CASE REPORT

Hypocalcemic cardiomyopathy☆

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Abstract The association between hypocalcemia and heart failure is rare. There are few reported cases in the literature of this association, which is termed hypocalcemic cardiomyopathy.

We report the case of a 61-year-old woman with no relevant medical history, admitted for progressively worsening exertional dyspnea, orthopnea and edema of the lower limbs over a period of one month. Physical examination showed diffuse muscle spasms, with no signs of latent tetany.

Further investigation revealed ionized calcium 0.54 mmol/l (normal 1.12–1.30), phosphorus 9.8 mg/dl, parathyroid hormone <2.5 pg/ml and CK >3000 U/l, with normal thyroid function. The electrocardiogram showed long QT interval and a pattern of left ventricular overload, and myocardial biomarkers were negative. The echocardiogram revealed regional wall motion abnormalities, coronary angiography was normal and a cranial CT scan detected calcification of basal ganglia and white matter.

She started diuretic and calcium replacement therapy which resulted in complete clinical recovery, with no need for heart failure therapy after normalization of serum calcium.

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Introduction

The clinical syndrome of heart failure (HF) results from congenital or acquired alterations to cardiac structure and/or function that are manifested by an imbalance between cardiac output and tissue oxygen requirements.\(^1,2\)

Among the different etiologies of HF are the cardiomyopathies, which are classified according to morphological type as dilated, restrictive and hypertrophic. Some forms of dilated cardiomyopathy, due to metabolic or toxic causes, are reversible (Table 1).\(^3\)

Calcium plays an essential role in myocardial metabolism, and hypocalcemia reduces myocardial contractility. However, HF of this etiology is rare, with few cases reported in the literature,\(^4\) but in most of these cases, correction of hypocalcemia led to resolution of HF.

Only one case has been reported in Portugal of dilated cardiomyopathy associated with post-surgical hypothyroidism, in which hypocalcemia, also in the context of post-surgical hypoparathyroidism, was the factor triggering decompensation of HF.\(^5\)

Case report

We report the case of a 61-year-old woman from Brazil, where she had been a mathematics teacher, resident for around a year in Portugal, where she worked as a cleaner. She had a history of surgery for bilateral pseudophakia over 15 years previously; she reported no other previous conditions, relevant family history or cardiovascular risk factors, was taking no medication, and did not drink or smoke.

She had been asymptomatic until three months before admission, when she began to experience worsening exertional dyspnea, associated with orthopnea in the three days before admission. She reported no paroxysmal nocturnal dyspnea, chest pain, palpitations, syncope, cough, expectoration or fever throughout this period.

Due to symptoms on minimal exertion she went to the emergency department, where examination showed mental confusion, psychomotor slowing, depressed facial expression, blood pressure 97/59 mmHg, rhythmic heart rate 79 bpm, respiratory rate 28 cpm, thinning of the outer third of the eyebrows, limb tremor and muscle spasms, but no Chvostek or Trousseau sign. Crackling rales were audible in the lower half of both lung fields, as well as an S3 gallop and a grade I/VI systolic murmur more clearly audible in the mitral area. The rest of the physical exam was normal.

Further diagnostic tests revealed normal myocardial necrosis markers, elevated BNP, rhabdomyolysis, severe hypocalcemia and type 1 respiratory failure (Table 2). The electrocardiogram (ECG) (Figure 1) showed long QT interval (QTc 0.53 s) and T-wave inversion in V2–V4 and DI. The posteroanterior chest X-ray (Figure 2) revealed interstitial infiltration in the lower third of both lung fields, suggestive of edema.

The bedside echocardiogram in the emergency department showed left ventricular dilatation (60/44 mm) with

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**Table 1** Metabolic etiologies of reversible cardiomyopathy.

<table>
<thead>
<tr>
<th>Congenital</th>
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<tbody>
<tr>
<td>Glycogenoses</td>
<td>Mucopolysaccharidoses</td>
</tr>
<tr>
<td>Fabry disease</td>
<td>Hemochromatosis</td>
</tr>
<tr>
<td>Danon disease</td>
<td>Friedreich ataxia</td>
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<table>
<thead>
<tr>
<th>Acquired</th>
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<tbody>
<tr>
<td>Hypothyroidism</td>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>Alcohol/drug toxicity</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Pheochromocytoma</td>
</tr>
<tr>
<td>Acromegaly</td>
<td>Beriberi</td>
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**Table 2** Initial laboratory assessment.

