Gastrointestinal lymphoma in childhood

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SYNOPSIS Thirteen cases of lymphoma of the bowel in infancy and childhood are presented. There is a marked preponderance in males. The tumour most commonly presents with abdominal pain and intestinal obstruction; the prognosis is poor. Histological findings characteristic of the 'Burkitt' type of lymphosarcoma do not apparently influence survival.

Primary neoplasms of the gastrointestinal tract are infrequent in childhood and comprise less than 1% of tumours seen in this age group. The majority of the recorded cases are tumours of the reticuloendothelial system. Several centres have published small series describing intra-abdominal lymphosarcomata alone or as part of a review of malignant lymphomata in childhood (Bailey, Burgert, and Dahlin, 1961; Jones and Klingberg, 1963; Rosenberg, Diamond, Dargeon, and Craver, 1958; Sullivan, 1962; Cutler, Stark, and Scott, 1945; Charache, 1956; Maxwell, 1954; Mestel, 1959).

We present here a review of 13 primary malignant gastrointestinal lymphosarcomata, with an assessment of their course, response to therapy, and histological appearance.

Materials and Methods

During the 10-year period 1960-69, 15 primary tumours of the gastrointestinal tract have been seen in this hospital (upper age limit is approximately 13 years). Two were teratomata arising in the gastric wall and have been reported elsewhere (Atwell, Claireaux, and Nixon, 1967; Berry, Keeling, and Hilton, 1969). From the remaining 13 cases, sections of the surgical specimens were stained with haematoxylin and eosin, haematoxylin-van Gieson, Gordon and

Sweet's reticulin stain, and the Unna-Pappenheim techniques. Necropsy material was available from one case (case 2).

Results

The clinical details, age at presentation, sex, duration of symptoms, operative findings, subsequent treatment, and progress are shown in Table I.

PATHOLOGICAL FINDINGS

Typical macroscopic appearances are seen in Figs. 1 and 2 (case 5) and Figs. 3 and 4 (case 7).

Microscopic findings are summarized in Table II. Ten tumours are lymphoblastic lymphosarcomata and are composed of closely packed round cells having prominent nuclei with little cytoplasm (Fig. 5). Five of these tumours contain large phagocytic reticular cells giving a 'starry sky' appearance and in three instances other cytological characteristics of the 'Burkitt' type of lymphoma (ill-defined cytoplasmic border, small cytoplasmic vacuoles, prominent nucleoli, frequent mitoses, occasional pyroninophilia) are present (Fig. 6). Involvement of the muscle coats of the bowel wall leads to the appearance of altered muscle cells within the tumour in some instances.

