Case Report

Pericardial effusion in a patient of celiac disease and hypothyroidism: A case report

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ABSTRACT

Celiac disease (CD) can be defined as an autoimmune chronic disorder in gluten-intolerant individuals producing malabsorption of nutrients and vitamins. The presence of CD in individuals causes an alteration in the absorption and pharmacokinetics of certain drugs. This poses a great challenge in maintaining serum thyrotropin levels in hypothyroidism patients on replacement therapy with levothyroxine (LT4). In this report, we present the case of a 39-year-old woman with hypothyroidism, pericardial effusion, and (previously unrecognized) CD. Our patient was a known case of hypothyroidism with a history of previous hospitalization for an episode of acute gastroenteritis. In our clinic, after an initial workup, the patient was continued on LT4 supplement, oral iron, and multivitamins. During her follow-up visit, when an anti-tissue transglutaminase IgA-positive report was available, a gluten-free diet was advised. Following this, the clinical condition of the patient improved drastically, accompanied by a fall in elevated thyroid-stimulating hormone (TSH) levels. This case highlights the necessity of understanding the etiology of rising serum TSH levels, hence ruling out malabsorption. Pericardial effusion, being a rare complication of hypothyroidism and CD, may lead to adverse cardiac events, hence resulting in hospitalization and patient disability.

Key words: Anti-tissue transglutaminase, Celiac disease, Levothyroxine, Pericardial effusion

Celiac disease (CD), also popularly known as celiac sprue or gluten-sensitive enteropathy, has lately marked its importance as a pivotal factor responsible for various malabsorption disorders in the Indian population. While the available literature drew its attention toward western population in whom this disease was relatively common, the global prevalence continues to surge irrespective of any race. The prevalence of CD is around 1% globally, including in India, with some regional variations among various states [1,2]. North Indian states show a higher prevalence as compared to the north-eastern and southern parts of India [2]. Drug absorption and pharmacokinetics of some drugs have been seen to alter in patients with CD due to several factors, such as delay in gastric emptying, reduction in surface area for absorption, and altered gastric pH [3,4]. In addition to this, few studies have documented higher levothyroxine (LT4) dose requirements in patients with CD due to altered absorption of the drug from the gut [4]. This dose requirement was, however, reduced once patients were instituted on a gluten-free diet [5]. Pericardial effusion is reported in some patients as a rare complication of celiac sprue as well as hypothyroidism [6,7].

Access this article online	
Received - 04 November 2023 Initial Review - 21 November 2023 Accepted - 21 December 2023	Quick Response code
DOI: 10.32677/ijcr.v10i1.4342	

This case shows CD which was diagnosed in a known case of uncontrolled hypothyroidism and moderate pericardial effusion. Serum thyroid-stimulating hormone (TSH) levels and pericardial effusion were both reduced after increasing the LT4 dose and shifting the patient to a gluten-free diet.

CASE REPORT

A 39-year-old female presented in the thyroid clinic on December 9th 2022, with complaints of easy fatigability and dyspnea on exertion (New York Heart Association grade II) for about a week, soon after a short course of a recent hospital stay. Medical history included hypothyroidism. She had been admitted to a local hospital on November 23rd 2022, for an episode of acute gastroenteritis. During the stay, she was found to have severe normocytic normochromic anemia (hemoglobin – 6.8 g/dL, packed cell volume – 22.1%, mean corpuscular volume – 88.8 fL, and mean corpuscular hemoglobin – 27.5 pg.), moderate pericardial effusion (21.1 mm anterior to the right ventricle and 16.1 mm posterior to the left ventricle revealed by a 2D echocardiography), and positive typhoid antigen (*Salmonella typhi*). All laboratory investigations have been listed in Table 1. She was discharged in good general condition after giving blood transfusion, antibiotics,

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Table 1: Laboratory investigations during hospitalization

S. No.	Laboratory investigation	Day 0 (November 23rd, 2022)	Day 42 (January 4th, 2022)	Day 71 (February 22nd, 2022)
1.	Hemoglobin	6.8 g/dL	12.2 g/dL	-
2.	PCV	22.1%	-	-
3.	MCV	88.8 fL	-	-
4.	MCH	27.5 pg	-	-
5.	2D Echo	Moderate pericardial effusion (21.2 mm anterior to RV and 16.1 mm posterior to LV)	-	Mild to minimum circumferential pericardial effusion
6.	Typhoid antigen	Positive (*Salmonella* Typhi)	-	-
7.	TSH	312.5 µIU/mL	123.3 µIU/mL	14.7 µIU/mL
8.	T3	<0.5 pg/mL	-	-
9.	T4	<0.3 mg/dL	-	-
10.	Anti tTg IgA	-	>100 units	-

PCV: Packed cell volume, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, RV: Right ventricle, LV: Left ventricle, TSH: Thyroid-stimulating hormone, T3: Triiodothyronine, T4: Tetraiodothyronine

and other supportive treatment. Thyroid profile revealed high serum TSH or thyrotropin (TSH) value (312.5 µIU/mL) with concomitant decreased free triiodothyronine (<0.5 pg/mL) and tetraiodothyronine (T4) (<0.3 mg/dL) levels, and she was started on 50 mg of LT4.

