Role of computed tomography in staging and management of gastrointestinal lymphoma[1]

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Introduction

Gastrointestinal lymphomas, although uncommon, are an interesting group of diseases to the clinician because of their potential curability. In a previous study we have shown that the complete surgical removal of gastrointestinal (GI) lymphoma, even of unfavourable histology, results in a large number of long-term survivors (Blackledge *et al.* 1979). Other patients with inoperable disease can survive for long periods with adequate treatment to the sites of disease. Patients in whom the disease is not controlled, however, usually have a rapid demise. Conventional lymphoma staging, using the Ann Arbor classification, is of limited value because up to 80% of patients will have disease confined to the abdomen. The prognosis of a patient depends on the extent of disease within the abdomen.

Ideally, extensive staging should be carried out at the time of the diagnostic laparotomy. In most cases, however, the finding of lymphoma is unexpected and the full extent of disease is not assessed. Unless a second-look operation is contemplated in a patient who is likely to be malnourished and immunosuppressed, noninvasive staging investigations must be used. Computed tomography (CT) offers advantages over other techniques such as lymphography, radioisotope scanning and gray-scale ultrasonography in examining the abdomen. CT has a high degree of accuracy in identifying involved lymph nodes and, unlike lymphography, all lymph node areas in the abdomen can be examined (Best *et al.* 1978, Schaner *et al.* 1977, Alcorn *et al.* 1977). Although CT cannot detect diffuse infiltration of organs such as liver and spleen, it can detect enlargement and intraorgan deposits. We report here a series of 18 patients with gastrointestinal lymphoma who had CT performed during the course of their disease. The clinical and radiological findings are compared and the use of CT in the management of GI lymphoma is discussed.

Method

A total of 26 CT examinations were performed on 18 patients. Fifteen examinations were performed at presentation, 6 at a time when remission was being assessed, 4 at a time of suspected relapse and one as a check during remission. All patients had histologically proven GI lymphoma. The histology was classified using the Rappaport classification (Rappaport 1966) and the tumours were staged using the staging classification described previously (Table 1, Blackledge *et al.* 1979). Six patients were described as having favourable pathology lymphoma, that is diffuse well differentiated lymphocytic lymphoma or nodular lymphoma. Eleven patients had tumours of diffuse pathology, and in one case the diagnosis was thought to be mixed cellularity Hodgkin's disease. Once a histological diagnosis had been made and the extent of the patient's disease established, treatment was started in the form of chemotherapy. Those patients with favourable pathology lymphoma received cyclophosphamide, vincristine and prednisolone (CVP) given in a course every three weeks. Those patients with unfavourable pathology lymphoma received a six-week induction course of vincristine, adriamycin and prednisolone (VAP). At the completion of initial chemotherapy, most patients

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Table 1. Staging of gastrointestinal lymphoma (Blackledge et al. *1979)*

IA	Tumour confined to gastrointestinal tract
IB	Multiple tumours confined to gastrointestinal tract
IIA	Tumour with local nodes (gastric or mesenteric)
IIB	Tumour with perforation and adherence to adjacent structures
IIC	Tumour with perforation and peritonitis
III	Tumour with widespread nodal involvement (para-aortic or more distant nodes)
IV	Tumour with disseminated disease (e.g. liver, bone marrow involvement)

received abdominal radiotherapy. In the majority of cases this was whole abdominal treatment: 3000 rad were given over 24–27 days and the kidneys were shielded beyond 2000 rad. In some cases, the patients received subsequent maintenance chemotherapy in the form of chlorambucil for those patients with favourable pathology lymphoma, or cyclophosphamide, methotrexate and 6-mercaptopurine given orally for the unfavourable pathology lymphoma group. The patient with Hodgkin's disease received mustine, vinblastine, procarbazine and prednisolone (MVPP) given in courses every six weeks. A total of eight courses was given and this patient then received whole abdominal radiotherapy.

The scans were carried out in the University Department of Radiology at the University of Manchester. The patients were scanned as previously described (Best *et al.* 1978), using an EMI CT 5005 Whole Body Scanner. Briefly, this involved scanning the patients from the lung hila to the pelvis. Scans were performed at 2 cm intervals. Where there was an area thought to be of special interest, this area was scanned at 1 cm intervals. The patients were prepared for CT using a bulk laxative for two days (Isogel, 10 ml twice daily), and 250 ml of Gastrografin diluted 5% v/v was given orally one hour before the scan to delineate the gastrointestinal tract. Movement artefacts caused by intestinal motility were prevented by paralysing the bowel with an intramuscular injection of propantheline 30 mg. Conventional staging investigations included barium studies, bone marrow aspirate and trephine, liver function tests, haemoglobin, red cell indices, differential white count, platelets and ESR. In most cases, the patient's immunoglobulins were assessed and electrophoresis performed. In only one case was a monoclonal immunoglobulin found; this was of the IgM type.