Three tumours are considered to be reticulum

Case	Age/Sex	Duration of Symptoms	Clinical Picture	Investigations	Surgery	Radiotherapy	Chemotherapy	Course
1	1 yr 11 mth M	3 mth	Anaemia, anorexia, episode of diarrhoea, right-sided abdominal mass	Hb 61%; ESR 28 mm in 1 hr; barium enema: irregular outline of caecum and ascending colon, Marrow-granulocytic hyperplasia	Laparotomy: abscess cavity R side abdomen; biopsy of colon, liver, lymph node; defunctioning ileocolostomy	—	Vincristine cyclophosphamide and oncolytic M-P virus; prednisolone	Inguinal lymphadenopathy; large pelvic mass 4 months postoperatively alive 6 months postoperatively Died 2 yr 9 mth
2	3 yr 1 mth M ¹	2½ mth	Diarrhoea and vomiting, later episode of diarrhoea, abdominal pain: firm, tender, mobile central abdominal mass	Marrow: aplasia (terminally)	Laparotomy: masses in terminal ileum (adherent to sigmoid) and caecum and ascending colon; end-to-side ileocolic, end-to-end colocolic anastomoses	—	Cyclophosphamide	Recurrence at 3 mth Died 5 mth
3	3 yr 4 mth M	3 mth	Episodic central abdominal pain, vomiting, weight loss, mass in right hypochondrium	Occult blood positive; barium enema: ileocolic intussusception	Resection of intussusception: end-to-end ileocolic anastomosis	+	—	Recurrence at 2 wk
4	3 yr 4 mth M	1 yr 3 mth	Anorexia, pallor, failure to gain weight; abdominal distension and episodic diarrhoea for 2 mth; blood in stool × 1; right-sided non-tender abdominal mass	—	Resection of mass in ileocaecal angle; ileocolic anastomosis	+	—	Died 4 mth
5	3 yr 4 mth M	1 wk	Episodic abdominal pain, abdominal distension; mass in right iliac fossa	Barium enema: filling defect in terminal ileum and caecum	Resection of mass; ileocolic anastomosis	—	—	Died 2 mth
6	4 yr 5 mth M ¹	8 mth	Episodic vomiting, abdominal pain, anorexia, and loss of weight; firm, non-tender mass in right flank	WBC, 6,900/cmm, 4% atypical mononuclear cells Marrow: tumour cells present	Laparotomy: mass in terminal ileum and caecum, mesenteric lymphadenopathy; resection of mass and end-to-end ileocolic anastomosis	—	—	Alive and well 6 years postoperatively
7	6 yr 2 mth M	1½ mth	Severe episodic abdominal pain, vomiting, blood in stool × 1; masses in epigastrium	Barium enema—chronic intussusception	Intussusception incompletely reduced, right hemicolon resected; end-to-end ileocolic anastomosis	—	—	Died 2 mth
8	6 yr 6 mth F	1 mth	Increasing abdominal girth, anorexia, pallor; hepatomegaly and shifting dullness	—	Laparotomy: tumour in root of mesentery 2° in liver; biopsy taken	—	—	Alive 1 mth
9	7 yr 3 mth M	7 mth	Central abdominal pain, diarrhoea, left inguinal hernia, herniotomy, then further abdominal pain and vomiting; weight loss; no abnormal physical signs	Barium enema—narrow segment in terminal ileum with thickening of the wall	Laparotomy: dilated small intestine above a narrow segment of terminal ileum adherent to bladder; mesenteric lymphadenopathy; terminal ileum and ascending colon resected; end-to-end ileocolic anastomosis	—	Cyclophosphamide Vincristine	Died 1½ mth
10	7 yr 5 mth M	1 mth	Central abdominal pain, absolute constipation, vomiting; hypogastric and pelvic masses	Barium enema: filling defects in caecum and sigmoid	Laparotomy: masses in terminal ileum and rectum, 2° in omentum; biopsy of omental nodule	—	—	Lost to follow up 2 wk
11	8 yr 9 mth M	3 wk	Vomiting and constipation; hard, right-sided abdominal mass	Plain abdominal radiographs: fluid levels	Resection of mass in terminal ileum; end-to-end ileocolic anastomosis	—	Cyclophosphamide	Alive, 2 mth
12	13 yr M	5 wk	Abdominal pain associated with micturition; weight loss; masses in right loin and pelvis	Plain radiograph: mass indenting bladder; barium enema: mass at ileocaecal valve	Laparotomy: tumour of terminal ileum, bladder roof adherent, mesenteric lymphadenopathy; excision of mass in bladder roof, ileo-ileal anastomosis	+	—	Died, 2 mth
13	12 yr 10 mth M	5 mth	Abdominal pain, chest infection, severe diarrhoea and vomiting for 1 mth; well defined, non-fluctuant abdominal mass	—	Laparotomy: irregular firm tumour in ileum, tumour nodules in wall of appendix, colon, and caecum; resection of ileal mass, ileo-ileal anastomosis	+	—	

Table I Clinical features in present series

¹Brothers

Fig. 1 Case 5: white nodules can be seen through the serosa distorting the normal intestinal profile. Enlarged lymph nodes are seen in the mesentery.

Fig. 2 Case 5: Hemisection shows a homogeneous white tumour involving the bowel wall with ulceration of the overlying mucosa and affecting local lymph nodes by direct extension.

Fig. 3 Case 7: the terminal ileum (right) and caecum are diffusely thickened.

Fig. 4 Case 7: Hemisection shows an area of white tumour within the bowel wall at the apex of the intussusception.

Fig. 5 Typical appearance of lymphosarcoma (haematoxylin and eosin $\times 500$).

Fig. 6 Lymphosarcoma with histiocytes containing nuclear debris scattered in the tumour mass (haematoxylin and eosin $\times 540$).

