Colitis ulcerosa complicated by malignant lymphoma: case report and analysis of published works

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Abstract
A 51 year old woman with a two year history of ulcerative colitis developed a wide spread gastrointestinal non-Hodgkin’s lymphoma of low grade malignancy (MALT-lymphoma) involving upper and lower gastrointestinal tract, spleen, and bone marrow. After chemotherapy, clinical symptoms improved and lymphocytic infiltrates disappeared. Thirty nine cases of ulcerative colitis and 22 cases of Crohn’s disease complicated by gastrointestinal lymphomas reported in published works are reviewed. In inflammatory bowel diseases any dense lymphocytic infiltrates seen in biopsy specimens obtained from ulcerative colitis or Crohn’s disease should be assessed to exclude gastrointestinal lymphoma.

Keywords: colitis ulcerosa, non-Hodgkin’s lymphoma.

Although colonic carcinoma is the major longterm complication of ulcerative colitis, primary colonic lymphoma has also been shown to be associated with ulcerative colitis. As the clinical symptoms of chronic inflammatory bowel disease and malignant lymphoma of the large bowel can be very similar, diagnosis of lymphoma can be masked and correct treatment may be delayed. We report a case of a patient suffering from ulcerative colitis for more than two years when malignant lymphoma of the colon developed. The diagnosis was made after treatment failure of the colitis with corticosteroids, azathioprine, and sulphasalazine.

Case report
A 51 year old woman suffering from ulcerative colitis since 1989 was transferred to our hospital in 1991 because of ineffective longterm treatment with corticosteroids, azathioprine, and sulphasalazine. First endoscopy of the colon and histological examination in 1989 showed chronic inflammatory bowel disease with typical signs of ulcerative colitis (Figs 1 and 2) involving the entire colon and the terminal ileum. Different therapeutic strategies including total parenteral or enteral nutrition had not improved the symptoms, which were dominated by 10–15 bloody stools a day.

When we saw the patient in 1991, she presented with a slightly painful abdomen with normal peristalsis, no superficial lymphadenopathy, no hepatosplenomegaly. Laboratory examinations showed mild inflammatory

Figure 1: Endoscopic view of the colon with completely disappeared vascular pattern, highly increased vulnerability of mucosa, and slight mucosal damage representing an endoscopy index of 8 indicating distinct inflammatory activity according to Rachmilewitz.65

Figure 2: Typical ulcerative colitis with crypt distortion, crypt abscesses, and irregular surface. Haematoxylin and eosin, original magnification ×225.
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Colonoscopy showed a mild form of acute ulcerative colitis. Histological examination of the stomach and duodenal biopsy specimens showed not only typical polymorphonuclear inflammatory infiltration, but also distinct lymphocytic infiltration (Figs 3 and 4), which was even more evident in the colonic biopsy specimens (Fig 5A). In all sections the lymphocytic infiltration invaded the mucosa forming lymphoepithelial lesions and destroying the mucosal glands, typical evidence for the presence of primary gastrointestinal malignant lymphoma of MALT type (Fig 5B). Cells showed typical cleaved nuclei reminiscent of centrocytic cells (Fig 5C). Characteristic signs for acute ulcerative colitis were no longer detectable. Further immunocytochemistry confirmed this to be a B cell lymphoma (Fig 6). Histological examination of the bone marrow showed invasion of the malignant lymphoma, which had already led to a 40% suppression of bone marrow cells (Fig 7).

Summarising the results, our patient had developed a low grade B cell non-Hodgkin's lymphoma involving the upper and lower gastrointestinal tract and the bone marrow—that is, stage IV. The enlargement of abdominal lymph nodes and spleen was probably also caused by distant lymphoma spread.

**TREATMENT**

The patient received chemotherapy according to the CVP protocol: cyclophosphamide 400 mg/m², vincristine 1·4 mg/m², prednisone 60 mg/m². After three courses, there was a decrease in diarrhoea from 10 to 5 stools daily with no blood contamination. Continuation of the chemotherapy for another three courses did not result in any further decrease in stool frequency. Repeated colonoscopy and bone marrow investigation, however, showed a progressive reduction of the lymphocytic infiltration. After chemotherapy had ended, the colon endoscopically showed typical changes as seen after long standing chronic inflammation of the colon with reduced haustration, but no evidence for acute disorder. Histologically, the malignant lymphoma was no longer present. Bone marrow was also free of lymphocytic infiltration. Abdominal computed tomography showed normal size of spleen and normal lymph nodes.

**Discussion**

Primary gastrointestinal lymphomas occur between 1 and 4% of all gastrointestinal malignancies. The gastrointestinal tract is the commonest site of extranodal lymphomas. In western populations, the stomach is most commonly involved, while colorectal lymphoma comprises between 10 and 20% of primary gut lymphomas in the larger published series. This fraction, however, may be reduced to 3% if ileocaecal tumours are excluded. Most of the tumours show characteristic histological and immunohistochemical features: the B cell tumours are composed of a polymorphic population of centrocytic like...
cells, plasmacytoid cells, and blast cells. Isaacson defined these neoplasmas as 'malignant lymphomas arising in mucosa associated lymphoid tissue – MALToma'. An important and distinctive feature of these lymphoma cells is the tendency to invade mucosal epithelium and form characteristic lymphoepithelial lesions. Often these centrocyte like cells are present as clusters, both intraepithelially and intraluminally and obliterate partially the mucosal glands.