Results

There were 7 patients in whom the primary disease arose in the stomach, 10 with small intestinal primaries and one patient with primary disease in the rectum. Sixteen patients had a diagnostic laparotomy. In 2 patients the diagnosis was made by endoscopic methods. The number of times when different areas were involved with disease as assessed by CT is shown in Table 2. Masses associated with the bowel were seen in 2 patients with gastric lymphoma and one patient with small bowel lymphoma; this disease was near the terminal ileum. In 12

Table 2. Incidence of involved lymph nodes as shown by CT in patients with gastrointestinal lymphoma (26 examinations in 18 patients)

	No. of cases
Mesenteric nodes	6
Para-aortic nodes (+iliac)	13
Coeliac	3
Splenic hilar	1
Mass associated with gastrointestinal tract	3
Liver (1 with intrahepatic deposits)	3
Spleen	6
Normal scans	5
Patients with mesenteric and para-aortic nodes	3

CT examinations, there was disease in the para-aortic nodes; in 2 patients this extended into the high paravertebral or retrocrural area. In the 3 patients with coeliac axis node enlargement, the para-aortic nodes were also enlarged. A mass of enlarged nodes at the splenic hilum was the only evidence of disease outside the gastrointestinal tract in one patient. Splenomegaly was considered to be present when the spleen was shown on a scan below the costal margin; using this criterion, the spleen was enlarged in 6 patients. In 5 patients scanned at the time of initial diagnosis, the scans appeared normal. Two of these patients had had complete removal of their tumours at surgery. In 2 patients mesenteric node disease was found but not removed at operation; this was not seen by CT. In the fifth patient, the only evidence of disease was diffuse abnormalities of the small intestine and evidence of bone marrow infiltration.

Seven patients had scans at presentation and repeat scans either at a time of complete remission or during remission. The initial scans of these patients all showed evidence of disease. In 4 patients abdominal masses could also be felt. Five out of 7 patients responded to treatment, reduction in the lymph node masses being seen by CT in all 5 patients (Figure 1). In the two non-responders, progression of disease in mesenteric nodes was seen in one case, and the disease in the nodes of the other patient remained static. The 5 patients in whom the CT scan showed no evidence of disease remain alive and in complete remission 2–24 months following the CT examination.

In 4 patients, unexpected evidence of disease was found by CT outside the gut and mesenteric region. In 3 cases, this was in the para-aortic or retrocrural nodes. The spleen was enlarged in 2 cases. In 2 of the 4 patients, treatment was successful and repeat scans showed resolution of disease.

In the 15 patients in whom CT was performed at presentation, CT altered the stage from I or II to stage III in 5 cases (33%). With the exception of 3 patients who had relatively complete staging laparotomies, CT in those patients with positive scans showed more extensive disease in the abdomen than had been expected at surgery. In only 2 of 24 CT examinations were involved areas proven at laparotomy not detected. These were in the mesenteric nodes and para-aortic nodes.

Discussion

Gastrointestinal lymphomas represent only 1% of all gastrointestinal tumours. There are no particular presenting symptoms which distinguish lymphoma from carcinoma, and barium studies are rarely useful in predicting lymphomatous disease (Sherrick *et al.* 1965). With the exception of the small intestine, where lymphomas represent about 20% of malignant tumours, a diagnosis of lymphoma is usually unexpected at surgery. CT is unlikely to be able to help in the presurgical diagnosis of gastrointestinal lymphoma. Although CT can detect mass lesions

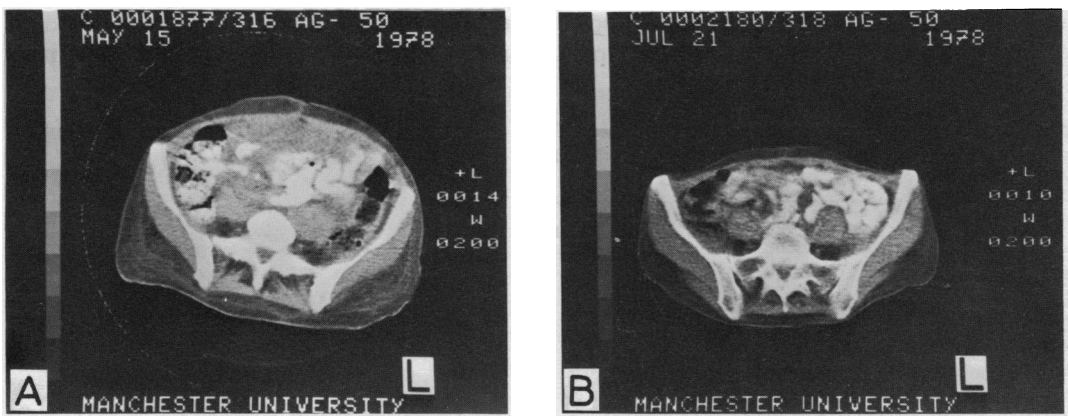

Figure 1. A, scan showing massive disease in the mesenteric region of a patient with primary gastrointestinal lymphoma of the stomach. The gut is clearly seen containing Gastrografin. B, the same patient following chemotherapy. The scan shows resolution of disease

with a high degree of accuracy, it does so on criteria of morphology and size. It cannot predict the histology of a lesion and its ability to establish a specific diagnosis is thus poor (Baker & Way 1978, Witkowski *et al.* 1978). It is not the examination of choice for examining the lumen of the GI tract and has no advantages over barium studies in these circumstances. The role of CT must be directed towards determining the extent of disease present. It is uniquely able to do this because of its ability to examine all areas of the abdomen. As a staging investigation, CT has a major role to play in gastrointestinal lymphoma.

