Open Journal of
Clinical & Medical
Case Reports

Volume 4 (2018)
Issue 8

ISSN 2379-1039

The association between celiac disease and aplastic anemia: A case report

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Abstract

Celiac Disease (CD), also known as gluten-sensitive enteropathy, is an immune-mediated small intestinal enteropathy which has diverse clinical presentation. It has been associated with several diseases such as Type 1 Diabetes Mellitus, Autoimmune Thyroiditis and Selective IgA Deficiency. CD is classified as classical, silent and atypical. The two latter forms are becoming more common. The silent form is an incidental finding in patient's presenting with symptoms attributable to other diseases. The author reports a case of 58 years old male who presented with generalized weakness, body aches, and chronic abdominal pain. On investigation, he is found to have pancytopenia with hypocellular bone marrow. A bone marrow biopsy revealed a picture of Aplastic Anemia (AA). A small intestine biopsy was done as part of evaluation for persistent anemia and it showed features of CD that was confirmed by serological markers. There are only few reported cases describing the association between Celiac Disease and Aplastic Anemia. A hypothesis can be generated to link the immune-mediated mechanism and the role of immunosuppressive therapy in both diseases.

Keywords

celiac disease; aplastic anemia; autoimmune; CD4+

Introduction

Celiac disease (CD) is an immune-mediated systemic disorder primarily affects the small intestine in genetically susceptible individuals [1]. It has a strong association with human leukocyte antigen (HLA) DQ2 encoded on D3 haplotype and HLA-DQ8 encoded on D4 haplotype [1,2,3,4]. It is triggered by the exposure to dietary gluten in patients with genetic predisposition. The highest prevalence of CD worldwide is in the middle-east as compared to UK and USA where the disease remains under diagnosed [4,5]. In a cross sectional prospective study done in UAE which included 1197 healthy individuals, the seroprevalence was 1:86 with female predominance [5].

The classical form of CD is manly associated with gastrointestinal symptoms such as chronic diarrhea, abdominal pain, and steatorrhea [3]. The non classical forms of CD, atypical and silent (asymptomatic), are more commonly identified. Individuals with atypical CD usually presents with symptoms secondary to extraintestinal manifestations (eg. skin disorder, osteopenia, anemia, vitamins deficiency, abnormal liver function tests) [6,7]. It is known in the literature that CD is linked with other

autoimmune diseases (eg. autoimmune thyroiditis, autoimmune hepatitis), but its association with Aplastic Anemia (AA) has rarely been reported [4,8]. Such patients are most likely to be having the non classical forms of CD and AA develops as part of the autoimmune process.

Case Report

A 58 year old Indian male presented to the hospital with history of mild diffuse lower abdominal pain for 1 month duration. The pain was gradual in onset, intermittent, and aching in nature. Associated symptoms include fatigue, lethargy, and unspecified weight loss. There was no history of fever, altered bowel habits, gastrointestinal bleeding, rash, or joint pain. His past medical history was significant for anemia of 2 years duration, but was not investigated. He did not have any surgical history. He was not using any regular medication nor had any allergies. Family history was negative for any chronic illnesses or malignancy. He was vegetarian, comes from low socioeconomic status, non-smoker, and non-alcoholic.

His vital signs on initial presentation; heart rate was 86 beats per minute, blood pressure 110/68 mmHg, temperature 36.8 degrees Celsius, and the respiratory rate was 18 breaths per minute. In general examination; patient was not in distress, well oriented, cachexic, and had conjunctival pallor. On abdominal examination, there was mild tenderness over the lower abdomen on deep palpation. There was no orgnaomegaly or lymphadenopathy. Per-rectal examination was negative for hematochezia or melena. Other systemic examinations were within the normal limits.

The initial blood test showed white blood count of 3.3X 10^3/cmm, hemoglobin 68g/L, platelets of 29 X 10^3/cmm, and peripheral blood smear was suggestive of aplasia. Blood chemistry was normal except for hypoalbuminemia. Iron profile, Vitamin B12, and Folate levels were normal. Screening for viral infections (EBV, CMV, HIV, Hepatitis) was negative. Extensive investigations including vascultic workup, thyroid panel, coagulation profile, and hemolytic workup were all negative. Paroxysmal nocturnal hemoglobinuria was ruled out by flow cytometry. The bone marrow aspiration showed hypocellular marrow suggestive of moderate Aplastic Anemia. Patient underwent gastroscopy as part of the workup of anemia. The esophagogastrodudenoscopy with biopsy showed the following: 1) pre-pyloric erosion, 2) chronic gastritis with focal cryptitis and increase of intraepithelial lymphocyte, 3) duodenal type mucosa with near total atrophy of villous architecture and increase of inflammatory cells in the lamina propria. Serology results for celiac disease showed anti Gliadin IgA >15 units/mL (N<12), anti Gliadin IgG >100 units/mL (N<12), anti Tissue Transglutaminase IgA >200 units/mL (N<10), anti-Endomoysium Antibodies IgA positive, and normal level serum IgA. Colonoscopy showed 2 small 5mm polyps in the rectum and sigmoid which were negative for malignancy.

