

CASE REPORT

Dilated cardiomyopathy associated with celiac disease: A case report

Salma Elnour  | Maram Hashim | Halah Ibrahim

Department of Internal Medicine,
Sheikh Khalifa Medical City, Abu
Dhabi, United Arab Emirates

Correspondence

Salma Elnour, Sheikh Khalifa Medical
City, PO BOX 48793, Abu Dhabi, United
Arab Emirates
Email: Sanour@seha.ae

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Abstract

Background: Celiac disease, an immune-mediated inflammation of the small intestine, occurs in genetically predisposed individuals, and is caused by sensitivity to dietary gluten and related proteins. The global prevalence is approximately 1%. Celiac disease is frequently associated with extra-intestinal manifestations, including iron deficiency anemia, dermatologic eruptions, type 1 diabetes mellitus, thyroid disease, and connective tissue disorders, but is rarely associated with cardiomyopathy. **Case presentation:** Our case describes a 33-year-old woman, who presented with exertional dyspnea and fatigue, and was diagnosed with severe iron deficiency anemia and dilated cardiomyopathy, secondary to celiac disease. **Conclusion:** High clinical suspicion is needed to identify celiac disease in patients diagnosed with dilated cardiomyopathy, as an improvement in cardiac function has been reported with strict adherence to a gluten-free diet.

KEYWORDS

case report, celiac disease, dilated cardiomyopathy, gluten-free diet, hypothyroidism, iron deficiency anemia

1 | BACKGROUND

Celiac disease (CD), an immune-mediated inflammation of the small intestine, occurs in genetically predisposed individuals, and is caused by sensitivity to dietary gluten and related proteins.¹ Globally, the prevalence of celiac disease is 1.4% based on serologic test results and 0.7% based on biopsy results.² Celiac disease is frequently associated with extra-intestinal manifestations, including iron deficiency anemia, dermatologic eruptions, type 1 diabetes mellitus, thyroid disease, neurologic symptoms, and various connective tissue disorders, but is rarely associated with cardiomyopathy.³⁻⁵

2 | CASE PRESENTATION

A 33-year-old Ethiopian woman presented to the emergency department after referral from her dentist for “looking pale.” She reported a 2-month history of exertional dyspnea and fatigue. She denied chest pain, shortness of breath at rest, palpitations, or orthopnea. There was no history of abnormal bleeding or bruising, heavy menses, melena, or hematochezia. The patient denied cough, fever, abdominal pain, diarrhea, or urinary complaints. She denied any rashes or weight loss.

The patient was employed as a housemaid. She had no past medical or surgical history and no previous

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hospitalizations. There was no family history of chronic or autoimmune diseases. She denied taking any prescription or over-the-counter medication. She denied alcohol or illicit drug use and was a non-smoker. The patient also denied sick contacts or recent travel.

On initial examination, she appeared pale, but otherwise healthy. Her body mass index was 20.5. She was afebrile with a temperature of 37 °C, blood pressure of 124/74 without orthostatic changes, heart rate of 88 bpm, and oxygen saturation of 100% on room air. Neck examination revealed a non-tender diffuse goiter, no lymphadenopathy, and jugular venous pressure was not elevated. Cardiovascular examination revealed a grade 3/6 pansystolic murmur, maximum at the apex with radiation to the axilla. Chest examination was clear on auscultation, with no peripheral edema. Abdomen was soft, non-tender with no organomegaly. Joint examination was unremarkable. There were no mucosal ulcers or skin rashes.

Initial laboratories revealed a microcytic anemia with hemoglobin of 32 g/dL (117–155 g/dL), MCV 49.7 fL (81–100 fL), MCH 11.1 pg (27–34 pg), with WBC count of $5.5 \times 10^9/L$ ($4.5\text{--}11 \times 10^9/L$), and platelets of $394 \times 10^9/L$ ($140\text{--}400 \times 10^9/L$). Liver and kidney function tests were normal. Iron studies revealed iron level 1.4 mmol/L (5.8–34.5 mmol/L), transferrin 3.7 g/L (2–3.6 g/L), transferrin saturation 0.02 (0.07–0.42), and ferritin 6 mcg/L (15–150 mcg/L). Vitamin B 12 level was 272 pmol/L (128–648 pmol/L), and folate level was 22.4 nmol/L (10.9–84.5 nmol/L). Hemolysis panel was unremarkable, with an LDH of 162 IU/L (135–214 IU/L) and haptoglobin of 0.64 g/L (0.3–2 g/L).