A staging classification should be related to prognosis. In our classification (Table 1), two major factors adversely affect prognosis. The first is local extension of a tumour outside the GI tract, with or without perforation. Those patients with perforation and peritonitis have a very poor prognosis. Since most of the patients in this group present as abdominal emergencies, laparotomy is carried out, and an accurate assessment of local extent, perforation and peritonitis is made. CT has little to offer in these circumstances, although in 3 cases in this study mass lesions extrinsic to the bowel were seen. The second major prognostic factor is lymph node involvement beyond the mesenteric or gastric nodes. Once lymph nodes beyond these are involved, the prognosis is worse. Para-aortic nodes, coeliac nodes and retrocrural nodes are all areas which may not be examined at surgery. The presence of disease within these nodes will adversely affect a patient's chance of survival. In this study, CT has proved a reliable and effective method of detecting disease in these regions. Previous authors have shown that there is a low false positive rate of detection of nodes in these areas (Best *et al.* 1978, Jones *et al.* 1978, Schaner *et al.* 1977). The presence of enlarged lymph nodes seen by CT is therefore of considerable prognostic significance.

Disease in the liver and spleen is less reliably detected by CT. Diffuse abnormalities are rarely seen and altered size or morphology or large intraorgan deposits are the only changes that CT reliably detects. Even increase in size of a large organ such as the spleen can be difficult to assess. This is because the organ must be measured over several scans and the degree of inspiration and position of the patient may alter the area shown on each scan. For this reason, relatively crude assessments of enlargement are made. The spleen is considered enlarged if it is below the rib margin as it would be clinically. There is evidence to suggest that this is not a reliable method of assessment since the incidence of splenic involvement in this study, 6 out of 25 scans, appears high when compared with the previous study where only 2 out of 104 patients had splenic enlargement at the time of initial diagnosis and only 10 out of 104 patients had palpable spleens at any stage of their disease (Blackledge *et al.* 1979). It is likely that the incidence of splenic disease is overestimated by CT using our protocol for scanning. This is because the protocol was designed to examine the whole reticuloendothelial system in the abdomen and because measurement of splenic size alone, without evidence of infiltration, is a poor indicator of splenic disease (Glatstein *et al.* 1970).

One area where CT appears very effective is in the assessment of response to treatment. It has been shown previously that the presence of residual disease as demonstrated by CT in clinical complete remission is an adverse prognostic factor in diffuse lymphomas (Best *et al.* 1978). In this study, a normal CT examination was associated with long-term survival. Residual disease, seen by CT at the end of treatment, progressed in all cases except one which has remained static nine months following the examination. In view of these findings, CT has altered treatment decisions; the presence of residual disease following remission induction by chemotherapy is now an indication to give further treatment with radiotherapy or chemotherapy. Although there have been no randomized trials, various papers have suggested that radiotherapy following surgery and chemotherapy may improve the survival of patients with gastrointestinal lymphoma. This is especially true in those patients with disease in regional lymph nodes (Freeman *et al.* 1972, Connors & Wise 1974, Bush & Ash 1969, Cupps *et al.* 1969, Nelson *et al.* 1977). Precise knowledge of the sites of disease may enable radiotherapy fields to be more accurately planned, thus avoiding some toxicity to the bowel, kidney or bone marrow.

CT is an investigation which is easily tolerated by patients. It can be performed, therefore, on people in whom further investigations would not previously have been carried out. The

usefulness of this is demonstrated in a patient not included in this study, with Hodgkin's disease. She had extensive lung parenchymal disease and was receiving treatment for this. A mass associated with abdominal pain was found on examination in the upper abdomen. A barium meal showed dilatation of the stomach with residual fluid and extrinsic compression to the fourth part of the duodenum. If CT had not been available, this would probably have been treated with radiotherapy. CT revealed a low density mass adherent to the posterior stomach wall and pancreas, compatible with oedematous change. Endoscopy revealed a benign gastric ulcer with surrounding inflammation. Further chemotherapy or radiotherapy would not have helped this condition and CT thus prevented unnecessary treatment.

Although CT cannot diagnose gastrointestinal lymphoma, it provides a useful and convenient investigation in the staging of the disease. In assessing remission status and in planning radiotherapy, it is the single most important investigative procedure now available.

Summary

Twenty-six computed tomography (CT) examinations in 18 patients with histologically proven gastrointestinal lymphomas are reported. Fourteen CT examinations were performed at the time of initial presentation, the others being performed during the course of the disease. CT did not help in the diagnosis of the disease but it is effective in assessing the extent and thus the stage of the disease. A normal CT scan during follow up is associated with good prognosis. CT may be of help in planning treatment, especially radiotherapy. It is an investigation easily tolerated by patients and can be used in circumstances where other investigations would be impossible.

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