Dilated cardiomyopathy as the first presentation of coeliac disease: association or causation?

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Global ventricular impairment is a frequent presentation in clinical practice, but dissection of causative mechanisms from clinical associations is challenging. We present the case of a 19-year-old man who presented with dilated cardiomyopathy as the first presentation of coeliac disease. The manifestation of iron deficiency anaemia prompted gastroenterology input and enabled accurate diagnosis. It is unclear whether coeliac disease was simply coexistent or directly implicated in pathophysiology. Mechanisms may relate to nutritional deficiencies or autoimmune myocarditis arising from cross-reactivity. We advocate early multidisciplinary involvement in such contexts to aid with management strategy. Despite adherence to a gluten-free diet, ventricular dysfunction persisted and he has been referred to a cardiac transplant centre.

KEYWORDS: Coeliac disease, cardiomyopathy, heart failure, micronutrient deficiency

Case presentation

A 19-year-old man was admitted via the Emergency Department (ED) with a 6-week history of exertional breathlessness, associated with orthopnoea, paroxysmal nocturnal dyspnoea and self-limiting coryzal symptoms. There was no history of chest pain, palpitations or syncope. His past medical history was unremarkable, with no background of alcohol excess or recreational drug use. On assessment, he was haemodynamically stable. Examination revealed a grade 3/6 pansystolic murmur, loudest in the apex with radiation to the axilla. There were bibasal coarse crackles on lung auscultation. Jugular venous pressure was not visualised but there was no peripheral oedema. Abdomen was soft and non-tender, with no suggestion of ascites.

Initial testing revealed a profound microcytic anaemia, with a haemoglobin of 6.5 g/dL and a mean corpuscular volume of 60 fL. Renal, liver and thyroid function were normal, as were inflammatory markers. Electrocardiogram (ECG) confirmed new left bundle branch block (LBBB) with a QRS duration of 146 ms. Chest X-ray showed borderline cardiomegaly with a cardiothoracic ratio of 0.52. There was thickening in the horizontal fissure and upper lobe diversion, but no florid pulmonary oedema or consolidation. Rectal examination was unremarkable.

Diagnosis

Based on the initial presentation, differential diagnosis includes cardiomyopathy with prior myocarditis potentially implicated in aetiology. However, this patient also has concurrent anaemia which is of unclear origin.

Initial management and prognosis

Three units of cross-matched blood were transfused with furosemide cover, and he was transferred to the coronary care unit. He was maintained on telemetry but no dysrhythmias were observed. Subsequent echocardiography showed a dilated left ventricle when indexed to body surface area with global hypokinesia and severe systolic dysfunction. There was moderate to severe functional mitral regurgitation into a severely dilated left atrium. Right ventricle was non-dilated with preserved function. Based upon initial findings, a working diagnosis of dilated cardiomyopathy (DCM) secondary to suspected myocarditis was made. He was commenced on conventional pharmacotherapy for heart failure.

Further blood profiling confirmed a low ferritin (21 μg/L) with normal folate and vitamin B12 levels. Haemolysis screen returned negative, although interpretation was limited in view of sampling post-transfusion. Serology excluded presence of autoimmune disease or viral infection. Thiamine, zinc, selenium and lead levels were normal.

After consultation with the haematologists, ferrous sulphate and ascorbic acid were commenced.

Further imaging via cardiac magnetic resonance imaging (MRI) (see Fig 1) corroborated findings from echocardiography, with a quantified ejection fraction of 23. Late gadolinium enhancement confirmed extensive, dense fibrosis affecting both endocardial and epicardial regions with associated myocardial oedema on T2 weighted (oedema) imaging (T2WI). In view of these novel findings, a decision was made to proceed with angiography which confirmed normal coronaries.

Case progression and outcome

The presence of iron deficiency anaemia prompted gastroenterology input, and a push enteroscopy was recommended to visualise the...
Coeliac disease is a multisystem, autoimmune disorder in which there is chronic and permanent intolerance to gluten. Although not typical, iron deficiency anaemia may be the first manifestation. There is the suggestion of familial aggregation for this disorder, with 10% prevalence amongst first-degree relatives stated in historical studies. It also demonstrates association with other autoimmune disorders, such as rheumatoid arthritis and thyroid disease.

DCM is defined by the presence of left ventricular dysfunction associated with chamber dilatation. The differentials are broad, but may include alcohol excess, chemotherapeutic agents and myocarditis. A small cohort of patients has true idiopathic DCM where the aetiology is unknown, although potentially related to an autoimmune pathogenesis.

Further investigations can aid with diagnosis of DCM. Chest X-ray may show cardiomegaly or pulmonary congestion in the context of decompensation. ECG classically confirms sinus tachycardia, but features such as left ventricular strain and bundle branch block (BBB) may also be observed. Ambulatory ECG monitoring is beneficial in identifying significant dysrhythmias, such as ventricular tachycardia, which are of prognostic significance. As with this patient, echocardiography is the mainstay for diagnosis although alternative imaging modalities such as cardiac MRI are considered for select cohorts, such as those with poor acoustic windows or where the underlying aetiology is unclear. Lastly, coronary angiography is appropriate in those with a convincing history or with a high-risk profile.

There is sparse data in the literature to investigate the relationship between coeliac disease and DCM. A single-centre study found a positive association between coeliac disease and idiopathic DCM compared to the general population, where diagnoses were confirmed via biopsy specimens. This corroborated with findings from a large Swedish cohort study, in which the risk of idiopathic DCM was found to be 73% greater in patients with coeliac disease and maintained in subanalyses after adjustment for confounders.

Various hypotheses have been suggested to explain underlying mechanisms. A causative aetiology may be related to the phenomenon of antigenic mimicry, with an autoimmune response directed at antigenic components of both myocardium and small bowel. Autoantibodies may have shared affinity to antigen epitopes in different tissues or, alternatively, different antigens could mimic TTG epitopes. Indeed, patients diagnosed with coeliac disease that adhere to gluten abstinence have been shown to demonstrate significant recovery of ventricular volumes and function, with adjunct suppression of dysrhythmic potential. Other propositions implicate nutritional deficiencies in pathogenesis. Chronic anaemia results in a hyperdynamic state due to neurohormonal activation secondary to peripheral vasodilatation, and can progress to cardiac failure. Malabsorption can additionally result in micronutrient deficits, such as thiamine, calcium, selenium and carnitine. These are perceived as critical mechanistic components of myocardial contractility and deficiency may have precipitant or exacerbating effects. Moreover, cardiac failure is associated with gut oedema, secondary to arterial insufficiency and venous stasis with associated endothelial dysfunction. This reciprocal negative interaction may potentiate nutritional deficits.

**Key learning points**

- This case is one of only a handful in the literature which explores the potential relationship between coeliac disease and DCM.
- It highlights the imperative need for adequate screening in all patients with DCM.
- In particular, index of suspicion should be raised in the context of concomitant nutritional deficiencies.
- A multidisciplinary approach was of significant benefit in formulating the correct diagnosis and instigating a targeted management strategy.
Coeliac disease and dilated cardiomyopathy

Consent to publish
The patient’s written consent was obtained prior to submission of this manuscript.

References

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