Case Report

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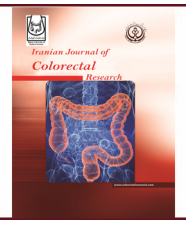

Celiac Disease and Other Autoimmune Manifestations in a Nine-Year-Old Girl

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Abstract

Background: Celiac disease is an autoimmune disease with a high incidence of multi-organ involvement; particularly, gastrointestinal manifestations and a doubled risk of malignancies. Here, we report a case of celiac disease with autoimmune hemolytic anemia (AIHA)
Case Presentation: A nine-year-old girl presented to us with a history of abdominal
pain, fever, nausea, and vomiting. Her examination findings were pallor and splenomegaly; her laboratory tests showed increased liver enzymes and macrocytosis with positive Coombs without a decrease in hemoglobin or high reticulocyte count. Poly-autoimmunity was considered, and AIHA and celiac disease were diagnosed throughout the admission following an in-depth workup. The patient responded to a strict gluten-free diet and pulse corticosteroids. This was a rare case of celiac disease presenting with such an array of signs and symptoms, with management also being distinctive and challenging.
Conclusion: Celiac disease is very rarely associated with conditions like Evans syndrome and autoimmune hemolytic anemia.Still, tests of autoimmune hemolytic anemia are recommendable when a patient has celiac disease-associated anemia with a normal hematocrit level.

Keywords: Celiac disease, Autoimmune hemolytic anemia, Auto immune disease

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Introduction

Celiac disease is an autoimmune disorder related to the use of glutamine and proline. It usually has many symptoms and complications, mainly in the gastrointestinal tract. Celiac disease mostly affects the small intestine mucosa, causing mucosal inflammation, crypt hyperplasia, and villi atrophy. The patients typically develop symptoms such as diarrhea, abdominal pain, and weight loss (1, 2).

One of the main complications in celiac disease patients is anemia, usually caused by a lack of iron or iron malabsorption. Rarely, we see anemia with an autoimmune background (1, 2). The relationship of autoimmune hemolytic anemia (AIHA) with celiac disease is a rare case. Diagnosing AIHA requires a detailed history, paraclinical evaluation, and clinical examinations. Paraclinical studies include evaluation

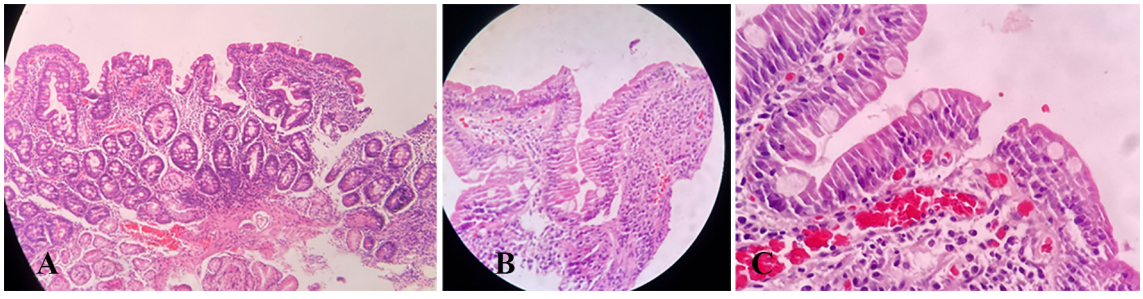

Figure 1: Microscopy of sample from the duodenum. Atrophy of villi and increased intraepithelial lymphocytes are evident.

of complete blood count, lactate dehydrogenase, total and indirect bilirubin, and haptoglobin. In addition, serological tests are used to measure the presence of antibodies against red blood cells (3).

Another autoimmune disorder with unknown pathophysiology is Evans syndrome, where AIHA and immune thrombocytopenia are associated with immune neutropenia. The syndrome is usually diagnosed after ruling out other etiologies (4).

Here, we report the rare case of a nine-year-old female with celiac disease and AIHA.