Patient received supportive management during hospital stay including multiple blood transfusions. He was discharged on multi-vitamins, calcium-vitamin D, and iron supplements. Patient was educated about his clinical condition and his immune-compromised status. He was advised to commence on strict gluten free diet and full dietitian consultation was provided. On further follow up over 1 year period, his overall clinical performance has improved. The blood investigations done on each visit showed improvement in the hemoglobin levels reaching 100 g/L, but he remained to have leucopenia and thrombocytopenia. As he was in stable general condition and showing clinical improvement, immunosuppressive treatment was not offered at this time. Moreover, due to his medical

insurance issues that will affect his long term follow up and management, patient decided to travel back to his home country.

Discussion

Celiac Disease is a multi-factorial disease. It is caused by an abnormal immune response that activates the lamina propria CD4+ lymphocytes following exposure to gliadin protein and related prolmains [1]. This mechanism triggers effector CD4+ T helper cell (Th1), which releases proinflammatory cytokines leading to inflammation in the mucosal lining of the small intestine. Additional CD4+ T cells with suppressor function known as, Type 1 regular T cells and Foxp3+, are implicated in the pathogenesis of CD. These regular T cells (Tregs) cause intestinal injury by the release of IL 10 and TFG- β [1,2,9]. Furthermore, it was found that cytotoxic T cells are also activated in this autoimmune disease inducing interferon (IFN)-γ production leading to epithelial cell apoptosis [1]. New studies have shown that other subset of effector T cells involved in the chronic inflammatory cascade, termed Th17, which also plays a major role in various other autoimmune diseases [1,9].

In Aplastic Anemia, autoimmunity plays a crucial role in the pathological process of the disease. The major contributing factor is CD8+ T lymphocytes which lead to CD34+ apoptosis by the release of proinflammatory cytokines resulting in bone marrow failure [10]. Studies have shown that CD4+ T helper cells (Th1, Th2, Th17, Tregs) are also involved in the pathogenesis of AA, but to a lesser degree [10]. Therefore, both AA and CD can be linked together as they share similar pathogenesis. A hypothesis can be generated that in adults who have undiagnosed CD, the ongoing chronic inflammatory process may eventually lead to bone marrow hypoplasia [Figure 1].

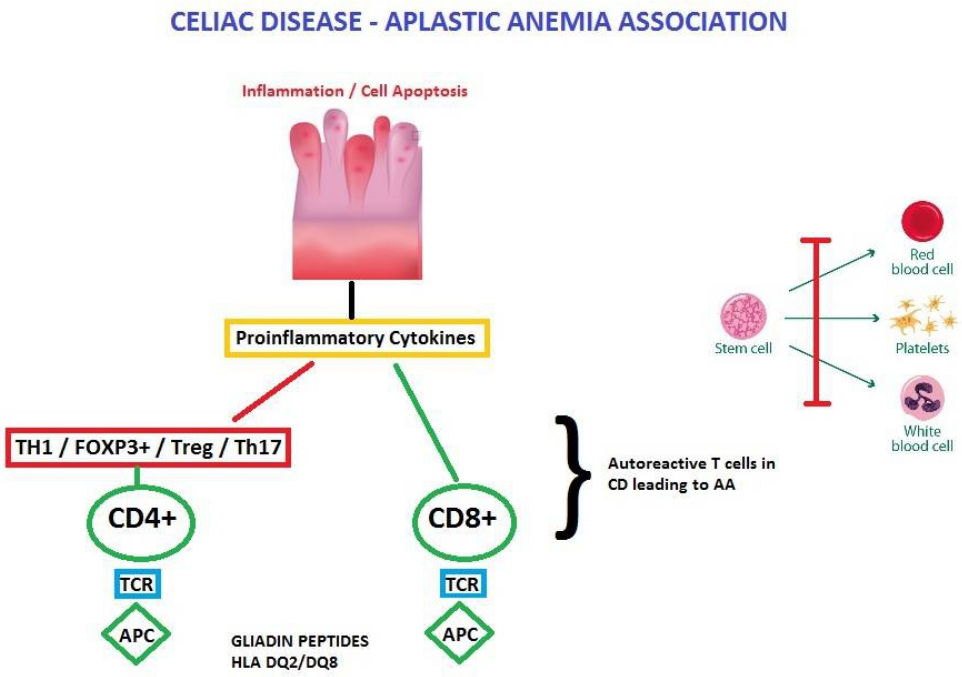
In the literature, 9 adult cases have been reported that further support this association CD-AA [8,11,12]. It can be concluded from these case reports that AA occur as a complication of CD secondary to abnormal immune responses and micronutrients deficiency. Moreover, treatment for AA can alter the disease process of CD. Immunosuppressive treatment (IST) used in AA can suppress the ongoing inflammatory process in CD relieving symptomatic patients. Also it has been described in the literature that there is resolution of celiac disease following bone marrow transplantation (BMT) done for other associated diseases [13]. Off the 5 cases reported by Salmeron et al., only a single patient had complete recovery from both diseases following treatment with gluten free diet and hemtopoietic stem cell transplantation [12]. There are no reports for the use of BMT or IST for isolated CD. The mainstay of treatment for CD remains gluten free diet unless it is a refractory disease in which other diagnosis should be worked up [8,12]. Once AA is established, treatment is BMT and/or immunosuppressive treatment.

