Celiac Disease with Acute Myeloid Leukemia: A Rare Association

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Abstract

Celiac disease is a malabsorption disorder, due to hypersensitivity to dietary gluten. Iron deficiency anaemia and predisposition to lymphoma are known haematological manifestations. There are a few reports on celiac associated leukaemia and still few of acute myeloid leukaemia (AML) associated with celiac disease (two cases). We are reporting probably the third case in literature of acute myeloid leukaemia associated with celiac disease in a 15 years old boy.

Keywords: Celiac disease; Acute myeloid leukemia; Lymphoma

Introduction

Celiac disease (CD) is a protein malabsorption syndrome with systemic manifestations. It results from intestinal sensitivity to the gliadin fraction of gluten from wheat, rye, barley and oats. Most children present during the second year of life, but the age at onset and the severity are variable. It is thought that intestinal damage and villous atrophy result from a cell-mediated immune response initiated by exposure to a polypeptide fragment of gliadin. The increased incidence of celiac disease in children with type 1 diabetes mellitus, IgA deficiency, and Down syndrome is consistent with possible immunologic factors in the development of celiac disease. Individuals with HLA DR4 and perhaps DR3 tissue types are at higher risk.

The association of CD and intestinal lymphoma is well known. The association between CD and intestinal T-cell Non-Hodgkin lymphoma (NHL), called enteropathy-associated T-cell lymphoma (ETL), appears to be particularly strong but these aggressive lymphomas are rare. There has been few case reports of leukaemia associated with celiac disease. However, only 2 cases of celiac disease in literature have been so far reported to be associated with acute myeloid leukemia. Whether development of leukemia in celiac disease is fortuitous, or whether it has an origin similar to that of other reported malignant diseases in the celiac syndrome is not clear.

Case

A 15 years old boy, a known case of celiac disease attended the haematology OPD with chief complaints of weakness, petechial rashes of 15 days duration. He was diagnosed as celiac disease 6 months back on the basis of small bowel biopsy and positive tissue trans-glutaminase antibody and had been on a gluten free diet for last 6 months. On examination he had pallor, generalized petechiae and hepatomegaly. He had been on a gluten free diet for last 6 months. On investigation he was found to be anaemic with Hb of 8.0 g%, TLC of 8000/μl and decreased platelets (15000/μl). His peripheral blood had 33% blasts. Clinical chemistry was within normal limits except for raised serum alkaline phosphatase, and serum was positive for tissue trans-glutaminase (122.6 au/ml).

He was investigated further on lines of acute leukaemia. Bone marrow aspiration revealed occasional megakaryocytes, few erythroid, myeloid cells and many blasts with high nuclear to cytoplasmic ratio, moderately abundant basophilic cytoplasm, round to indented nuclei with prominent nucleoli. Bone marrow biopsy showed chiefly fibrotic marrow with patchy cellularity, increased megakaryocytes with focal clustering; few areas showed normally maturing erythroid and myeloid cells with an area with aggregate of atypical cells. Reticulin grade was III. Immunophenotypically cells were positive for CD 13, CD133, CD117, CD34, and HLADR. Cytogenetics study was normal. The case was diagnosed as Acute Myeloid Leukemia associated with celiac disease. The patient didn’t opt for treatment and left against medical advice.

Discussion

Celiac disease is a disorder in which the proximal small bowel mucosa is damaged as a result of dietary exposure to gluten. It mostly affects people of northern Europe and their descendants in other parts of the world. The disorder does not present until gluten products have been introduced into the diet. The most common period of presentation is between 6 mo and 2 yr of age, and it is a permanent intolerance to gluten. The disorder is associated with major histocompatibility complex class II alleles DQA1*0501 and DQB1*0201 [1].

Various haematological manifestations of celiac disease include anemia secondary to malabsorption of iron, folic acid or vitamin B12, thrombocytosis, thrombocytopenia, leukopenia, venous thromboembolism, hyposplenism, and IgA deficiency. Many cases have been reported in literature of lymphoma occurring in patients of celiac disease. Recent epidemiologic studies suggest a relative risk developing an NHL as a complication of CD ranging from 2.1 to 6.6. Patients with celiac disease have a 50- to a 100-fold increased risk of developing malignant lymphoma compared with the general population. The exact risk is unknown as the precise prevalence and incidence of celiac disease in the population is also unknown [2]. Patients with celiac disease are at increased risk of being diagnosed with lymphoma of T-cell type [3,4]. There is a strong relationship between CD and enteropathy type T cell lymphoma (ETL). One study showed that the odds ratio (OR) of being diagnosed with ETL was 19.2 among patients with CD. A more recent Swedish study showed the standardized incidence ratio (SIR) for ETL to be 51. Even though the relative risk of developing ETL is most significantly increased in CD patients, non-ETLs, including B-cell NHL and extraintestinal T-cell NHL, are more common in aggregate than ETL in these patients. Multiple studies suggest that there may be a reduction of risk with long-term adherence to a GFD. The benefit of a GFD may be slow in accruing in those who are diagnosed later in life and, in at least 1 study; the risk of NHL seemed to persist. Fundia
et al. suggested that CD has chromosome instability affecting specific points that could be related to the high prevalence of malignancies in this disorder. In their study, they found that fourteen spontaneous chromosome aberrations and 5 induced fragile sites specific for CD patients presented a strong coincidence (70%) with bands involved in T- and B-cell malignant lymphoma rearrangements.

There are very few cases reported in literature of acute leukemia associated with Celiac disease. The association does not appear to be common; it is difficult to tell if that is due to the low level of suspicion of celiac disease in general, or if it is due to a rare association. Gupte et al. reported a case of 12 years old girl diagnosed with celiac disease who developed acute myeloid leukemia 4 months after her diagnosis. Molitor et al. [5] described a case of T cell large granular leukaemia in a 70 years old female, diagnosed with celiac disease 3 months prior. Re G et al. [6] reported a case of hairy cell leukaemia after a history of celiac disease. Kline et al. [7] reported a case of celiac disease that developed acute myeloid leukaemia 3 years after diagnosis of celiac disease. He was treated with conventional chemotherapy followed by allogenic stem cell transplantation and her symptoms of celiac disease improved as well [7]. Autologous HSCT was reported recently in a series of 7 adults with refractory CD with aberrant T cells [8].

The issues in management of acute leukaemia with celiac disease have not been dealt with separately in literature because of paucity of cases. Probably, management does not differ from other cases. Conventional chemotherapy is the mainstay of treatment with HSCT, if possible. HSCT has resulted in improvement of symptoms of celiac disease as well. However, co morbidities need to be especially cared about, with special emphasis on nutritional aspects.

To conclude, in any patient with celiac disease, having hematological complaints, with organomegaly on examination, a possibility of lymphoma should be kept. Bone marrow examination should form a part of work up, as some of these patients may be harbouring more sinister leukemias.

References