
Case Report

Concomitant Hodgkin's Lymphoma and Atopic Dermatitis in a Child with Celiac Disease

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Celiac disease is an autoimmune disease associated with increased risk of several diseases including a variety of malignancies. This is the first report of the concomitance of atopic dermatitis and Hodgkin's lymphoma in a child with celiac disease.

Here, we report an 11-year-old boy with chronic diarrhea, glossitis, chronic dermatitis, and megaloblastic anemia who later developed Hodgkin's lymphoma.

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Introduction

Celiac disease (CD) is an autoimmune disorder characterized by malabsorption induced by the intake of gluten proteins present in wheat, barley, and rye. Studies show that it is not merely a gastrointestinal disease and that it is not as rare as it was once considered.¹ CD is associated with increased rates of several diseases, such as iron-deficiency anemia, osteoporosis, dermatitis herpetiformis, several neurologic and endocrinologic diseases, other autoimmune disorders, and various malignancies, most importantly intestinal lymphoma.² Here, we report a child with Hodgkin's lymphoma and severe atopic dermatitis associated with CD.

Case Report

An 11-year-old boy was admitted for anemia work-up in September 2000. At that time, he was suffering from chronic diarrhea, abdominal distension, glossitis, and chronic dermatitis. Initial laboratory examinations revealed a macrocytic anemia with a hemoglobin level of 10 g/dL and a

mean corpuscular volume of 100.7 fL. A bone marrow aspiration revealed a hypercellular bone marrow with erythroid hyperplasia and megaloblastic changes. The serum folate level was within the normal range, but serum vitamin B12 level was low (110 pg/mL). He was treated with parenteral vitamin B12 and his anemia and glossitis were resolved after a few weeks.

On January 2002, he returned with diarrhea, abdominal distension, dermatitis, and anemia. This time, anemia was normochromic and normocytic with a low ferritin level (7.5 µg/L), low serum iron (28 µg/dL), and an elevated total iron-binding capacity (402 µg/dL). Due to the chronicity of diarrhea and anemia, consultation with a gastroenterologist was requested and gastrointestinal endoscopy with biopsies was performed. Histopathologic examination revealed a chronic active gastritis with *Helicobacter pylori* colonization, atrophy of duodenal villi, and chronic inflammatory infiltrates in the lamina propria compatible with CD (Figures 1 and 2).

The patient was treated with a gluten-free diet and all his clinical symptoms including abdominal distension, diarrhea, and anemia were resolved.

During the treatment of his CD, the patient developed a cervical lymph node. Serologic tests for cytomegalovirus and Epstein-Barr virus were negative. A lymph node biopsy, with a three-month delay due to initial patient's refusal, was performed. The histopathologic findings were consistent with Hodgkin's disease, mixed

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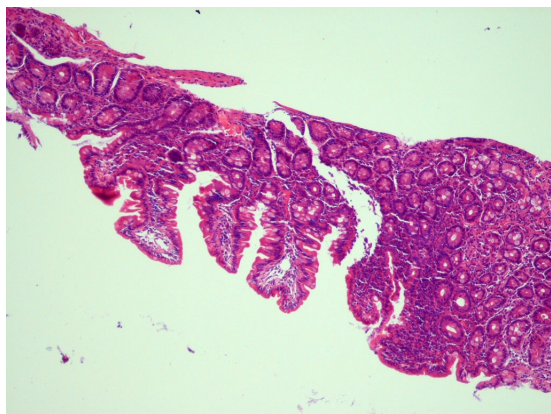


Figure 1. Complete loss of villi in portion of small bowel mucosa (H&E stain ×100).

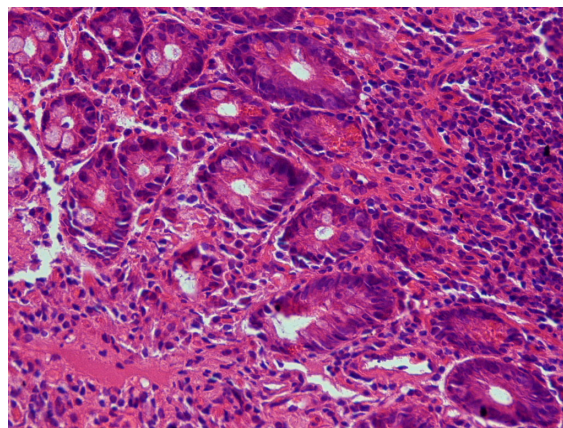


Figure 2. Crypts fairly well preserved with increased number of inflammatory cells (H&E stain ×400).

cellularity type. Due to the involvement of mediastinal and para-aortic lymph nodes indicative of stage III-2A of Hodgkin's disease, he underwent therapy with MOPP/ABVD protocol. Radiation therapy was not administered.

Approximately four years after the termination of chemotherapy, the patient is now in complete remission for Hodgkin's disease. The symptoms of the CD are also completely resolved using a gluten-free regimen, but he is still suffering from severe pruritic dermatitis which is more noticeable on his face and upper parts of the body. The clinical characteristics of this dermatitis—chronic and relapsing eczema with severe pruritus, xerosis, and an elevated serum IgE—were completely compatible with atopic dermatitis. During these years, his serum IgE levels were always more than 1000 IU/mL and was last measured to be 2380 IU/mL.

Discussion

Untreated CD is associated with increased risk of malignancy, particularly lymphoma, mostly with origins from gastrointestinal mucosa. The pathogenesis behind this association is not fully understood, but greater permeability to environmental carcinogens, chronic antigenic stimulation, and release of proinflammatory cytokines are among the suggested mechanisms.³ Also, a correlation between the duration of gluten exposure and the incidence of malignancy has been found. Considering that the relative risk of lymphoma is reduced by a gluten-free diet, celiac patients must be adequately educated about the importance of a gluten-free diet.

There are few cases in the literature reporting an association between CD and pediatric

malignancies.⁴ Virtually all lymphomas that complicate CD are non-Hodgkin type. Indeed, Hodgkin's disease in association with CD has been reported only anecdotally in adults.⁵

The association between atopic dermatitis and CD was first reported more than three decades ago.⁶⁻⁸ Although there is no consensus on the existence of such an association and even though there are reports which state that atopy is not more common in patients with CD,⁹ it has been shown that the incidence of CD in atopic patients is greater than expected. In a study on 401 consecutive atopic patients with no clinical signs of malabsorption, four patients (1%) had evidence of CD which is significantly higher than that in the normal population.¹⁰ The most probable mechanism for this association is the deficiency of local mucosal immunity due to abnormal IgA responses.

It has been reported that the incidence of atopic dermatitis is not higher in patients with Hodgkin's disease. However, interestingly, it has been shown that atopy is a favorable prognostic factor for survival in Hodgkin's disease and the rate of "B" symptoms is lower in those Hodgkin's disease patients who also have atopy.¹¹

Elevated serum IgE levels are not necessarily diagnostic of atopic dermatitis. In particular, several reports have shown that IgE is the immunoglobulin class most frequently found to be elevated in Hodgkin's disease.^{12,13} However, successful treatment of Hodgkin's disease generally results in normalization of serum IgE levels.¹⁴ Consistently elevated levels of IgE in our patient both before developing Hodgkin's disease and after treating the disease support the notion that this was most likely related to his atopy.

To the best of our knowledge, this is the first case of concomitant Hodgkin's lymphoma, CD, and atopic dermatitis. Although atopic dermatitis is common, the association between severe atopic dermatitis and a systemic autoimmune condition and a hematologic malignancy is of clinical interest.

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