In our clinic, the patient was advised a serum TSH, vitamin B12 levels, iron profile, hemogram, random blood sugar, as well as, serum anti-tissue transglutaminase (tTG) IgA levels as an initial workup and was continued on LT4 supplement, oral iron, and multivitamins. She was also given therapy for deworming.

On her follow-up visit on January 4th 2023, her investigations revealed markedly high anti-tTG antibodies (>100 units with a reference range of <4 units), an improved TSH value (123.3 µIU/mL), and hemoglobin (12.2 g/dL). Revised treatment was given, and the patient was started on a gluten-free diet. The patient had a far better general condition and showed relief of dyspnea, as well as, fatigability on February 4th 2023. Serum TSH was further reduced to a near-normal value of 14.7 µIU/mL. A follow-up 2D echo performed on February 2nd, 2023, revealed marked improvement in pericardial effusion.

DISCUSSION

CD, as a result of both genetic and environmental factors, is seen in about 0.5–1% of the total world population [1]. However, the database from various epidemiologic studies conducted in parts of Africa, the Middle East, Asia, and South America hint that the disease has been profoundly underdiagnosed. A prevalence of 2–5% has been seen in patients with autoimmune thyroid disorders [5].

The role of human leukocyte antigen (HLA) and non-HLA genes has been well established in the pathogenesis of this disease. The population at risk involves individuals with diabetes, autoimmune disorders, or a family history of CD. More than 95% of patients with CD are positive for HLA-DQ-2 and/or HLA-DQ-8. The presence of elevated serum levels of antibody (anti-tTG IgA) in a patient exhibiting clinical features of malabsorption while on a gluten-containing diet marks the basis for the diagnosis of CD in an individual.

The detection of CD in patients with uncontrolled thyrotropin values has become an integral part of caregiving. A TSH value that is not within an appropriate range produces symptoms and discomfort in many, including menstrual abnormalities, infertility, unusual forgetfulness, and behavioral changes. Many of these symptoms are inevitable during the treatment course of such hypothyroid patients and often lead to disharmony at work or otherwise.

The association of CD and hypothyroidism has been studied by Counsell *et al*., in a case series in which the first report describes the case of a 27-year-old woman who presented with constipation and menorrhagia where her laboratory reports showed mild iron deficiency and autoimmune hypothyroidism (TSH–109 mU/l). Despite adequate pharmacological therapy, she continued to lose weight (28 lb) and developed diarrhea [7]. Further investigations also showed continued iron deficiency and new folate deficiency, and distal duodenal biopsy specimens showed subtotal villous atrophy. However, a significant clinical response was noted after a gluten-free diet was advised to the patient. A previous report described an 80-year-old woman who presented with a history of diarrhea resistant to all previous therapies and assumed to be due to thyroxine treatment. Her laboratory investigations showed biochemical euthyroidism with TSH–2.0 mU/l and T4–90 nmol/l and mild iron and folate deficiency [7]. Similar to the first report, partial villous atrophy was observed, and a drastic clinical and histological response was noted after the patient was shifted to a gluten-free diet. Another case reported by Sabawoon *et al*. hinted toward the association of hypothyroidism-induced pericardial effusion and warned about the necessity of early recognition and management in such cases [8]. In the case described here, the patient had significant fatigue and dyspnea attributable to pericardial effusion, which in turn resulted from CD, as well as, high TSH levels in the body. Pericardial effusion, although in rare cases, can manifest itself as a complication of hypothyroidism and, in severe cases, may result in cardiac tamponade.

The pathophysiology of hypothyroidism-induced pericardial diseases can be explained by the low levels of thyroid hormones causing increased permeability of the epicardial vessels and decreased lymphatic drainage of albumin. This leads to the

accumulation of fluid in the pericardial space, hence resulting in pericardial effusion. In the above-mentioned case, moderate pericardial effusion in the time course resolved to a minimum pericardial effusion with effective thyroxine replacement and treatment of the underlying CD. CD was diagnosed to be the underlying cause of uncontrolled TSH which was shown to have improved when a gluten-free diet along with thyroxine replacement therapy was advised.

CONCLUSION

Malabsorption remains to be a well-recognized cause of increased LT4 dose requirements in resistant hypothyroidism. Treating the etiology of malabsorption does, in most cases, control the serum TSH levels and also resolve the symptoms related to hypothyroidism, which might include pericardial effusion. This case reflects the necessity of diagnosing the underlying pathology of rising serum TSH levels, with malabsorption being the one to be ruled out often. Pericardial effusion, being a complication of many conditions itself, leads to adverse cardiac consequences demanding hospitalization and patient disability. Understanding the cause may, however, treat effusion with ease, both at the care provider's and patient's end.

ACKNOWLEDGMENT

The authors are grateful to the patient who has consented to include her medical details in this case report and also to the Division of Clinical Research and Medical Management, Institute of Nuclear Medicine and Allied Sciences.

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Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Kanwar RS, Kakkar K. Pericardial effusion in a patient of celiac disease and hypothyroidism: A case report. Indian J Case Reports. 2024; 10(1):19-21.