ECG showed sinus rhythm with left bundle branch block. Serial troponin levels were normal. An echocardiography was performed, which showed a severely dilated left ventricle and severely reduced left ventricular systolic function, with left ventricular ejection fraction of 15–20%. There was severe global hypokinesis of the left ventricle and grade II left ventricle diastolic dysfunction. Doppler samples suggested elevated left ventricular filling pressure. There was mild-to-moderate mitral regurgitation. Pulmonary artery systolic pressure was normal at 30–35 mmHg. A small pericardial effusion was noted.

The patient was admitted to the general medical ward for severe symptomatic iron deficiency anemia. She received 4 units of cross-matched red blood cells. Her hemoglobin subsequently increased to 96 g/L. Further workup showed anti-gliadin IgA 379.6 cu (normal <19.9 cu), anti-gliadin IgG 708.4 cu (normal <19.9 cu), anti-tissue transglutaminase IgA 3671.9 cu (normal <19.9 cu), and anti-tissue transglutaminase IgG 2356.4 cu (normal <19.9 cu). She underwent an upper endoscopy, which revealed normal mucosa. A duodenal biopsy showed total villous atrophy, crypt hyperplasia, and intraepithelial

lymphocytosis, consistent with celiac disease. No granulomas were seen. The dietician was consulted, and the patient was started on a gluten-free diet.

CT cardiac coronaries were performed and revealed a dilated left ventricle and left atrium, absent coronary calcification, with no evidence of coronary anomaly or atherosclerotic disease. The cardiac CT also did not reveal any extra-cardiac abnormalities, such as pulmonary hemosiderosis. Cardiac MRI showed a dilated cardiomyopathy with severely dilated left ventricle, severely reduced left ventricular ejection fraction of 26%, and increased indexed LV mass and mid septal wall enhancement, with small pericardial effusion. The patient was started on a medication regimen that was financially feasible, which included valsartan, bisoprolol, ivabradine, and spironolactone.

To work up the goiter, thyroid function tests were done and showed TSH 22.4 milli (0.27–4.2 milli) and T4 7 pmol/L (12–22 pmol/L), with elevated thyroid autoantibodies TPO Ab 44 IU/ml (normal <34 IU/ml), and Thyroglobulin Ab 1816 IU/ml (normal <115 IU/ml). Other autoimmune workup was performed and showed low C3 0.77 g/L (0.9–1.8 g/L), normal C4, and elevated rheumatoid factor of 64 IU/ml (normal <14 IU/ml). Antinuclear antibody and double-stranded DNA were negative. Ultrasound of the thyroid revealed diffuse thyromegaly, with increased vascularity. The patient was started on levothyroxine supplementation.

On discharge, the patient was doing well with no symptoms of heart failure. Her hemoglobin remained stable after transfusion. The patient was educated about celiac disease and the importance of a strict gluten-free diet, and was scheduled for outpatient follow-up.

3 | DISCUSSION

This case of severe anemia and cardiomyopathy, without gastrointestinal symptoms, highlights the extra-intestinal findings that should raise a high clinical suspicion for celiac disease. Celiac disease has a wide spectrum of clinical presentations, with both gastroenterological and extra-intestinal manifestations.^{1,4,5} Different clinical categories of CD have been described in literature, ranging from silent CD, which is generally asymptomatic, to classic or typical CD, which is characterized by intestinal symptoms, and atypical or subclinical CD, which also includes extra-intestinal symptoms.¹ It is believed that up to five times more patients present with silent or atypical disease than with the classic form.⁶ When a diagnosis of CD is suspected, initial screening should involve laboratory evaluation for autoantibodies, specifically IgA total and antitransglutaminase IgA. Endomysial (EMA)-IgA and serum tissue transglutaminase (tTG)-IgA are additional

antibody tests have similar sensitivities. Although the EMA-IgA test has the highest diagnostic accuracy, it is not as widely available and is more expensive than the tTG-IgA test.⁷ Upper endoscopy with small bowel biopsy can help to confirm the diagnosis of CD in patients with suspected disease. Genetic testing for CD can be performed. However, genetic testing is not diagnostic, as studies have shown that only 3% of the 40% of European carriers of the HLA-DQ2 and HLA-DQ8 haplotypes, which are linked to increased CD risk, develop the disease.⁸ It should be confined to specific screening scenarios (family members of CD patients) and in controversial diagnoses.

