

Case Report

Primary hypoparathyroidism presenting with heart failure and ventricular fibrillation

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A 24-year-old female presented with sudden heart failure and ventricular fibrillation. A complete work-up suggested the existence of primary hypoparathyroidism in an otherwise previously healthy young woman. Left ventricle enlargement was detected by echocardiography with an ejection fraction of 30%. Electrolyte disorders dominated the laboratory results, with severe hypocalcemia, hypokalemia, hypomagnesemia and other changes, which were corrected with infusion therapy. An improvement of her overall condition prompted a switch from electrolyte infusion therapy to the oral route after the first week of treatment. The patient was discharged under calcium, calcitriol, diuretics and angiotensin-converting-enzyme-inhibitors oral maintenance therapy. Two months after discharge, her ejection fraction remained low (33%), although the end-systolic volume had returned to normal values, and her general status had substantially improved. Within a period of 4 months her cardiac function improved significantly and the follow-up surveillance echocardiography showed an ejection fraction of 53%, with normal left ventricle dimensions.

INTRODUCTION

Primary hypoparathyroidism (PHPT) is characterized by an abnormally low level of secretion of the parathyroid hormone (PTH), a hormonal factor that is very important in calcium balance and homeostasis. PTH regulates calcium metabolism through several routes including activation of osteoclasts that results in bone resorption, the renal absorption of calcium in distal tubule, stimulation of 1- α hydroxylase; thus influencing the formation of 1, 25-dihydroxy vitamin D, as well as the inhibition of proximal tubular transport of phosphates. In the absence of PTH, these effects cannot occur. Therefore, the consequence of PTH deficiency is hypocalcemia [1].

The etiologies most frequently related to PHPT include neck surgery with excision of all parathyroid glands, irradiation and hungry bone syndrome following a parathyroidectomy for hyperparathyroidism [2]. Less frequently, it may have an autoimmune basis or be caused by genetic mutations. In such cases, skeletal malformations are also present [3, 4].

Clinical manifestations of PHPT are variable but proportionally related to the severity of hypocalcaemia that derives from the hormone deficiency. Symptoms may be trivial and thus initially neglected, but tetany, laryngeal spasm, seizures,

heart failure and ventricular arrhythmias are some of the life-threatening occurrences in this setting [5, 6].

CASE REPORT

A 24-year-old Caucasian female presented to the emergency room (ER) of our hospital following a 2-week history of dyspnea, persistent cough and orthopnea. In the ER, she had two episodes of ventricular fibrillation and a defibrillator was used to convert her cardiac rhythm. From her history, the most relevant detail was bilateral ocular cataracts diagnosed 4 months before, but no seizures or cardiac complaints had occurred before this 2-week period. She did not have any family history for dilated cardiomyopathy or sudden cardiac death and no metabolic screening was previously done for the cataracts.

On examination, she was pale and was breathing at 26 breaths per minute. The pulse rate was 125/min, with an arterial blood pressure of 80/50 mmHg; without pulsus paradoxus. On lung auscultation crackles were heard bilaterally up to the level of the middle fields. The jugular veins were not dilated. The heart sounds were distant and a 2–3/6

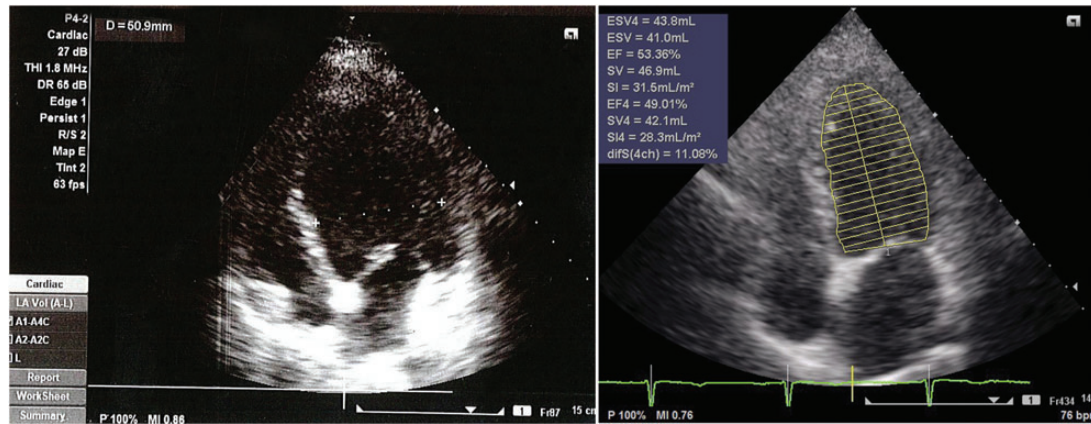


Figure 1: Left insert; Admission echocardiography, with enlargement of left heart chambers. Right insert; Cardiac echocardiography 6 months after the episode, with considerable improvement of EF.

Table 1: Plasma values of electrolytes upon admission and after the first week of treatment

Electrolyte (total plasma values)	Upon admission	After the first week of treatment	Normal values
Calcium	1.3 mmol/l	2.8 mmol/l	2.2–2.7 mmol/l
Potassium	2.5 mmol/l	3.6 mmol/l	3.5–5.0 mmol/l
Sodium	132 mmol/l	141 mmol/l	136–142 mmol/l
Magnesium	0.6 mmol/l	1.1 mmol/l	0.70–1.10 mmol/l
Phosphate	5.2 mmol/l	1.8 mmol/l	0.81–1.45 mmol/l

holosystolic murmur was heard at the apex. The abdominal and neurological examinations were normal.