Diagnosing CD requires a high degree of suspicion and must be confirmed with serology and intestinal biopsy. Early screening and diagnosis of CD is crucial to avoid long term complications such as infertility, malignancy, and hematological complications [3]. Celiac disease should be included in the routine work up of patients presenting with AA, especially in the silent/atypical CD presentations. Patient's who develop CD should be started on gluten free diet with micronutrient supplements. Other treatment modalities, IST and BMT, should be considered in individuals who develop AA. This can be challenging and cost effective especially for patients coming from undeveloped countries. More studies are still required to confirm this phenomenon of CD-AA association and our understanding of the underlying mechanism.

Acknowledgements

I would like to thank Al Mafraq Hospital for the support given to complete up the case report.

Figures



References

1. Mazzarella G. Effector and suppressor T cells in celiac disease. World J Gastroenterol. 2015; 21: 7349–7356.

2. Ciccocioppo R, Di Sabatino A, Corazza GR. The immune recognition of gluten in coeliac disease. Clin. Exp. Immunol. 2005; 140: 408–416.

3. Rubio-Tapia, A. Hill ID, Kelly CP, Calderwood AH. Murray JA. American College of Gastroenterology. ACG clinical guidelines: Diagnosis and management of celiac disease. Am J Gastroenterol. 2013; 108: 656–676.

4. Murch S, Jenkins H, Auth M, et al. Joint BSPGHAN and Coeliac UK guidelines for the diagnosis and management of ceoliac disease in children. Arch Dis Child 2013; 98: 806-811

5. Abu-Zeid YA, Jasem WS, Lebwohl B, Green P, ElGhazali G. Seroprevalence of celiac disease among United Arab Emirates healthy adult nationals: A gender disparity. World J Gastroenterol. 2014; 20: 15830–15836.

6. Admou B, Essaadouni L, Krati K, et al. Atypical celiac disease: From recognizing to managing. Gastroenterol. Res. Pract. 2012; 2012: 637187.

7. Rostami Nejad M, Hogg-Kollars S, Ishaq S, Rostami K. Subclinical celiac disease and gluten sensitivity. Gastroenterol Hepatol Bed Bench. 2011; 4: 102–108

8. Basu A., Ray Y., Bowmik P, Rahman M, Dikshit N, Goswami RP. Rare Association of Coeliac Disease with Aplastic Anaemia: Report of a Case from India. Indian J Hematol Blood Transfus. 2014; Sep; 30: 208–211.

9. Hisamatsu T, Erben U, Kühl A.A. The Role of T-Cell Subsets in Chronic Inflammation in Celiac Disease and Inflammatory Bowel Disease Patients: More Common Mechanisms or More Differences. Inflamm Intest Dis 2016; 1: 52-62.

10. Kordasti S, Marsh J, Al-Khan S, et al. Functional characterization of CD4+ T cells in a plastic anemia. Blood 2012

119: 2033-2043.

11. Grey-Davies E, Hows JM, Mars JCW. Aplastic anaemia in association with coeliac disease: a series of three cases. Br J Haematol. 2008; 143: 258–260

12. Salmeron G, Patey N, de Latour RP, et al. Coeliac disease and aplastic anaemia: a specific entity? Br J Haematol. 2009; 146: 122–124.

13. Ben-Horin S, Polak-Charcon S, Barshack I, et al. Celiac disease resolution after allogeneic bone marrow transplantation is associated with absence of gliadin-specific memory response by donor-derived intestinal T-cells. J Clin Immunol. 2013 Nov; 33: 1395-402.

Manuscript Information: Received: February 02, 2018; Accepted: April 20, 2018; Published: April 30, 2018

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Citation: Kiblawi MH. The association between celiac disease and aplastic anemia: A case report. Open J Clin Med Case Rep. 2018; 1403.