Case report

Rectal malignant lymphoma in chronic ulcerative colitis

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SUMMARY Carcinoma of the colon as a complication of ulcerative colitis is relatively common, whereas malignant lymphoma is apparently rare; there are approximately 20 recorded cases. We report a case of follicular lymphoma of the rectum in a 73 year old woman with a 21 year history of ulcerative colitis. In view of the possible immune basis of ulcerative colitis, it is important to report and accurately classify cases of lymphoma arising in association with it.

Carcinoma of the colon as a complication of ulcerative colitis is relatively common, whereas malignant lymphoma is apparently rare. Primary malignant lymphoma of the large intestine is itself rare.1 2 There are now approximately 20 recorded cases of large intestinal malignant lymphoma arising in patients with long-standing ulcerative colitis3-16 and one case of malignant lymphoma arising in the terminal ileum of a patient with a ileostomy after colectomy for ulcerative colitis.17 We report a follicular lymphoma of the rectum arising in a 73 year old woman with a 21 year history of ulcerative colitis, and include immunohistochemical and ultrastructural findings to support the diagnosis.

Methods

The colon and rectum were opened before fixation in 10% formol saline. Paraffin sections were prepared, and stained by haematoxylin and eosin, periodic acid-Schiff after diastase digestion, Gomori's reticulin method, and methyl-green-pyronin. Material for electron microscopy was selected from the tumour and fixed in 4% glutaraldehyde, post-fixed in osmium tetroxide, and the sections stained by uranyl acetate and lead citrate.

Paraffin-embedded tumour material was used for immunohistochemical investigation. A controlled trypsin-immunoperoxidase PAP technique modified from the PAP method of Mason et al.18-20 was used to determine the distribution of heavy chains of immunoglobulins (Ig) G, A, M, D, and E, kappa and lambda light chains, lysozyme, and albumin. Trypsin (type II crude pancreatic) was purchased from SIGMA Chemical Company, rabbit anti-human antisera, rabbit PAP, and normal rabbit serum from DAKO, goat anti-rabbit immunoglobulins from Nordic Immunological Laboratories, goat anti-human antisera from Kallerstat Laboratories, and 3,3' diaminobenzidine from BDH Chemicals.

Case report

A 73 year old Caucasian woman presented in December 1979 with a 21 year history of ulcerative colitis. Rectal biopsy and barium enema in 1974 had confirmed the diagnosis and shown narrowing and shortening of the whole colon. In 1978 digital examination suggested thickening of the rectal wall, but a biopsy and barium enema showed ulcerative colitis only (Fig. 1). By December 1979 her complaint was a constant feeling of pressure in the rectum, and rectal examination revealed a large smooth annular mass which was biopsied. Histologically, there was a small area of monomorphic lymphoid cells in the submucosa, and a diagnosis of malignant lymphoma was made. Superficial lymph nodes and radiograph of the chest were normal, and laboratory investigations showed a haemoglobin of 12.5 g/dl, white cell count of 4.8 × 109/1 with normal differential, and erythrocyte sedimentation rate of 46 mm in one hour. Panproctocolectomy was performed and no abnormality of liver, spleen, or abdominal lymph...
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and a smaller mass 4 cm proximally. The cut surface showed a uniform pale appearance with very little mucosal ulceration (Fig. 2). The remainder of the bowel showed typical features of the long-standing ulcerative colitis.

LIGHT MICROSCOPY
The tumour was composed of lymphoid cells: many cells showed a small irregular or cleaved nucleus, though about 40% of cells were larger with a rounded or irregular nucleus (Fig. 3). In addition, plasma cells and histiocytes were present within and around the tumour mass. The reticulin stain demonstrated evidence of follicle formation. These features enable the tumour to be classified as a follicular lymphoma of mixed small and large follicle cells (National Lymphoma Investigation Classification21). Local lymph nodes showed normal reactive changes only. The colonic and rectal mucosa showed features of long-standing, quiescent ulcerative colitis (Fig. 4).

ELECTRON MICROSCOPY
The tumour cells showed irregular and indented nuclear outlines with the chromatin in small clumps centrally and around the margin. The cytoplasm contained few organelles but numerous ribosomes; a few cells contained short lengths of rough endoplasmic reticulum. Golgi zones and well-developed stacks of this reticulum were not a feature. Mature histiocytes and plasma cells were identifiable among the tumour cells.

GROSS PATHOLOGY
The specimen showed an 8 cm annular mass infiltrating the mucosa and muscle of the rectal wall nodes was seen. Subsequently, isotope scans of liver and spleen and lymphangiography have also failed to show any evidence of disease. No further treatment has been given, and the patient shows no evidence of lymphoma at 12 months' follow-up.

Fig. 1  Barium enema in 1978 showing long-standing ulcerative colitis.

Fig. 2  Operation specimen after fixation. Longitudinal section of rectum showing pale tumour infiltrating the wall; two foci are present.
IMMUNOHISTOCHEMISTRY

There was no evidence that the tumour contained immunoglobulin heavy or light chains, or lysozyme. Plasma cells containing IgG, IgM, IgA, kappa, or lambda light chains, and histiocytes containing lysozyme were present within the tumour. The adjacent mucosa contained plasma cells staining predominantly for IgA and kappa or lambda light chains. All negative control sections and endogenous negative control cells were negative.

Discussion

Malignant lymphoma of the large intestine in association with chronic ulcerative colitis is very rare, whereas adenocarcinoma is an accepted risk.22 There are only about 20 recorded cases of
lymphoma, though an accurate estimate is difficult because previously reported cases are included among new series\textsuperscript{8,10} and this distinction is lost in later reviews.\textsuperscript{13,16}

Since the first two cases of ulcerative colitis associated with malignant lymphoma appeared in 1928\textsuperscript{3} case reports have been complicated by frequent changes in the classification of lymphomas, though in about half the cases detailed classification was not attempted.\textsuperscript{15} About four cases of Hodgkin’s disease are recorded, but this diagnosis must now be in doubt in view of recent series of intestinal lymphoma.\textsuperscript{17,23} Henry and Farrer-Brown\textsuperscript{23} reviewed 125 cases of intestinal lymphoma and reclassified all five cases of Hodgkin’s disease as plasma cell tumour. Contrary to this, Isaacson and Wright\textsuperscript{24} published a series of 18 cases of malignant histiocytosis associated with malabsorption, and suggested that some of Henry and Farrer-Brown’s cases were, in fact, malignant histiocytosis with reactive plasma cells. In this context, it is disquieting that a recent report of histiocytic lymphoma in chronic ulcerative colitis\textsuperscript{16} gives no indication whether the authors mean malignant histiocytosis or ‘histiocytic’ in the Rappaport sense.\textsuperscript{25} Assuming they mean the latter, it is likely that all the lymphomas associated with colitis are of B-lymphocyte origin.

Our case fulfils Dawson’s criteria of a primary malignant lymphoma of the intestinal tract.\textsuperscript{26} Detailed study of the tumour shows a follicular lymphoma with a reactive infiltrate of plasma cells and histiocytes. It is thus also of B-lymphocyte origin.

In view of the small number of reported cases, it is questionable if malignant lymphoma is causally related to ulcerative colitis. However, if all the lymphomas are of the same histogenesis then a common aetiology is possible. Marked lymphoid follicular hyperplasia, a B-lymphocyte phenomenon, is common in chronic ulcerative colitis\textsuperscript{9} and may be related to the development of malignant lymphoma.

It is important to be aware of the possibility of malignant lymphoma in ulcerative colitis in order to evaluate correctly any lymphoid infiltrate seen in a biopsy.

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