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Case Report

Coeliac disease presenting with colonic lymphoma

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Coeliac disease is associated with an increased risk of small bowel lymphoma and adenocarcinoma.[1] The earliest association between coeliac disease and malignant lymphoma was reported by Fairley and Mackie (1937).[2] Histological stains enabled the identification of T-cell lymphoma, now designated as enteropathy-associated T-cell lymphoma (EATL) as the most common neoplasm (96%) associated with coeliac disease in one series,[3] and B-cell lymphoma accounting for the remaining 4%. The cause for this association remains uncertain. HLA genotyping has indicated that lymphoma is more common in DQA1*0501, DQB1*0201 individuals.[4]

Small bowel malignancy typically occurs in the fifth to seventh decades of life. Recent studies using population screening have provided an estimate of prevalence of coeliac disease (in particular, 1 in 122 in Northern Ireland [5]; 5.3 in 1000 in Sweden [6] and 4.9 - 5.7 in 1000 in Italy [7]). The common presentations of lymphoma are an exacerbation of their underlying disease (e.g. diarrhoea, pain, abdominal mass, weight loss) or a surgical complication (e.g. perforation, obstruction). We report a case of coeliac disease presenting with colonic lymphoma.

CASE REPORT A 63 year old man presented with one-month history of nausea, vomiting, diarrhoea and weight loss. He had a history of heavy alcohol consumption and previous bouts of morning diarrhoea for two years. Physical examination was unremarkable. Full blood picture, electrolytes and liver function tests were normal; the albumin was low. Following admission, he developed intermittent pyrexia and persistent diarrhoea despite anti-diarrhoeal medication.

On admission, antibodies to endomysium and tissue transglutamase (31Eu/ml, normal: 0-25) were positive. Endomysial antibodies were measured by immunofluorescence with a titre 1:5 or greater taken as positive, and tissue transglutamase was measured by immunosorbent assay (ELISA). OGD was performed, and duodenal biopsy showed partial villous atrophy. Colonoscopy showed a large flat ulcer at the distal transverse colon and biopsies revealed mucosal inflammation with no evidence of malignancy. He was commenced on a gluten-free diet. Ten days later, he developed two large episodes of bright red bleeding per rectum which required blood transfusion; however he continued to bleed and 48 hours later, laparotomy was undertaken.

At laparotomy, the ulcerated area of colon was identified and transverse colectomy was performed. It was also noted that a segment of ileum was thickened. No procedure was carried out on the small bowel. Histological examination confirmed an ulcer with appearances suggestive of malignant lymphoma. The lymphoma was covered by thick inflammatory exudates; probably explaining the initial benign colonoscopic biopsies. Some of the cells were positive for CD68. The majority of cells did not stain for either B- or T-cell markers. Therefore, it was regarded as a non-B, non -T cell lymphoma.

Due to the appearance of the small intestines at laparotomy, a small bowel series was carried out which was normal. Postoperatively, he became

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very depressed and his appetite waned and he was commenced on enteral feeding. Three weeks later he had a sudden deterioration and died due to pneumonia. Autopsy failed to show any further evidence of systemic lymphoma.

DISCUSSION

Lymphoma accounts for approximately 0.2 to 0.6% of large bowel malignancies.[8] The mean age of presentation is 55 years with a male preponderance.[9] So far, two risk factors have been identified: inflammatory bowel disease[10] and immunosuppression (post-kidney transplant, HIV, immune disorder).[11, 12] In coeliac disease a lymphocytic infiltrate develops in the gastric and colonic mucosa;[13] to date no association has been described between coeliac disease and colonic lymphoma. Immunological changes (rises in CD3+ and CD25+ lymphocytes and pro-inflammatory cytokines) have been noted in rectal mucosa of untreated coeliac patients, after a gluten challenge in the form of gluten enema had been given.[14]

As described above, microscopic inflammation is present in the colon of those with coeliac disease. It is possible that such inflammation could predispose to malignant transformation. As yet, this hypothesis remains untested. Colonic adenocarcinoma has been described in patients with coeliac disease.[15] In this report, three patients suffering from coeliac disease were found to have a right sided colonic adenocarcinoma. One patient was diagnosed with coeliac disease ten years previously and ulcerative colitis six years after that. The remaining two had the diagnosis of carcinoma and coeliac disease made within months of each other. There is one other documented case of colonic lymphoma in coeliac disease.[16] This was histologically a very different lesion from this case, being a diffuse differentiated T-cell lymphoma, which was treated primarily by chemotherapy.

There are several histopathological classifications of lymphoma due to the diverse morphology and cellular polymorphism of the disease. Descriptions such as malignant lymphomatous polyposis, tumours of mucosa-associated lymphoid tissue, tumours of 'centrocyte-like cells', 'maltoma' and polymorphic B-cell lymphomas have been used. Most immunohistochemical studies of gastrointestinal lymphoma have reported that the majority of tumours are of B-lineage via immunoreactivity with one or more B-cell markers.[17] However, some cases of high-grade lymphoma failed to stain with anti-leukocyte common antigen. In this case, tumour cells may stain positive for other antibodies that recognise leucocyte common related antigen. Yet, there is no specific combination of antibodies that allows positive identification of any of the histological subgroups.[18]

Prognostic data of primary colorectal lymphoma in the literature is scarce. Although histological stage significantly correlates with survival, in several series different pathological classifications were used. In another series, the presence of tumour cell MT2 immunoreactivity appeared to be a better determinant of prognosis than histological grade.[17] Surgical resection is recommended for localised colo-rectal lymphoma as it may provide important prognostic information, offer a chance for cure, with or without adjuvant therapy, and prevent surgical complications.[18] The value of chemotherapy, either alone or as adjuvant therapy for colonic carcinoma has not been prospectively evaluated. Radiotherapy and/or chemotherapy may also be of value for lymphoma with advanced stage and high-grade lymphomas.[17]

CONCLUSION

We have highlighted an uncommon disease occurring in the context of coeliac disease. This is the first report of coeliac disease in association with solitary colonic lymphoma, although there may be a possibility of the tumour occurring coincidentally in a patient with coeliac disease. A recent retrospective study in Northern Ireland had demonstrated that a third of patients with apparently spontaneous small bowel lymphomas had unrecognised coeliac disease.[19] This case may suggest that a similar search for coeliac disease in patients with colonic lymphoma might be appropriate.

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