Iron deficiency anemia (IDA) is one of the most common clinical manifestations of CD and is present in over half of patients at the time of diagnosis. This is likely because the duodenum is the site of iron absorption and the major site of inflammation in patients with CD.^{1,2} IDA can be the only sign of CD, particularly in patients with atypical CD. Some studies have suggested that the degree of villous atrophy correlates with anemia severity.⁹ For example, in a study of 405 adult celiac patients, Harper et al. documented a significantly higher prevalence of IDA (34%) in patients with subtotal/total villous atrophy, when compared with patients with partial villous atrophy (13%; $p > 0.001$).¹⁰ Annibale et al. also found a significant inverse correlation between hemoglobin concentration and the pathologic severity of duodenal biopsies in patients with CD.⁹

Recent studies, with advanced diagnostic cardiac imaging, have highlighted the relationship between CD and cardiovascular diseases. Severely dilated left ventricle, left ventricular dysfunction, very low ejection fraction, pulmonary hemosiderosis, and heart block have all been reported in cardiomyopathy patients with CD.¹¹ Several mechanisms have been proposed to explain the etiology and progression of cardiomyopathy in celiac disease. Firstly, severe nutritional deficiencies, due to chronic malabsorption, can cause cardiomyopathy.³ It has also been suggested that derangements in intestinal permeability in patients with CD may allow the absorption of luminal antigens or infectious agents, and lead to myocardial damage through immune-mediated mechanisms.³ Finally, direct myocardial injury may result from an immune response against an antigen present in both the myocardium and the small intestine.³ Understanding the relationship between celiac disease and cardiomyopathy can help explain the effects of a gluten-free diet in patients with cardiac manifestations. One case series described the effect of a gluten-free diet on cardiac performance in three patients with idiopathic dilated cardiomyopathy and celiac disease. In the two patients that strictly observed the gluten-free diet, a 28-month follow-up showed an improvement in echocardiographic parameters and quality of life

measures. The third patient did not observe the gluten-free diet and presented with worsening echocardiographic parameters and cardiologic symptoms, and required additional medication therapy.¹² These data suggest that a gluten-free diet may have a significant beneficial effect on cardiac performance in patients with CD and idiopathic dilated cardiomyopathy.¹²

Autoimmune disease is also strongly associated with CD, with an approximate prevalence of 20% in adults.¹³ Hypothyroidism, likely caused by autoimmune thyroiditis, is the most common autoimmune manifestation and occurs in 5%-15% of patients with CD.¹³ The mechanism underlying the correlation between CD and autoimmune thyroiditis is believed to be independent of gluten exposure, and is most likely related to a common genetic predisposition.¹⁴ It is notable that hypothyroidism can also affect the heart and vascular system.¹⁵ Patients with severe and longstanding hypothyroidism can develop pericardial effusion and low cardiac output, primarily due to bradycardia, decreased cardiac contractility, and reduced ventricular filling.¹⁵ As such, hypothyroidism may have also contributed to the cardiac dilatation and reduced ejection fraction seen in our patient. Treatment with thyroxine has been shown to reverse hypothyroidism-induced cardiovascular changes.¹⁵

Though not diagnosed in our patient, many other extra-intestinal manifestations of CD have been reported. Over a third of adults with CD, for example, present with neurologic symptoms, such as peripheral neuropathy, epilepsy, and cognitive disorders.⁵ Dermatitis herpetiformis, recurrent aphthous stomatitis, and metabolic bone disorders are also associated with CD.¹⁶ A gluten-free diet can have a beneficial effect in reducing many of these complaints.

4 | CONCLUSION

Clinicians should be aware of the many extra-intestinal manifestations of celiac disease, and proceed with screening tests and dietary treatment accordingly. Our case highlights some of the conditions associated with CD. These include iron deficiency anemia, dilated cardiomyopathy, and hypothyroidism. Cardiomyopathy associated with celiac disease is a serious and life-threatening condition if left untreated. A high degree of clinical suspicion is required to make the diagnosis. In patients with dilated cardiomyopathy and iron deficiency anemia, screening for CD is important, as a gluten-free diet can improve heart function.

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None.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ETHICS APPROVAL

Ethical approval is not required at our institution to publish an anonymous case report.

CONSENT

Written consent was obtained from the patient.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

ORCID

Salma Elnour  <https://orcid.org/0000-0001-7250-1515>

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