

Case Report

Unmasking the triad: a case of severe iron deficiency anemia revealing underlying autoimmune hypothyroidism and celiac disease

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ABSTRACT

Anemia is the most common hematologic disorder worldwide, iron deficiency being the leading one. Often, anemia is the presenting sign of a more serious underlying condition, which is left untreated and can generate consequent morbidity. Heavy menstrual bleeding (HMB) plays a major role in iron deficiency, especially in women of reproductive age. In this report, we presented an interesting case of a 43-year-old female who presented to the gynecology department of a tertiary care hospital in Islamabad with symptoms of easy fatigability, generalized body weakness, and HMB for the past 3 months. She was admitted to the gynecology ward because of severe iron deficiency anemia. Haemoglobin (Hb) 6.1 g/dl with low mean corpuscular volume (MCV), low serum iron and ferritin levels, and high total iron-binding capacity (TIBC). She was treated with IV iron therapy for iron deficiency and tranexamic acid to stop bleeding. Due to the absence of an obvious gynecological cause, she was referred to the medical outpatient department (OPD) for further evaluation. Further investigations revealed markedly reduced T4 levels and positive anti-thyroid antibodies, dyslipidemia, and grade 2 fatty liver disease. She was initiated on levothyroxine, statins, and proton pump inhibitors (PPIs). Despite Hb improvement, she complained about persistent body aches, muscle pain, and backache. On additional workup, serum calcium and vitamin D levels were low, and anti-tissue transglutaminase IgA and IgG tests appeared positive. She was started on a lifelong gluten-free diet with calcium and vitamin D supplementation. Follow-up and monitoring for osteoporosis and nutritional deficiencies were done.

Keywords: Iron-deficiency anemia, Autoimmune diseases, Hypothyroidism, Celiac disease, Anti-tTG IgA

INTRODUCTION

Iron deficiency anemia (IDA) remains the most common and prevalent hematologic disorder globally, especially in women of reproductive age. While often linked to insufficient nutrient intake or menstrual losses, IDA may serve as an early indicator of complex underlying pathologies.^{1,2} Among the other causes of IDA, endocrine and autoimmune causes are often overlooked. The connection between thyroid problems and menstrual irregularities in reproductive age women is very important clinically. Thyroid disorder, mainly hypothyroidism, can contribute to IDA through heavy menstrual bleeding by affecting the coagulation cascade as well as slowed red blood cell production. In autoimmune hypothyroidism

(Hashimoto's thyroiditis), the presence of anti-thyroid antibodies gradually damages the thyroid gland, deteriorating thyroid function. As in our case, the detection of positive anti-thyroid antibodies validated the autoimmune origin of her hypothyroidism. Autoimmune diseases frequently occur together because of common genetic and environmental risk factors, a process referred to as autoimmune clustering. Those diagnosed with one autoimmune condition are more likely to develop other autoimmune disorders as well. Celiac disease and autoimmune thyroiditis are two of the most commonly occurring autoimmune disorders that often appear together. They both have shared immunogenetic markers, like HLA-DQ2 and HLA-DQ8 haplotypes, which help

explain their co-occurrence in individuals who are vulnerable.

CASE REPORT

On the 14 November 2024, a 43-year-old female presented to the gynecology/obstetrics outpatient department (OPD) with heavy menstrual bleeding, easy fatigability, and generalized body weakness from the past 3 months. She was experiencing excessive menstrual bleeding and irregular cycles over the past three months, worsening with progressive development of easy fatigability and generalized body weakness. These symptoms remained throughout the day up to the level that started affecting the patient's day-to-day activities. On examination she looked pale and lethargic, well oriented, and sitting comfortably. Her blood pressure was 130/80 mmHg, pulse rate was 82 beats per minute, respiratory rate was 19 breaths per minute, and her temperature was 98.3 °F. There was no jaundice, clubbing, lymphadenopathy, or palpable pelvic mass.

Routine laboratory test was done which shows hemoglobin of 6.1 g/dl, mean corpuscular volume (MCV) 67 fl. Iron studies show total iron-binding capacity (TIBC) high, serum iron levels low, serum ferritin levels low and reticulocyte count 1%. Initial management includes IV iron therapy, tranexamic acid for bleeding control and then refer to medicine OPD for anemia workup.

The patient was referred to medical OPD for detailed evaluation of the symptoms of anemia and additional symptoms which includes shortness of breath, palpitations, easy fatigability and constipation. On further inquiry patient mentioned that she is having these symptoms for the last 9 years worsening progressively over the period of last 3 months. In addition, she also had complaints of gastro intestinal symptoms like dyspepsia, nausea and intermittent episodes of vomiting. Her past medical and surgical history was unremarkable. On clinical examination she exhibited pallor with a lemon-tinged skin appearance, her blood pressure was 120/80 mmHg, heart rate 92 beats per minute, respiratory rate 20 breaths/minute. There was mild facial puffiness, loss of eyebrow hair, rough dry skin and thyroid was not palpable. On systemic examination there was flow murmur at left parasternal border, mild epigastric tenderness and delayed relaxation of ankle jerk.

Based upon history and examination her thyroid function test was done which shows thyroid stimulating hormone (TSH): 100 µIU/ml (0.4 to 4 mu/l normal), T3: 56 ng/dl (80 to 220 ng/dl), T4: 0.4 ng/dl (0.8 to 1.8 ng/dl) and antithyroid antibody test was positive. Lipid profile shows low density lipoprotein (LDL): 156 mg/dl, total cholesterol: 280 mg/dl and ultrasound abdomen reported fatty liver (grade 2).