The ECG 2 h after cardioversion showed a sinus rhythm. The patient's heart rate was 89 b.p.m. and the QT corrected interval 450 ms. The initial echocardiography performed in the ER suggested diffuse hypokiniesis of the left ventricle and an impressive enlargement of the left cardiac chambers (*Left insert*, Fig. 1). No increase in the right cardiac chambers' volumes was suggested by this examination.

Upon admission, the patient's ejection fraction was 30% (normal 55–70%), with an end-systolic volume of the left ventricle of 135 ml (normal values of our center, for adult women, 42 ± 12 ml), suggesting a serious cardiac condition. Blood analysis showed hemoglobin values slightly below normal (10.2 g/dl; normal 12–15.6 g/dl). Electrolyte studies detected remarkable abnormalities, with profound hypocalcemia and hypokalemia, and hyperphosphatemia, hypomagnesemia and hyponatremia of a lesser gravity (see Table 1).

I.v. administration of calcium gluconate at a rate of 0.3 mEq/min was started, and the patient's serum calcium levels were monitored every 6 h. Other supportive therapeutic measures were added, such as saline infusions that included potassium and magnesium supplements. The patient received

i.v. calcium infusions over 6 days, and her plasma calcium values returned to normal during this period (Table 1). The suspicion of a PHPT was confirmed through the PTH value, which was found to be 0.5 pg/ml (normal values 11–54 pg/ml), thus significantly below normal, on a sample taken the day of admission. Calcitriol was added the second day of infusion therapy.

The biochemical studies including urea, creatinine, bilirubin, hepatic transaminases and protein electrophoresis were normal. Owing to her young age, a full set of autoimmune parameters was analyzed, including anti-Ro, antinuclear antibodies, rheumatoid factor and erythrocyte sedimentation rate, all of which were within normal values. The patient's thyroid hormone levels and ultrasound showed no abnormality and thyroid-peroxidase antibodies and anti 21-hydroxylase antibodies were negative.

After the initial i.v. therapy, the patient was switched to oral supplements of calcium (as carbonate calcium, 1 g daily) and calcitriol (0.25 μ g daily). A potassium-sparing diuretic (spironolactone 50 ml twice daily), a loop diuretic (furosemide 40 mg/daily) and an angiotensin-converting-enzyme inhibitor (zofenopril 15 mg/daily) were added to the maintenance therapy. Spironolactone was added for two reasons; in the setting of the heart failure, and for its potassium-sparing effects, considering the initial electrolyte disorders and also the administration of furosemide which could probably aggravate them.

A 24 h Holter ECG monitoring, physical examination and laboratory tests on the discharge showed no abnormalities. Close monitoring of her medical status from her family physician was recommended.

Based on the laboratory and echocardiography findings, a diagnosis of heart failure due to hypocalcemia was suspected. Two months after the episode, the patient was re-examined by the cardiologist. The left ventricle seemed to have regained much of its functionality, with an end-systolic volume of 80 ml. However, the ejection fraction remained abnormally low (33%). During the follow-up visit, she was breathing

normally, and no conduction disorders were detected. The echocardiogram repeated after 4 months showed a significant cardiac function improvement with an ejection fraction of 53% and normal left ventricle dimensions (*Right insert, Fig. 1*). Based on these findings and the improvement of cardiac function a diagnosis of heart failure due to hypocalcemia was warranted.

DISCUSSION

Hypocalcemia, together with hypokalemia and hypomagnesemia, is an important factor accounting for myocardial cytotoxicity in stressor states [7]. This hypothesis, formulated half a century ago by Fleckenstein, is still a milestone of the theoretical framework to explain non-coronary causes of myocardial necrosis. Hypocalcemia and hyperphosphatemia are due to the deficiency of PTH. Other electrolyte disorders can be explained by reduced effective arterial blood volume and reduced renal blood flow in patients with congestive heart failure. Compensatory mechanisms are activated including the renin–angiotensin–aldosterone system, vasopressin release and enhanced sympathetic nervous system. These factors evoke sodium and water retention contributing to hyponatremia of hemodilution, induced hypokalemia and hypomagnesemia.

Heart failure of unknown origin and of sudden onset in a young patient has a large differential diagnosis. Myocarditis is the most probable cause, but medications, drug abuse and other toxic factors should be cautiously scrutinized, with a long list of chemicals imputed [8]. End-systolic volume is generally considered to be more reliable regarding to prognosis of left ventricle failure, and a value of <130 ml is considered to be a good prognostic factor [9]. In our case, the end-systolic volume on admission was higher than this, but the case had a relatively good outcome. The young age of the patient, the lack of neurological complications and the intensive therapy contributed to this outcome.

Nevertheless, 2 months after the episode, the ejection fraction was still low, but sometimes it can take up to 6 months for the cardiac function to return to normal in case of heart failure due to hypoparathyroidism. An echocardiogram repeated after 4 months showed significant improvement of cardiac function

(ejection fraction 53%) and normal left ventricle dimensions that confirmed the diagnoses of heart failure due to hypoparathyroidism. The patient was recommended continuous oral therapy with calcium supplements and calcitriol. Guidelines for the long-term treatment of PHPT are available, and therapeutic options seem efficacious for the stable control of plasma calcium levels [10].

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