

## CASE REPORT

# Aggressive Burkitt-Like Lymphoma of Colon in a Patient With Prior Celiac Disease

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**Background:** Celiac disease (CD) and immunosuppression are the two risk factors for gastrointestinal, as well as non-gastrointestinal, non-Hodgkin's lymphomas (NHL). Recent large retrospective studies confirm that celiac disease significantly increases risk of developing small bowel lymphomas by 30 to 40 percent and other gut malignancies by 83-fold. **Case Report:** A 75-year-old man with a history of CD of two-year duration presented with pallor, fatigue, and 20-pound weight loss of three weeks duration. There was a vague non-tender mass in the right hypochondrium, and his stools tested positive for occult blood. The lab values were within normal range, except for hemoglobin of 11mg/dL, MCV 75, mildly elevated SGOT of 61 IU/L, and LDH of about 5000 IU/L. Work-up including computerized tomography (CT) scan, positron emission tomography (PET) scan, and colonoscopy were performed. **Results:** A CT scan of the abdomen showed extensive carcinomatosis, scattered lymphadenopathy, and small pleural effusions. PET scan results coincided with CT findings. Colonoscopy revealed a friable nodular mass in the hepatic flexure, histopathology of which confirmed a high-grade B-cell lymphoma. Flow cytometry following immunostaining was positive for CD10, CD19, CD20, CD45, CD79a, and Ki-67. FISH assay demonstrated t(14:18) translocation and bcl-2 rearrangement. The bone marrow biopsy showed evidence of disease. The patient was treated with rituximab, plus cyclophosphamide, Adriamycin, vincristine, and prednisone (CHOP-R), with intrathecal methotrexate prophylaxis. Currently, the patient remains in remission. **Conclusion:** This is the first case of aggressive Burkitt-like lymphoma (BLL) occurring in a patient with celiac disease in his eighth decade of life. It is possible that chronic inflammation, profound immunosuppression, and nutritional deficit could lead to development of high-grade B-cell lymphoproliferative disorders. Further molecular studies are warranted to investigate the link between certain polymorphisms of human leukocyte antigens (HLA) in B-cell populations in the gut, and this might be useful to identify high-risk individuals in the population of patients with CD.

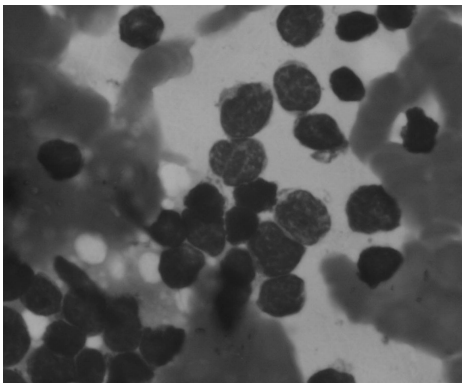
## BACKGROUND

Celiac disease and immunosuppression are the two risk factors for gastrointestinal as well as non-gastrointestinal

non-Hodgkin's lymphomas (NHL)<sup>†</sup>. Although there has been conflicting data from studies [1,2], recent large retrospective studies confirm that celiac disease (CD) significantly increases risk of developing

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<sup>†</sup>Abbreviations: CD, celiac disease; FISH, fluorescent in situ hybridization; BLL, Burkitt-like lymphoma; HLA, human leukocyte antigens; NHL, non-Hodgkins lymphoma; CT, computerized tomography; EATCL, enteropathy associated T-cell lymphoma; PET, positron emission tomography.



**Figure 1. Bone marrow examination showed infiltration with B lymphocytes coinciding with Burkitt's-like lymphoma.**

small bowel lymphomas (more commonly T-cell type) by 30 to 40 percent and other gut malignancies by 83-fold [3,4]. Lymphoma accounts for only 0.6 to 0.8 percent [4] of colonic malignancies with one case of Burkitt-like lymphoma (BLL) reported so far [5]. The possible mechanisms for the development of lymphomas are not clear but might be related to the chronic inflammation of the bowel, leading to a sequential multi-step process culminating in oncogenic mutations. Here, we report a case of aggressive BLL of the colon in a patient with prior CD.

## CASE REPORT

A 75-year-old man with history of celiac disease presented with pallor, fatigue, and 20-pound weight loss of three weeks duration. CD was diagnosed two years prior, at which point the patient underwent extensive evaluation for unexplained microcytic hypochromic anemia and was found to have an elevated endomysial antibody titer. A small bowel biopsy showed celiac disease. The patient was then placed on a gluten-free diet and the anemia resolved completely.

