Cardiology in the Young

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High-output cardiac failure in the setting of iron deficiency anaemia: a case report

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Brief Report

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Abstract

We present a case of a child with high-output heart failure and severe iron deficiency anaemia-induced dilated cardiomyopathy managed with serial blood transfusions, preload and afterload reducing agents, inotropic therapies, and long-term iron supplementation. The complete resolution of echocardiogram findings of moderate enlargement of all cardiac chambers and moderately depressed left ventricular systolic function was achieved.

The global prevalence of iron deficiency anaemia is nearly 17 per cent in children under 5 years of age, classifying iron deficiency anaemia as a moderate public health issue as defined by the World Health Organization.[1] There is a widely studied association between iron deficiency anaemia and cardiomyopathy with severe anaemia being a strong prognostic factor in those with existing cardiac dysfunction.[2] There remains, however, a paucity of literature clarifying the mechanism of iron deficiency in the development of cardiomyopathy and prevalence of iron-deficiency mediated cardiomyopathy in the paediatric cohort.

Case description

A 4-year-old male with developmental delay, poor weight gain, and inadequate medical care presented with acute lethargy and hypoxic respiratory failure. Two weeks prior to presentation, he began experiencing decreased appetite and increased fatigue. In the setting of limited food acceptance with aversive behaviour, the patient was consuming 40–60 ounces of whole milk daily. His weight (14 kg) was at the 2.63 percentile and his weight-for-length z-score was −1–1.9. The physical exam was remarkable for developmental delay (non-verbal with motor and social delay), generalised pallor, dry mucous membranes, poor dentition, tachypnoea with subcostal retractions, tachycardia with II/VI holosystolic murmur at the left sternal border, hepatomegaly, and symmetric wasting of extremities with decreased muscle bulk throughout. He was diagnosed with chronic malnutrition and moderate subcutaneous fat loss. He was found to have severe microcytic anaemia (Hgb 1.1 g/dL, mean corpuscular volume 63 fL) with profound iron deficiency (Fe < 10 ug/dL, Ferritin < 3 ng/mL, red cell distrubtion width 26.5%). Further evaluation of nutritional status showed pre-albumin 6 mg/dL, carnitine 24 nmol/mL, and copper 60 mcg/dL. The B-type natriuretic peptide was elevated at 66,118 pg/mL. Genetic testing for a comprehensive cardiomyopathy panel was clinically unremarkable with a variant of unknown significance in gene coding for dystrophin – not predicted to alter protein function.

A chest X-ray revealed marked cardiomegaly with prominent pulmonary vasculature. Electrocardiogram demonstrated ectopic atrial rhythm, right axis deviation, and right ventricular hypertrophy without evidence of ischaemic changes. Transthoracic echocardiogram showed moderate enlargement of all cardiac chambers, moderately depressed left ventricular systolic function (left ventricular ejection fraction of 46 % by biplane Simpsons method), mild tricuspid valve regurgitation, moderate mitral valve regurgitation, mild to moderate aortic valve insufficiency, mildly dilated coronary arteries, and small pericardial effusion.

He was diagnosed with acute on chronic decompensated heart failure due to severe iron deficiency anaemia. He was initially given oxygen supplementation with increased fraction of inspired oxygen of 80–100 per cent to augment tissue oxygen delivery in the setting of low haemoglobin. Given the severity and suspected chronicity of the patient's anaemia, gradual serial transfusions of 5 mL/kg packed red blood cells were pursued to maintain haemodynamic stability and prevent pulmonary oedema. Iron deficiency anaemia was managed with intravenous iron, followed by oral ferrous sulphate. Heart failure was managed with diuretics for preload reduction and intravenous milrinone infusion to augment cardiac contractility and lusitropy. During this course of treatment, hypertension developed likely secondary to renin-angiotensin-aldosterone system activation from systemic vasodilation. Central causes were considered, however, remained unlikely given normal head CT imaging. He was later transitioned to enteral goal-directed medical therapy with angiotensin-converting enzyme

(ACE) inhibitors (Enalapril) and potassium-sparing diuretic (Spironolactone). From a nutritional standpoint, he was started on total parenteral nutrition with close electrolyte monitoring. Multivitamins, enteral iron, and carnitine supplementation were introduced. He ultimately required gastrostomy tube placement for chronic oral dysphagia and immature oral skills.

Over the course of a 4-week admission, he had improved left ventricular systolic function with persistent dilated left heart at the time of discharge. Echocardiogram showed moderately dilated left atrium and left ventricle, low normal left ventricular systolic function, left ventricular ejection fraction of 52 per cent by Simpson method, trace mitral regurgitation, and trivial aortic insufficiency. The B-type natriuretic peptide was 4905 pg/mL and haemoglobin stable at 8–9 g/dL at the time of discharge. Repeat echocardiogram imaging six months later showed complete normalisation of the left heart size and left ventricular systolic function. Given the interval improvement, further diagnostic imaging including cardiac MRI was not pursued.

Discussion

Considering the incidence of iron deficiency anaemia in paediatrics and recognising the sequalae of high-output heart failure secondary to severe iron deficiency anaemia, we present this case to highlight the significance of anaemia screening within this cohort.[1,3]

The haemodynamic manifestations of severe anaemia include a decrease in systemic vascular resistance and increase in cardiac output to optimise oxygen delivery to peripheral tissue, generating a high-output cardiac state. Peripheral vasodilation is, in part, secondary to vasodilatory effects of nitric oxide on vascular endothelium.[4] In a study with children ages 5 months–5 years with iron deficiency anaemia predominantly in the setting of inadequate nutritional iron intake, features of overt congestive heart failure were observed in subjects with haemoglobin levels less than 6 g/dL.[5] High-output heart failure in chronic iron deficiency anaemia was observed in this case. The resultant peripheral vasodilation and reduced renal perfusion triggered renin-angiotensin-aldosterone system activation and subsequent vasoconstriction requiring ACE inhibition.

Spironolactone was used for its role in cardiac remodelling through the inhibition of myocardial damage precipitated by aldosterone and increase of norepinephrine uptake in cardiac myocytes.[6] Spironolactone has a previously described role in iron regulation through suppression of hepatic hepcidin, thereby increasing iron availability and overall transferrin saturation.[7]

The sequalae of iron deficiency anaemia on myocardial tissue have been studied in animal models with histopathologic evaluation of iron-deficient subjects demonstrating muscle fibre atrophy, fibroblast proliferation, and global features of dilated cardiomyopathy.[8] Mechanisms of disrupted mitochondrial function, upregulation of hypoxia-inducible genes requiring iron cofactors for inhibition, and alterations in fatty acid metabolism were described in animal subjects with inactivated transferrin receptor in cardiac myocytes[9,10]. Echocardiogram findings of left ventricular dysfunction in these subjects were presumed to be a consequence of cellular changes from iron deficiency.[9,10] In a similar study, following the deletion of cardiac myocyte-specific hepcidin, a hormone involved in iron hemostasis, increased mortality with left ventricular enlargement, and reduced left ventricular ejection fraction ensued in recombinant mice.[10]

In a previously described case, a child with dilated cardiomyopathy from iron deficiency anaemia underwent heart transplantation for progressive left ventricular dilation despite the correction of the underlying anaemia.[3] The presented case supports the reversibility of cardiac dysfunction. Nonetheless, we hope to emphasise the effects of iron deficiency on myocardial tissue and haemodynamics.

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Competing interests. None.

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