Autoimmune Hemolytic Anemia as Presentation of Celiac Disease

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Abstract

Celiac disease is a multisystem disorder in children and adults; it is considered as one of the most important malabsorption syndromes related to an auto-immune mediated response to gluten-containing food in a genetically predisposed patient. The most common involved system is the Gastrointestinal tract. Association with other autoimmune diseases such as thyroid disease and diabetes mellitus type 1 is well known but autoimmune mediated hemolytic anemia that responded to a gluten-free diet was interesting to be found.

A six years old male previously healthy child, presented with pallor and reduced activity, dark-colored urine, with clinical and laboratory features of hemolytic anemia, and multiple blood transfusions within a year of medical care-seeking to finally diagnosed with celiac disease and responded to a gluten-free diet of about 8 months now with no need of blood transfusion.

Key words: Autoimmune Hemolytic Anemia, Celiac Disease

Introduction

Celiac disease (CD) is an autoimmune multisystem disorder triggered by the gluten and other related prolamins substances present in wheat and other cereals, in those patients who are genetically predisposed.[1] Clinical features vary considerably; GI symptoms are more common in those diagnosed in the first 2 years of life,[2] as the patient grows the extraintestinal manifestation dominates, without accompanying gastro-intestinal (GI) symptoms. Short stature, delayed puberty, peripheral neuropathy, osteopenia and osteoporosis are the nonhematologic-al presentations reported in celiac patients. On the other hand, wide spectrum hematological manifestations are well established, mostly anemia (iron deficiency, folate deficiency, B12 and pyridoxine deficiency), thrombocytosis due to hypersplenism, hemorrhage due to vitamin K deficiency, or folate mediated thrombocytopenia. Although these nonimmune hematological problems are relatively common, autoimmune-mediated hematologic disorders have been reported infrequently.[3]

This paper reports a very rare association between CD and autoimmune hemolytic anemia, and the possibility of considering CD in the differential diagnosis of autoimmune hemolytic anemia (AIHA).

Case presentation

A six-year-old male child, known case of asthma and atopy with no chronic medication use (apart from occasional oral steroid use for asthmatic exacerbation) presented with sudden onset pallor, easy fatigability, exertional dyspnea, and repeated vomiting, with a low-grade fever over a week. The patient was initially examined to be found severely pale, ill-looking, having a soft abdomen with no organomegaly, no lymphadenopathy and with normal vital signs for his age apart from tachycardia 150 BPM. The patient was sent for laboratory tests that show WBC 10.4 $*10^9$/L, 47% granulocytosis, 43% lymphocytosis, Hb level was 6.3 g/dl, platelet count was $630*10^9$/μL. Bblood film at that time showed a severe iron deficiency anemia, hypochromic microcytic RBCs with anisopoikoilocytosis, normal-looking WBC and platelet with mild thrombocytosis.

The patient received a blood transfusion and started oral iron supplementation as S. iron was 57 mcg/dl (normal range 59-150), and serum ferritin was 70 mcg/dl (normal range 30-220). A week later on a follow-up visit, the patient was still symptomatic, Hb level was 7.1 g/dl, with no improvement in his general condition; further investigation had been done to show ESR of 90 mm/hr., positive CRP, normal liver function test, with negative Coombs test, and non-deficient level of G6PD enzyme, normal renal function test. Hence, another transfusion was done, and about 20 days later the patient had severe pallor, jaundice, and dark-colored urine. A new blood film showed a feature of hemolytic anemia with retic count of 7.1% and corrected retic 4%, which required an in-patient management for blood transfusion, intravenous fluid with frequent monitoring of PCV and renal function test. Besides, more advanced investigation was done with normal thyroid function test, deficient level of vitamin D, and positive Anti Ds DNA IgG and IgM level.

The patient was diagnosed with Autoimmune hemolytic anemia and started on oral prednisolone 2 mg/kg/day with a further search for the underlying cause. G6PD enzyme deficiency was excluded for the non-deficient enzyme level measured 2 weeks from the hemolytic attack; the patient had no respiratory symptoms or any features of mycoplasma or other infections that may cause hemolytic disease. In addition, there was no joint pain or skin changes, no neurological manifestations, and no features of serositis to collect criteria of SLE. Further, the patient had a negative latex test of Rheumatic disease; so, all these diagnoses had been excluded.

A month later, another attack of hemolysis occurred while on steroid with Hb level as low as 5.7 gm/dl, a trial of IVIG 1 gm/kg for two days. Meanwhile, a screening test for CD was done to show positive anti-tissue transglutaminase antibody IgG and the patient was tapered from steroid, and started on strict adherence to a gluten-free diet, with a gradual rise in Hb. After 8 months, the patient had been free of blood transfusion and the Hb level was kept in the range of 10-11 mg/dl.

Follow-up: the patient is free of symptoms with normal activity. A final diagnosis of celiac-associated hemolytic anemia was finally done.

Discussion

Patients with CD often have more autoimmune illnesses than healthy people. Many theories have been presented to explain why the CD or intestinal mucosal atrophy impairs antigen delivery underneath the intestinal mucosa, resulting in immune system activation or autoimmune. As a result, CD and autoimmunity are two distinct conditions. The most common

autoimmune illnesses is linked to celiac disease are type 1 diabetes and autoimmune thyroiditis. Nonetheless, AIHA is uncommon among CD individuals. [4]

Shah et al [5], have made a description of 21 cases with possible associations between CD positive serology and AIHA. However, they suggest a further exploration to prove this association.

In Ivanovski et al. [6] an 11-year-old girl with untreated CD who had hemolytic anemia was described and, accordingly, it was advised that patients with Coombs negative "immune" hemolytic anemia should be serologically checked for CD. The anemia improved after starting a gluten-free diet, as it did in this case.

Pallor and general weakness were the predominant symptoms in our case, and CD was diagnosed with a high anti-tTGAb titer. After eight months on a gluten-free diet, our patient's growth and complete blood count all returned to be normal. The failure of our patient to respond to corticosteroids and IVIG could be explained by the fact that the patient was fed, i.e., constantly confronted with gluten, and anti-tTGAb production was unrestricted until the gluten-free diet was introduced.

Conclusion
- Late presentation of CD mostly occurs as a non-GI complaint.
- CD should be kept in mind for differential diagnoses of Hemolytic anemia.
- Strong base scientific evidence needs to be present before initiating a specific therapy, to reach a clear non-cloudy diagnosis.

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