

Hypocalcaemia as a Reversible Cause of Acute Heart Failure in a Long-Term Survivor of Childhood Cancer

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ABSTRACT

Hypocalcaemia is known for its neuromuscular symptoms, which are rapidly alleviated by intravenous supplementation. Calcium is also essential for both cardiac cell excitability and contraction. We present a case of acute heart failure due to hypocalcaemia in a young male with a complex medical history.

LEARNING POINTS

- Hypocalcaemia is a rare cause of acute heart failure.
- All clinical decisions, although correct and necessary, may have grave consequences in the short and long term.
- Childhood cancer survivors have an excess risk of developing multiple complications, namely heart failure and lung fibrosis.

KEYWORDS

Hypocalcaemia; heart failure; long-term survivor; childhood cancer

CASE DESCRIPTION

We present the case of a 23-year-old Caucasian male who was diagnosed with Hodgkin's lymphoma at the age of 3. He first received chemotherapy with vinblastine, etoposide, bleomycin and prednisone plus radiotherapy, but due to an unsatisfactory response after four cycles he was changed to vincristine, prednisone, procarbazine and doxorubicin. He was considered in full remission at the age of 5. About 10 years later, at a follow-up visit, a new cervical lump was found. The lymph node histology was compatible with thyroid papillary carcinoma and staging showed extra-thyroid invasion, with lung and nodal metastasis. Total thyroidectomy with bilateral cervical lymph node dissection was performed in 2005, combined with eight cycles of radioiodine from 2005 to 2012. After surgery, he was started on levothyroxine, calcium carbonate and calcitriol.

During follow-up our patient started complaining of mild exertional dyspnoea. Lung computed tomography (CT) showed diffuse lung fibrosis; pulmonary function tests (PFTs) were suggestive of mainly restrictive lung disease. He was then admitted to our heart failure and pulmonary hypertension specialty clinic in 2013. At admission he complained of fatigability, dyspnoea at rest and orthopnoea.

Echocardiogram estimated a pulmonary artery systolic pressure (PASP) of 60 mmHg, with a markedly dilated right ventricle and mild right systolic dysfunction, but preserved left systolic function. Cardiac catheterization confirmed a PASP of 70 mmHg, a high pulmonary vascular resistance index (7.32 Wood units) but no response to stimulation with iloprost.

A diagnosis of pre-capillary pulmonary hypertension and lung fibrosis due to radiotherapy and chemotherapy was made. Symptomatic treatment with furosemide 80 mg per day was started and he was discharged.

A few weeks later our patient was re-admitted because of severe worsening of dyspnoea, de novo diplopia and muscle cramps. Physical examination showed blood pressure 108/62 mmHg, heart rate 82 beats per minute, and oxygen saturation of 94% with a fraction of inspired oxygen of 0.21; rales were audible in the lower halves of both lungs and there was no peripheral oedema. Trousseau's sign was elicited while measuring blood pressure. Arterial blood gas analysis showed very low ionized calcium, confirmed by serum measurements: 0.48 mmol/l (normal range: 1.13–1.32 mmol/l). Echocardiogram showed severe systolic cardiac dysfunction, with an estimated ejection fraction of 16%; cardiac magnetic resonance (MR) excluded constrictive pericarditis and confirmed global and severe systolic dysfunction. A diagnosis of acute heart failure and neuromuscular irritability due to severe hypocalcaemia was made. Intravenous calcium supplementation was initiated under close cardiac monitoring.

Our patient showed an uneventful recovery. At discharge he had mild exertional dyspnoea, serum ionized calcium level was 1.16 mmol/l and an echocardiogram showed improved systolic function with an estimated left ventricle ejection fraction of 42%.

DISCUSSION

What is already known

Clinicians are aware of tetany as a hallmark presentation of acute hypocalcaemia. Neuromuscular irritability symptoms – such as muscle spasms and cramps, perioral numbness, paraesthesias of hand and feet, clumsiness and, in severe cases, carpopedal spasm and seizures – must be promptly recognized and addressed. The classic physical findings of this neuromuscular irritability are Chvostek and Trousseau's signs. Chvostek's sign is sensitive but less specific, while Trousseau's sign is less frequent but more specific, and implies more severe and sustained hypocalcaemia^[1].

What is new

Severe hypocalcaemia is a rare but possible cause of acute heart failure. The absolute quantity of ionized calcium that crosses the sarcolemma and the transverse tubules of cardiac cells is insufficient to bring about full activation of the contractile apparatus. Calcium influx into the cardiac cell triggers the release of calcium from the sarcoplasmic reticulum, in a process called calcium-induced calcium release. As a consequence, cardiac muscle contraction ensues^[2,3]. When hypocalcaemia is present, cardiac performance – estimated by ejection fraction – is reduced. All cases of heart failure due to hypocalcaemia published so far demonstrated full systolic dysfunction recovery with calcium supplementation^[2-4].

Why is it significant

This case illustrates how medical iatrogenesis parallels our practice, no matter how thorough and correct it is. This patient presented with acute heart failure due to hypocalcaemia, and we hypothesize that it was precipitated by starting furosemide, since this drug indirectly promotes calcium release to the lumen of the ascending loop of Henle. The literature also suggests that the calcium-lowering effect of furosemide tends to be greater in the presence of established hypoparathyroidism.

This patient also serves as an example of how live-saving treatments in childhood often have grave consequences in the long run. In fact, Mertens et al. showed that childhood cancer survivors have an all-cause absolute excess risk of 8.8 deaths per 1,000 person-years, which is 10.8 times greater than that in general population^[5]. The diminished health status and premature death risk seem to derive from both disease recurrence and other causes of death, 21.3% of which can be attributed to treatments, such as anthracycline-related heart failure and pulmonary restrictive disease and/or lung fibrosis after chemotherapy and radiotherapy exposure^[5,6]. It is also known that organ damage might not be clinically evident until many years later^[6]. Consequently, long-term follow-up of childhood cancer survivors is vital to quickly detect and address complications and to promote secondary prevention (smoking cessation, weight loss and exercise, for example). Cohort studies and case reports also have a role in determining which treatment modalities carry the highest risk and which co-morbidities are to be expected^[6].

In conclusion, we present a rare cause of acute heart failure in a young patient with a complex medical history. It is also a model case for keeping in mind that all medical decisions, even when live-saving, have consequences in the short and long term.

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