The initial management plan includes levothyroxine replacement therapy (tab. thyroxin 50 µg, 1/2-tab OD), tab.

atorvastatin 10 mg OD, iron and folic acid supplementation, and PPIs for dyspepsia. On subsequent follow-up after a month and a half, the patient's Hb improved from 6.1 to 9.4 g/dl and then 10.6 g/dl with MCV 68 fl. Serum iron, serum ferritin, and TIBC were reported as normal. TSH levels decreased from 100 to 56 µIU/ml and then 4.3 µIU/ml. Symptoms of the patient also improved, like chest discomfort, menstrual irregularities, and breathlessness. But the emerging complaint was persisting body aches, muscle pain, backache, and continued fatigue despite Hb improvement. Additional workup includes low serum calcium, low vitamin D levels, and positive anti-TTG IgA and IgG antibodies. Upper GI endoscopy refused by the patient. Management was expanded to include calcium and vitamin D supplements and a strict gluten-free diet.

Table 1: Results of laboratory investigations.

Laboratory investigations	Results	Reference ranges
Complete blood count		
RBC count	3.12	3.8-4.8
Hemoglobin	6.1	12.0-15.0
Hematocrit	21	36-46
MCV	67	80-95
MCH	20	27-31
MCHC	29	32-36
Platelet count	205,000	140,000-425,000
Absolute lymphocyte count	810	1500-4000
Thyroid function tests		
TSH	>100	0.3-5.2

Table 2: Results of screening for celiac disease.

Laboratory investigations	Results	Reference ranges
Tissue transglutaminase (tTG) IgA antibodies test		
Anti-tTG IgA	Positive	Negative: <15, positive: ≥15

DISCUSSION

Anemia refers to the reduced oxygen level in blood. Anemia, particularly IDA, is globally more common in women than in men due to factors like menstrual blood loss, and pregnancy.^{3,4} Anemia is associated with many diseases, including hypothyroidism.^{5,6} The association between anemia and hypothyroidism is a strong association.⁷⁻⁹ Thyroid hormones play a crucial role in hemoglobin levels through erythropoiesis by stimulating the expression of the erythropoietin gene and erythropoietin production, as well as bone marrow suppression. In this case, the patient's main presenting symptoms were menorrhagia, generalized weakness, and easy fatigability. Abnormal uterine bleeding, including menorrhagia, is usually quite a common condition in premenopausal women, while the other 2 symptoms point

towards anemia.¹⁰ As the initial examination conducted in the gynecology department did not show any remarkable results except indicating the presence of anemia, this could have easily overlooked any underlying and associated causes, which can only be uncovered on detailed examination. After referral to the medicine department, clinical assessment revealed the presence of constipation and, later on, other GI symptoms such as nausea, vomiting, and dyspepsia. Other than that, dry skin, loss of eyebrow hair and delayed reflexes were also observed. All these pointed to hypothyroidism, which was confirmed on thyroid function tests. The patient also had dyslipidemia and grade 2 fatty liver, confirmed on lipid profile and abdominal ultrasound. The association between thyroid disturbances and menstrual irregularities has been established in multiple studies.¹¹⁻¹³ This is because hypothyroidism affects the coagulative cascade by shifting the hemostatic system towards a hypocoagulable and hyperfibrinolytic state.¹⁴ On follow-up after one and a half months, the patient still had persistent backache and fatigue. This was despite therapy in which the patient's hemoglobin levels improved significantly. This meant that additional workup had to be done. We know that the presence of one autoimmune disease is an indication to investigate any other autoimmune conditions, as they are associated with each other, as per multiple studies.¹⁵⁻¹⁷ Thus, this was assessed in the additional workup on the follow-up. The workup revealed the presence of celiac disease, as anti-tTG IgA and IgG were positive, and this explained the earlier symptom of gastrointestinal upset.

Hypothyroidism and celiac disease are closely related to each other due to genetic predisposition, which is present in interrelated autoimmune conditions.^{18,19} The strongest link between autoimmune hypothyroidism and celiac disease is the autoimmune link of genetic predisposition, but there are more links that associate the two conditions. One such explanation is the nutrient deficiencies that celiac disease causes by damaging the intestinal villi, which reduces the nutrients for T3, T4 synthesis, as well as levothyroxine in patients with hypothyroidism. In our case, we understand that the presence of celiac disease should've been investigated when it was found that autoimmune hypothyroidism was present, instead of after 1 and a half months later, as autoimmune conditions tend to be closely associated with each other. Constipation is a symptom of hypothyroidism, but in our case, despite improvement in thyroid levels, other constitutional symptoms were still there, which raised the suspicion of a different cause, and that was celiac disease.

CONCLUSION

This case underscores the importance of exploring systemic and autoimmune causes in patients with persistent IDA. The concurrent diagnosis of autoimmune hypothyroidism and celiac disease illustrates how autoimmune disorders can overlap, leading to hematologic issues. A thorough assessment and prompt treatment not only enhanced the patient's condition but also averted

further complications. Clinicians should remain vigilant for endocrine and gastrointestinal origins in cases of ongoing anemia, but often financial constraints prevent early detailed workup.

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