To distinguish between primary and secondary gastrointestinal lymphoma, the definition of primary gastrointestinal lymphoma by Dawson is quite applicable, which consists of a normal chest x ray, no evidence of hepatosplenomegaly or superficial lymphadenopathy, a normal white blood cell count (that is, no evidence for leukaemia), and a predominant tumour mass in the bowel with only local lymphadenopathy. Diagnostic problems may occur, however, to discriminate between primary gastrointestinal lymphoma, which has generalised and nodal lymphoma, with secondary gastrointestinal manifestation. This case fulfils these criteria, except for the mild splenomegaly and bone marrow infiltration, which was caused by distant spread.

The combination of gastrointestinal malignancy and chronic inflammatory bowel disease is of increasing interest. It is already well known that, after 25–30 years of ulcerative colitis, the cumulative risk of developing cancer is about 10%. Adenocarcinoma complicating Crohn's disease is increasingly recognised, especially in the small intestine. The nature of the relation between inflammatory bowel disease and intestinal lymphoma, however, is less certain. The first instance of this association is Barken in 1927 who reported two cases in ulcerative colitis with malignant lymphoma. To date, there are 26 publications reporting 39 cases of non-Hodgkin’s lymphoma (35 cases) or Hodgkin’s lymphoma (four cases) complicating ulcerative colitis. Four of these case reports even describe the additional occurrence of...
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Colon cancer. Most lymphomas in ulcerative colitis, like carcinoma in colitis, arose on the basis of extensive long standing disease (mean duration of colitis at the time of lymphoma diagnosis 12 years; mean age at lymphoma diagnosis 50-3 years). They differ from sporadic colorectal lymphoma in a number of ways; colitis associated lymphomas are more often multiple (38% v 10%, except for malignant lymphomatous polyposis), left sided (compared with the caecal predominance in sporadic lymphoma), high grade (80% v 35%) in an advanced stage at diagnosis. This case does not entirely match these criteria, especially as a long history of ulcerative colitis before the lymphoma is lacking.

The small numbers of reported cases make it difficult to prove a definite association between ulcerative colitis and colon lymphoma, although various mechanisms of pathogenesis have been postulated. These include repeated episodes of prolonged stimuli of the MALT tissue and lymphoid hyperplasia.

There are fewer reports about an association with gastrointestinal lymphoma with regard to Crohn’s disease. We found 20 publications describing 25 cases of this combination. 18 non-Hodgkin’s lymphoma, and four Hodgkin’s lymphoma. In these cases, it is even more difficult to prove an association between the two diseases. Yet, there are some findings supporting this concept: all reported tumours have arisen at sites of active inflammatory bowel disease and the comparative incidence of lymphoma in different parts of the gut seems to reflect the incidence of Crohn’s disease. Furthermore, it is interesting to note that Crohn’s tissue homogenates have been reported to induce B cell lymphomas in athymic mice suggesting, at least in experimental animals, that a link between Crohn’s disease, immunosuppression, and malignant lymphoma exists. Another factor to be considered is the prolonged use of corticosteroids and azathioprine. A convincing relation has been established between immunosuppressive drug treatment and an increased incidence of malignant tumours in patients after organ transplantation. Recently, an increasing number of cases have been reported in homosexuals in association with the acquired immune deficiency syndrome (AIDS).

Before starting any treatment, profound staging is required. This includes upper and lower endoscopy with multiple biopsy specimens from all different parts, contrast radiography of the small intestine, cervical, thoracic and abdominal computed tomography, bone marrow cytology and histology, scintigraphy of the skeleton, endosonography, and in addition liver biopsy.

Treatment of inflammatory bowel disease combined with gastrointestinal lymphoma follows primarily the guidelines of lymphoma treatment: at stage I and II surgery either alone or in combination with radiotherapy should be performed. Chemotherapy should be the primary treatment for cases of malignant lymphomatous polyposis as this type of lymphoma is usually widespread throughout the gastrointestinal tract. Radiotherapy or chemotherapy, or both may also be of use for cases with advanced stage and high grade lymphomas. Yet, prognosis seems to be poor.

Adenocarcinoma combined with chronic inflammatory bowel disease obviously has a better survival than colorectal lymphoma.

In conclusion, malignant lymphoma of the bowel is a rare but significant complication of inflammatory bowel disease, apparently being more common in chronic ulcerative colitis than in Crohn’s disease. It is quite conceivable that the changed lymphoid populations in inflammatory bowel disease represents the clones in which lymphoma arises. Therefore, it is important to evaluate any lymphocytic infiltrate seen in a biopsy specimen, especially when anti-inflammatory treatment seems to be ineffective.
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Intestinal
degeneration
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disease. Arch
Surg
NeplJ3Med
1985;
colitis
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Gastroenterology
1985;

34-6.


Hughes R. Rectal tumour malignancy: a case possibly originating


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