarely involved. Although reversible congestive heart failure caused by hypocalcemia has been described in previous case reports in adults,[2-4] idiopathic hypoparathyroidism-inducedhypocalcemia cardiomyopathy especially in children was very rare. We presented a case of hypoparathyroidism-inducedcardiomyopathywhich was improved by calcium and vitamin D replacement.

Myocardial dysfunction due to hypocalcemia has been documented in many experimental animal studies, and also in various clinical reports.[2-10] The role of calcium in heart muscle contraction and relaxation is well established.[11] Calcium inside the sarcoplasmic reticulum of the myocardial cells initiates contraction after binding to the troponin–tropomyosin complex resulting in the cross-linkage between the muscle proteins actin and myosin. The strength of the cardiac contraction depends on the amount of influx of the extracellular calcium. The sarcoplasmic reticulum of the cardiac cells cannot sequestrate adequate quantity of the calcium ions to initiate contraction. This is also results in the need for extracellular source of calcium ions. Calcium regulates and carries ionic currents that are responsible for the myocardial action potential and chronicity. Low extracellular [Ca^{2+}] is thought to shift the activation of the action potential to a lower membrane electro-potential thereby increasing excitability. Within the cardiovascular system, hypocalcaemia both impair myocardial contractility and prolong the QT interval, predisposing to ventricular arrhythmias.

Hypocalcaemia as a cause of cardiac dysfunction can easily be overlooked because the clinical symptoms of hypocalcemia, such as fatigue and muscle weakness, are often regarded as subjective and ambiguous in the absence of tetany. Our patient had a 2-year history of tetany and convulsion before admission but was misdiagnosed of epilepsy and treated with anti-epileptic drugs. She was not found to have sever hypocalcaemia until this admission.

She had a syncope with torsade de point when examined after admission and prolonged QT on electrocardiogram (ECG). Later laboratory examination showed a severe hypocalcemia, hyperphosphatemia and remarkably lower level of intact parathyroidhormone.The patient had no history of thyroid surgery,chronic renal failure or other autoimmunity disease symptoms. Finally, the diagnosis of idiopathic hypoparathyroidism was made which was treated with areplacement of calcium and Vitamin D.

In our case, serum level of hypocalcaemia was corrected within several days after calcium supplement. The patient feels well and the LV systolic function improved quickly in one months. However, the improvement of LV chamber size, longed QT interval and inverse T wave was achieved by far later.

Calcium and vitamin D treatment was continued after for over 2 years, LV systolic function and chamber size become more and more normalized although the anti-heart failure drugs stopped early. In the experience of Gurtoo et al,[12] discontinuation of calcium supply leaded reappearance of heart failure. Calcium and vitamin D treatment is most important in treatment of hypokalemia induced cardiomyopathy.

CONCLUSION

We conclude that even though dilated cardiomyopathy is irreversible in most cases, there are few reversible metabolic conditions such as hypocalcaemia of which early diagnosis and aggressive treatment improve the cardiac function significantly

Compliance with ethical standards

*No conflicts and interest.

*Case report involved human participants.

*Informed consent was obtained from all individual participants included in the study.

REFERENCES

1. Lipshultz SE, Sleeper LA, Towbin JA. et al. The incidence of pediatric cardiomyopathy in two regions of the United States. N Engl J Med. 2003; 348:1647-165512711739.
2. Brown J, Nunez S, Russell M and Spurney C. Hypocalcemic rickets and dilated cardiomyopathy: case reports and review of literature. Pediatr Cardiol 2009; 30: 818-823.
3. Price DI, Stanford LC Jr, Braden DS, Ebeid MR and Smith JC. Hypocalcemic rickets: an unusual cause of dilated cardiomyopathy. Pediatr Cardiol 2003; 24: 510-512.
4. Tziomalos K, Kakavas N, Kountana E, Harsoulis F and Basayannis E. Reversible dilated hypocalcaemic cardiomyopathy in a patient with primary hypoparathyroidism. Clin Endocrinol (Oxf) 2006; 64: 717-718.
5. Gulati S, Bajpai A, Juneja R, Kabra M, Bagga A and Kalra V. Hypocalcemic heart failure masquerading as dilated cardiomyopathy. Indian J Pediatr 2001; 68: 287-290.
6. Kosecik M and Ertas T. Dilated cardiomyopathy due to nutritional vitamin D deficiency rickets. Pediatr Int 2007; 49: 397-399.
7. Gupta P, Tomar M, Radhakrishnan S and Shrivastava S. Hypocalcemic cardiomyopathy presenting as cardiogenic shock. Ann Pediatr Cardiol 2011; 4: 152-155.
8. Verma S, Khaddar A, Chopra K, Remit M and Singh S. Hypocalcemia nutritional rickets: a curable cause of dilated cardiomyopathy. J Trop Pediatr 2011; 57: 126-128.
9. Çakërri L, Husi G, Minxuri D, Roko E and Vyshka. G. Primary hypoparathyroidism presenting with heart failure and ventricular fibrillation. Oxf Med Case Reports 2014; 2014(4): 77–79.
10. Velayuthan S, Gungor N and McVie R. Hypocalcemic cardiomyopathy as initial presentation of primary hypoparathyroidism. Pediatrics International 2014; 56:e23–e25.
11. Opie LH. Mechanisms of cardiac contraction and relaxation. In: Braunwald E, editor. Heart disease: a textbook of cardiovascular medicine. Philadelphia: WB Saunders; 2008. p. 509-539.
12. Goswami R, Gurtoo A and Agarwal SK. Worsening heart failure in a case of rheumatic heart disease - the hypocalcaemic link. International Journal of Cardiology 1992;35: 126-127.

Authors Contribution:
ZC- Concept, collected data and review of literature and helped in preparing first draft of manuscript; **SKY-** Concept and design of the study, reviewed the literature, manuscript preparation and review of manuscript; **XL-** Concept of study and review of study; **QY-** Critical revision of the manuscript and study.

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