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
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<tbody>
<tr>
<td>LDH cholesterol (U/l)</td>
<td>989</td>
</tr>
<tr>
<td>CK (U/l)</td>
<td>3784</td>
</tr>
<tr>
<td>NT-proBNP (pg/ml)</td>
<td>3994</td>
</tr>
<tr>
<td>TSH (U/ml)</td>
<td>1.32</td>
</tr>
<tr>
<td>Troponin (ng/ml)</td>
<td>&lt;0.04</td>
</tr>
<tr>
<td>pH</td>
<td>7.46</td>
</tr>
<tr>
<td>PO(_2) (mmHg)</td>
<td>67</td>
</tr>
<tr>
<td>PCO(_2) (mmHg)</td>
<td>29</td>
</tr>
<tr>
<td>Ca(^{2+}) (mmol/l)</td>
<td>0.54 (1.13–1.32)</td>
</tr>
<tr>
<td>TSH: thyroid-stimulating hormone</td>
<td></td>
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</table>
diffuse hypocontractility, more marked in the apex, moderately impaired global systolic function (fractional shortening 26%), but no valvular abnormalities or pericardial effusion (Figure 3). A high-resolution thoracic computed tomography (CT) scan showed a low probability of pulmonary embolism. Serological tests for infectious agents commonly found in myocarditis and Chagas disease were negative.

Symptomatic treatment for HF was started with diuretics, angiotensin-converting enzyme (ACE) inhibitors and nitrates, but there was little symptomatic relief and the hypocalcemia was investigated further. Hypocalciuria and hyperphosphatemia were also detected due to reduced parathyroid hormone levels (Table 3). Investigation of the etiology of hypoparathyroidism ruled out cancer, infiltration, and polyglandular and autoimmune syndromes, and a diagnosis of idiopathic hypoparathyroidism was made. Renal ultrasound showed no alterations and a cranial CT scan (Figure 4) detected extensive supratentorial calcification, more evident in the basal ganglia, suggesting typical chronic hypoparathyroidism.

With a provisional diagnosis of HF of unknown etiology and hypocalcemia secondary to idiopathic hypoparathyroidism, the patient continued the above medication, to which were added intravenous calcium carbonate, a phosphate-binding agent (sevelamer) and vitamin D. Progressive normalization of calcium–phosphate metabolism was observed, accompanied by complete reversal of HF symptoms and normalization of ECG and echocardiographic findings (left ventricular size 50/32 mm, no wall motion abnormalities and fractional shortening 36%). Therapy for hypoparathyroidism was maintained but diuretics, nitrates and ACE inhibitors were discontinued. The patient remained asymptomatic.

Cardiac catheterization revealed no significant coronary lesions and normal left ventricular function (ejection fraction 64%).

The association between correction of hypocalcemia and disappearance of HF symptoms, in the absence of an alternative etiology for the latter, confirmed that hypoparathyroidism and resulting hypocalcemia were the cause of her HF.

**Discussion**

Regulation of serum calcium levels depends mainly on parathyroid hormone, in the short term by calcium

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Diagnostic investigation of hypocalcemia.</th>
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<tr>
<td>Ca++ (mg/day)</td>
<td>89.9 (100–320)</td>
</tr>
<tr>
<td>Phosphorus (mg/dl)</td>
<td>9.8 (2.4–5.1)</td>
</tr>
<tr>
<td>Magnesium (mg/dl)</td>
<td>1.9 (1.3–2.7)</td>
</tr>
<tr>
<td>PTH (pg/ml)</td>
<td>&lt;2.5 (14–72)</td>
</tr>
<tr>
<td>Anti-parathyroid antibodies</td>
<td>–</td>
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PTH: parathyroid hormone.
which may explain the psychomotor slowing and depression, which can result in hypoparathyroidism and rickets.

Transient left ventricular dysfunction in one patient revealed myocardial biopsy in one patient revealed myocardial damage. Various causes of acute hypocalcemia were reported, including iatrogenic and autoimmune hypoparathyroidism and rickets. In some cases coronary insufficiency was not formally excluded by angiography, but in most cases the association with HF was strong.

In the case presented, the fact that the patient received combined therapy for HF and hypocalcemia makes it difficult to determine the precise effect of each treatment on the symptomatic improvement observed. However, in some cases in the literature there was no response to conventional therapy, but there was an unequivocal association between the introduction or discontinuation of calcium replacement therapy and improvement or worsening of HF, respectively.

Although in this case, as in most others, there was normalization of ventricular systolic function, this is not always the case. There is no explanation for this in the literature, but it has been suggested that prolonged exposure of the myocardium to severe hypocalcemia may lead to structural damage, as seen in autopsies of cows that died from hypocalcemic cardiomyopathy, which detected widespread microscopic foci of myocardial necrosis. Myocardial biopsy in one patient revealed dilated sarcoplasmic reticulum and size variability in the mitochondria, which may have been secondary to metabolic abnormalities.

Another interesting point is the appearance of acute symptoms of hypocalcemia, including HF, in a patient with signs of chronic disease like calcification of basal ganglia. Decompensation frequently occurs in situations of increased calcium demand such as alkalosis, as seen in our patient, and can perpetuate and worsen hypocalcemia. Rhabdomyolysis can be both cause and consequence of hypocalcemia, by altering membrane electrical activity, increasing the electrical excitability of muscle fibers and resulting in tremors, perpetuating the primary abnormality in a vicious cycle. The duration and severity of hypocalcemia are thus clearly important in triggering cardiac decompensation.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data and that all the patients included in the...
study received sufficient information and gave their written informed consent to participate in the study.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Conflicts of interest

The authors have no conflicts of interest to declare.

References