Case

A nine-year-old girl was brought in by a non-consanguineous parent to our institute in June 2021. The patient had no history of a deceased child in her family or abortion. She had been admitted to an institute four years ago because of knee joint and ankle pain, which had caused movement impairment. Examinations had shown an increase in liver enzymes. Still, she recovered with treatment. A follow-up two months afterward showed improvement in the liver enzymes, while six months ago, the patient was hospitalized because of fever, diarrhea, abdominal pain, and vomiting. A laboratory test indicated increased liver enzymes. Medications were used to control the fever, and the patient was referred to our institute for further workup. Upon arrival, the patient was stable, appeared well, and was non-febrile. Abdominal tests indicated splenomegaly, though there was no hepatomegaly. Based on lab tests, liver enzyme levels were increased: aspartate transaminase (AST)=101 U/L (reference range 15-50), alanine transaminase (ALT)=136 U/L (reference range 7-56), and alkaline phosphatase=1860 U/L (normal range 180-1200). Macrocytosis and a 3+ direct Coombs test were recorded, though the patient's hemoglobin level was normal (Figure 1).

Diverse diagnoses were taken into account at first, among which were chronic liver disease and celiac disease. The lab results were circumscribed based on the differential diagnoses to avoid extra financial burden to the family. Therefore, thyroid function tests, serum albumin, iron profile, vitamin B12, bilirubin count, total serum protein, and autoimmune antibodies like anti-Smith antibody, anti-nuclear antibody, anti-smooth muscle antibody, and anti-double-stranded antibody were checked. The results were in the normal ranges except for elevated anti-tissue transglutaminase (TTG) antibodies (IgA titer of TTG=300 U/ml and IgG titer of TTG=350U/ml). Moreover, viral markers were checked, all of which were in the normal range. Eventually, a liver biopsy was considered.

Following the liver biopsy, the pathological reports did not show any sign of hepatitis. Given that anti-TTG antibodies had been examined earlier, an intestinal biopsy was carried out to confirm Celiac disease. In addition, upper GI endoscopy was carried out to check the GI tract. According to intestinal biopsy, there was a moderate villous abnormality and increased intraepithelial lymphocytes (IEL; 25/100 enterocytes). Moreover, lymphoplasma infiltration in the duodenum (D2 segment) was revealed by endoscopy along with villous swelling in the intestines (Marsh 3b). Given the evidence, celiac disease was diagnosed, and a gluten-free diet was implemented. In addition, the patient was started on corticosteroid therapy. After six months on a gluten-free diet, her growth became normal, as did her liver function test and complete blood count. Informed consent was obtained from all participants.

Discussion

As an autoimmune disease, celiac disease demonstrates symptoms like chronic diarrhea, failure to thrive, abdominal pain, and weight loss. The severity of the disease in pediatric patients is higher than that of adults. While an intestinal biopsy is still the primary means of diagnosis, it can be confirmed without biopsy in the case of children. Currently, the only treatment of the disease is a gluten-free diet, while some have recommended corticosteroids as an add-on treatment (1).

Iron deficiency is usually the cause of anemia in celiac patients; however, some reports have also confirmed AIHA. In the case of AIHA, the patient demonstrates non-specific symptoms such as paleness, fatigue, shortness of breath, jaundice, splenomegaly, and peripheral edema. In addition, evidence of hemolysis needs to be examined as a part of the paraclinical examination. The paraclinical tests must include assays for a complete blood count, reticulocyte count, peripheral blood smear, indirect bilirubin, and lactate dehydrogenase (2).

Celiac disease patients usually have more autoimmune diseases compared with normal individuals. Many hypotheses have been proposed to explain that celiac disease or intestinal mucosal atrophy causes impaired antigen delivery under the intestinal mucosa, which leads to immune system stimulation or autoimmunity. Therefore, celiac disease and autoimmunity can be seen as two separate phenomena. Diabetes mellitus type 1 and autoimmune thyroiditis are the most common autoimmune disorders associated with celiac disease (5). Still, AIHA is also rarely seen in celiac disease patients (2).

Currently, there are few cases of celiac disease along with conditions like Evans syndrome and AIHA. Except for one patient, these patients have responded to corticosteroids and a gluten-free diet (2). The main symptoms in our case were splenomegaly, pallor, and general weakness, and the diagnosis of celiac disease was achieved with a small bowel biopsy following a high anti-TTG titer. Our patient responded to a gluten-free diet and pulse corticosteroids, with normalized growth, liver function test, and complete blood count after six months.

Conclusion

Celiac disease is very rarely associated with conditions like Evans syndrome and autoimmune hemolytic anemia. Still, tests of autoimmune hemolytic anemia are recommendable when a patient has celiac disease-associated anemia with a normal hematocrit level.

Conflicts of interest: None declared.

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