Untreated celiac disease (CD) is associated with a wide variety of malignant complications. The malignancies most frequently associated with CD include T-cell lymphoma and adenocarcinoma of the small intestine and esophagus. However, other sites including oral and isolated lymphomas involving the central nervous system have been reported in association with CD. Treatment of celiac disease with a gluten-free diet is thought to reduce the chance of CD-associated malignancies. Colon malignancies are generally not considered to be associated with CD. However, the results of one study suggest an association between CD and right colon carcinoma compared with colon carcinoma in patients without CD, which occur most frequently in the descending colon. This is a case of multifocal lymphoma of the colon in association with celiac disease.

CASE REPORT

The patient is a 63-year-old European-American woman who presented initially with a 5-day history of left abdomi-
nal pain and passage of mucus with bowel movements. She noted a decrease in appetite and weight loss of 18 to 25 pounds over the 6 months prior to presentation. Review of systems revealed “lifelong” constipation, which had become progressively worse over the previous 3 months and was associated with decreased stool caliber and passage of some bright red blood per rectum. Her history was notable for hypothyroidism. Family history was positive for breast cancer but otherwise negative for malignancy, autoimmune disorders, and digestive diseases. Complete blood cell count (CBC) included a hemoglobin of 7.9 g. Laboratory studies were normal without evidence of malnutrition. Colonoscopy disclosed multiple large necrotic ulcers in the ascending, transverse, and descending colon with necrosis and inflammation. Initial biopsy specimens were negative for malignancy.

The patient was transferred to our institution 5 days later. She had increasing fatigue and weakness over the previous 3 to 6 months and there were instances of fevers, chills, and night sweats. Colonoscopy revealed deep ulcerations throughout the colon (Fig. 1). Biopsies revealed an anaplastic large cell lymphoma. Immunophenotyping showed a CD3+, CD4- T-cell lymphoma. CT of the abdomen disclosed lymphadenopathy and thrombosis of the mesenteric veins. No other metastases were found so the lymphoma was considered stage 2B. Treatment was started with allopurinol, prednisone, then cyclophosphamide, hydroxydaunomycin, Oncovin, and prednisone (CHOP). Small bowel contrast radiography was normal. Esophagogastroduodenoscopy (Fig. 2A) was performed within 24 hours of the initiation of chemotherapy because of GI bleeding, and biopsies of the duodenum revealed a flattened duodenal mucosa, inflamed lamina propria with numerous plasma cells and lymphocytes, and an increase in intraepithelial lymphocytes (Fig. 2B). No infectious agents were seen. Anti-gliadin antibody was positive at IgA 117 (normal 0-19) and IgG 47 (0-19). The patient was discharged home a few days later. A gluten-free diet was not started because of the patient’s poor performance status.

DISCUSSION

T-cell lymphoma is a relatively rare form of lymphoma, accounting for less than 25% of all lymphomas. Small intestinal T-cell lymphomas although rare, are most frequently found in association with CD. Although an association of T-cell lymphoma of the colon and CD has not been described previously, several lines of evidence suggest that there may be a connection between the two conditions in our patient.

Celiac disease can result in changes in parts of the GI tract other than the small intestine. It has...
been associated with lymphocytic infiltration of the gastric and colonic mucosa. These lymphocytes seem to be increased in number in response to gluten exposure, probably by a cytokine-dependent mechanism. Additionally, gluten challenge to the rectal mucosa via gluten enemas in patients with untreated CD produces immunologic changes in the rectal mucosa including an increase in CD3+ and CD25+ lymphocytes and proinflammatory cytokines that resolve over time. However, the rectal response to gluten enema is greatly reduced in treated patients, suggesting that continued luminal exposure to gluten is necessary to maintain the proliferation of lymphocytes and the responsiveness of the mucosa to gluten challenge. Celiac disease has also been reported to occur more frequently in lymphocytic colitis than in the general population.

The changes in the immune system associated with CD are suggestive of a pre-malignant state of the lymphocytic system. The stimulus of gluten in CD induces proliferation of both lamina propria and intraepithelial compartments of the intestinal mucosa. Although either site may be the origin of the lymphomatous changes it is thought that clonal expansion of intraepithelial lymphocytes bearing a unique phenotype is largely responsible. What triggers the malignant change from a proliferative state is unclear. However, it may be the same cells that are involved in the ulcerative jejunitis that are subsequently found in the ensuing lymphomas. CD is associated with increased chromosomal fragility, which may also predispose patients with this disease to malignant degeneration. To change the outcome of this disease process and its high mortality, early identification and treatment of CD will be necessary as well as a method of recognition of an intermediary phase in the process of malignant degeneration. Unfortunately, 60% of patients with enteropathy associated T-cell lymphomas present with simultaneous CD, not previously diagnosed.

This case, as well as the suggestion that colon adenocarcinoma associated with CD is more likely to occur in the right side of the colon, appear to indicate that CD may be associated with colonic malignancy. A prospective study in a large cohort of patients with CD would be necessary to estimate the risk. If high, this might alter the approach to colon cancer screening in these patients. It is likely that our patient had silent CD for many years, although her only GI complaint prior to 6 months before her presentation was constipation.

REFERENCES