Case	Site	Histological Appearance
1	Caecum and ascending colon, 2° liver	Lymphosarcoma
2	Terminal ileum and caecum	Reticulum cell sarcoma
3	Terminal ileum and caecum	Lymphosarcoma ¹
4	Terminal ileum and caecum	Lymphosarcoma
5	Terminal ileum and caecum, 2° mesenteric nodes	Lymphosarcoma ¹
6	Terminal ileum, caecum, ascending colon	Reticulum cell sarcoma
7	Terminal ileum and caecum	Lymphosarcoma
8	Root of mesentery, liver 2°	Lymphosarcoma
9	Terminal ileum	Lymphosarcoma
10	Ileum, rectum, omental 2°	Lymphosarcoma ¹
11	Terminal ileum and caecum	Lymphosarcoma ¹
12	Ileum 2°, bladder vault	Reticulum cell sarcoma
13	Ileum, nodules in caecum and colon, appendix	Lymphosarcoma ¹

Table II Histology of present series
¹Burkitt-like morphology

cell sarcomas, and are composed of pleomorphic reticulin cells; binucleate cells are seen. Reticulin fibres are seen between cells and thicker condensations of reticulin divide cell masses.

Bone marrow examination was normal in cases 3, 4, 9, 11, 12, and 13. The narrow aspirate in case 1 showed granulocytic hyperplasia but no tumour infiltration. Appearances were within normal limits in case 2 initially but terminal aplasia was found. In case 6 the tumour cells were found terminally. Bone marrow examination was not performed in cases 5, 7, 8, and 10.

Necropsy was performed on case 2; he died two years and nine months after resection of an ileocaecal tumour. Bone marrow aplasia and pulmonary fibrosis had developed and was apparently associated with cytotoxic drug therapy.

There was cultural and histological evidence of disseminated moniliasis with involvement of the central nervous system. Residual tumour was not found.

Tumour had involved bone marrow terminally in case 6, with the appearance of tumour cells in the blood. Metastases occurred in cases 1, 3, 4, 8, 10, and 12. Transcoelomic spread of tumour to other abdominal viscera was probable in case 13.

Discussion

The age range at presentation was from 1 year 11 months to 12 years 10 months in our series.

Twelve of the 13 patients were male; a similar degree of male preponderance was noted in the series described by Mestel (1959), 11 males and two female cases, but was less marked in other studies. Bailey *et al* (1961) found a male-to-female ratio of 3.4:1, and Jones and Klingberg (1963) had a male-to-female ratio of 2.6:1.

The 13 tumours constitute 0.6% of all tumours

seen at this hospital since 1957 (excluding leukaemia) and 37% of the lymphomata.

The presence of Burkitt-like morphology was not associated with a better prognosis and the phagocytic activity of histiocytes included in the tumour does not appear to be evidence of an effective host response to the tumour.

Two of the cases were brothers (cases 2 and 6): the familial tendency to develop lymphomata has been discussed elsewhere (Rigby, Rosenlof, Pratt, and Lemon, 1966) and will not be considered further here.

Abdominal pain and distension were the most frequent presenting symptoms, as in most series of both adult and childhood age groups (see Mestel, 1959, for bibliography).

Investigation showed no distinctive features, and in general findings were those of intestinal obstruction and intussusception.

Primary treatment was surgical and was designed to achieve complete resection (cases 2, 3, 4, 5, 6, 7, 9, 11, and 12) or palliation (cases 1 and 13). In cases 8 and 10 biopsy only was performed and no further treatment was given. Cases 3, 4, 5, and 13 were treated by radiotherapy and cases 1, 2, 9, 11, and 12 by cytotoxic drugs in addition. Four patients are alive but two have been diagnosed only in the last few months. Of the remaining two, case 1 is alive with evidence of extensive disease after six months. There is one long-term survivor (case 7) who is free of disease six years after radical surgery alone. These dismal results compare with those found in other series (Charache, 1956; Mestel, 1959). Bailey *et al* (1961) have achieved some success with surgery and radiotherapy in a small series (three long-term survivors from nine cases).

These cases presented over a period of 10 years, and policy regarding chemotherapy and radiotherapy probably reflects common usage at that time, except in cases 8 and 10 where extensive metastatic spread was present at laparotomy and specific antitumour therapy was withheld. Bone marrow examination was not performed in all cases, and the use of antitumour therapy was not based on the findings in the blood.

In general this is a tumour with an exceedingly grave prognosis. Its relative infrequency and the varied methods of treatment employed prevent a rational assessment of the efficiency of various therapeutic regimes but it seems likely that radical surgery with radiotherapy aimed at preventing local recurrence is a rational mode of treatment in view of the present state of knowledge of this disease.

C. L. Berry is the Gilson scholar of the Worshipful Society of Apothecaries of London.

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Addendum

Since the preparation of this paper, case 9 has died, eight months after diagnosis.