On physical examination, a vague nontender mass in the right hypochondrium was found and his stools tested positive for occult blood. The laboratory values were within normal range, except for hemoglobin (11mg/dL), MCV 75, SGOT (61 IU/L) and LDH (5000 IU/L).

CT scan of abdomen showed extensive carcinomatosis. There were also small pleu-

ral effusions and scattered lymphadenopathy. PET showed diffusely hyper-metabolic foci coinciding with CT findings. Colonoscopy revealed a friable nodular mass in the hepatic flexure and proximal transverse colon. However, histopathologically the mass consisted of a high-grade B-cell lymphoma. Flow cytometry following immunostaining reported positive CD10, CD19, CD20, CD45, CD79a, and Ki-67. FISH assay demonstrated t(14:18) translocation and bcl-2 rearrangement. The bone marrow biopsy showed evidence of disease (Figure 1). The bone marrow biopsy was also positive for CD10, CD19, CD20, CD38, CD45 and HLA-DR.

The patient was treated with rituximab cyclophosphamide, Adriamycin, vincristine, and prednisone (CHOP-R) according to protocol, with intrathecal methotrexate prophylaxis. The patient is currently in remission.

## DISCUSSION

This is one of the very few documented cases of an aggressive colonic Burkitt-like lymphoma in a patient with a history of celiac disease. CD is an inflammatory condition of the small intestine in which there is gluten-mediated damage to small intestinal villi. It is a common disorder affecting as much as 1 percent of the population [6,7]. The association between CD and intestinal lymphoma was first described by Fairley and Mackie in 1937 [8]. A recent large multi-center retrospective study involving over 9,800 patients in Europe indicates that celiac disease patients have an increased risk of NHL (Odds ratio 2.6, 95 percent CI 1.4-4.9) [4].

According to Catassi et al., enteropathy-associated T-cell lymphoma is the most common with an incidence rate of 0.5- to 1 million, constituting 35 percent of all small bowel lymphomas, followed by B-cell and adenocarcinomas [2]. Koo reported a case of operable colonic lymphoma confined to the transverse colon [5]. We report this rare case in which a patient with a history of CD developed colonic BLL with extensive peritoneal involvement. There are three interesting and unique features: While CD is usually

a disease more common in the fourth and fifth decades of life, our case was diagnosed in his eighth decade. Secondly, his lymphoma was diagnosed two years after the diagnosis of celiac disease, in contrast to literature, if celiac disease is diagnosed first, lymphoma occurs within five to 10 years with a probable time lag of up to 60 years [9]. Lastly, the median age for incidence of BLL is 55 years, while our patient was in his eighth decade of life.

Several oncogenic mechanisms might predispose the a digestive tract afflicted with CD to malignancy: increased permeability of environmental carcinogens like Epstein-Barr virus, chronic inflammation, release of pro-inflammatory cytokines, defective immune surveillance (post-kidney transplant and Human Immunodeficiency Virus patients) and nutritional deficiencies caused by the disease or the gluten-free diet [10]. Increased ribosomal DNA transcriptional activity *in vitro* in mucosal cells from patients diagnosed with CD has been demonstrated [11]. All the above-mentioned mechanisms culminate in proneoplastic mutations in B-cell populations such as deletion of 9p21, 17p23(P53) and gain of 1q chromosome. Howell and associates have previously demonstrated that apart from certain HLA genotypes (DQA1\*0501 and DQB1\*0201) predisposing to CD and EATCL, additional HLA-DR/DQ alleles might independently operate to cause lymphomas [12]. Likewise, further molecular typing studies are warranted to point out the nature of B-cell populations in the gut in patients who develop BLL. This can help to identify high-risk individuals among patient populations with diagnosed CD to aid in earlier therapeutic intervention and better prognosis.

## CONCLUSION

This is the first case of aggressive BLL occurring in a patient with celiac disease in his eighth decade of life. It is possible that chronic inflammation from CD predisposes individuals to the development of both high- and low-grade B-cell lymphomas, although

this hypothesis is yet to be proven. Prognosis of these patients could be improved by identifying certain unique HLA genotypes associated with development of high grade B-cell lymphomas by closer monitoring and earlier intervention.

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