MALIGNANT LYMPHOMA OF THE INTESTINE:
A report of three cases.

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Tumours arising in the small intestine are uncommon; those of them originating in the lymphoid tissues are said to be even less frequent than adennocarcinomas. This infrequent incidence, together with the particular problems they pose with regard to their pathology and diagnosis, seems to us to warrant the report and comment on three cases which we have treated over the past eight years.

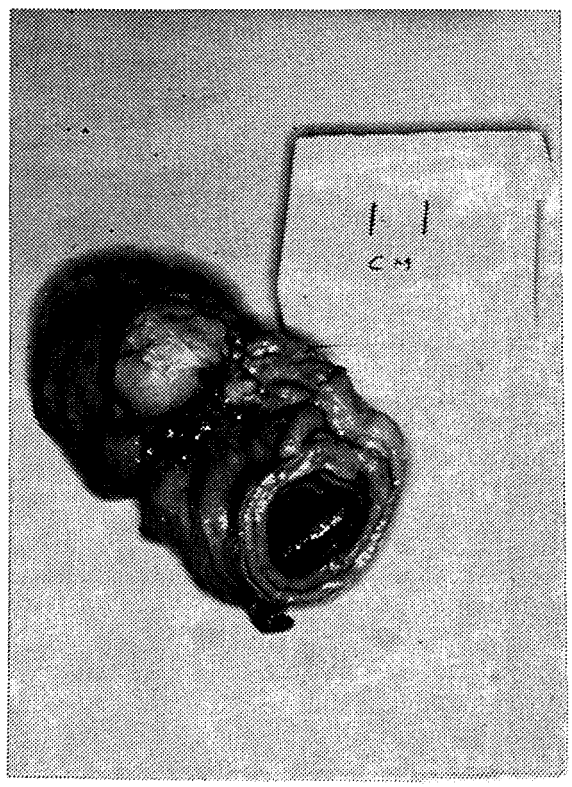
Case Reports

Case 1. Male aged 46, seen first on the 26.7.62, complaining of bouts of colicky abdominal pain and increasing constipation over a period of two months. There was occasional neausea, a fair appetite and no vomiting but the patient was afraid to eat as food seemed to precipate the onset of pain. There was some loss of weight. About twenty months previously he had had an attack of intense diarrhoea lasting some ten weeks.

On examination he was a well nourished man of good physique. There was no facial flush and no finger clubbing. His chest was clear. His abdomen was full, and there was some slight, ill defined tenderness in the right lower quadrant. Bowel sounds were hyperactive.

He was seen again on the 22.8.62. The pain was now getting worse, and a swelling had appeared in the right axilla which was getting larger, but was not causing pain. Examination confirmed the presence of a soft, enlarged, non-tender lymph node about 4cm in diameter, in the right axilla. The neck, left axilla, and both groins were free from enlarged nodes. The liver and spleen were not enlarged.

A blood count showed a haemoglobin of 76%, white cells 9,000, with no im-



Case 1. — Resected segment of small bowel.

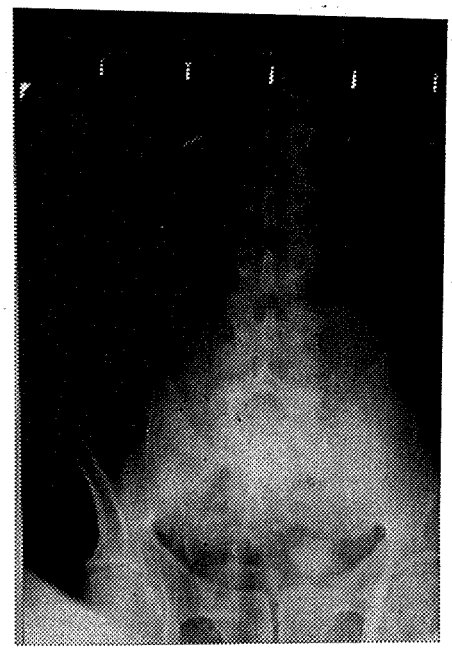
mature white cells. ESR was 38mm in the first hour. Barium meal and follow through showed some hold up and dilatation of the lower ileum.

Laparotomy (J.A.M.) was performed on the 25.8.62 under general anaesthesia. The abdomen waas explored through a right paramedian incision. There was no free fluid. The small intestine was the seat of five lesions, four of which were in the ileum, and one in the jejunum. The lesions were well defined, thickening the bowel wall, narrowing its lumen, and presenting a whitish, pearly appearance on the serosal aspect. There were numerous, moderately enlarged, firm glands in the root of the mesentery. The liver and spleen were palpably normal. An ileo-transverse colostomy was performed, short-circuiting the ileal lesions, and the abdomen was closed. The enlarged node in the right axilla was excised. Histological examination of this node was reported "Lymphosarcoma — the picture is uniformly dominated by the presence of small round lymphocyte-like cells. Infiltration of the capsule is a prominent feature." (Dr. F. Calleja). The operation wound healed satisfactorily, but the patient developed diarrhoea.

In October 1962 he was referred to London, where he had radiotherapy to the right axilla and right groin (2000r in 14 days). Between the 17th and 29th October 1962, he was given 12 m.c. of P_{32} by intravenous injection. He returned to Malta in December 1962. His diarrhoea had lessened, but his general condition was not good. However he slowly began to show a remarkable and progressive improvement, recovering his apetite and putting on weight. His energy was also returning, and he was back to a full day's work after about three months. He was subsequently lost sight of for two years.

On the 13.3.65 he was seen again, when he complained of severe colicky abdominal pain and vomiting which had started some nine hours previously. Absolute constipation was present. General examination showed a well nourished, but dehydrated man, with a slightly distended and tense abdomen, and hyperactive bowel sounds. Plain X-Ray of the abdomen on the 14.3.65 showed fluid levels in the small intestine.

Laparotomy performed that same day revealed the seat of the obstruction to be an infiltrated, short segment of ileum, which was adherent to the anterior abdominal wall; this was mobilised and resected, and continuity restored by end to end anastomosis. He made a fair recovery from this operation. His subsequent course was marked by episodes of abdominal pain and diarrhoea. At first he responded to cyclophosphamide and corticosteroids, but eventually took a downhill course, and died on the 6.10.65.



Case 2. — 14. 3. 65. Plain X-ray abdomen showing multiple fluid levels.

Case 2. Male aged 51 was referred to the Surgical Outpatient clinic on the 5.5.62 for Ca Rectum by his General Practitioner. He gave a history of intermittent attacks of diarrhoea sometimes lasting a week, over the previous six months. The stools were at times blood stained, but there was never any constipation or tenesmus. His appetite had lessened, but there was no nausea or vomiting. There was some loss of weight. There was no previous illness of note. He said he had noticed increased

growth of three cysts in the scalp which he had had for many years.

On examination, his general condition was fair. He was high-coloured, his tongue was clean and moist, and there was no cervical lymph node enlargement. His jugulars showed no engorgement. Temperature was 98°F, pulse 72 per minute, blood pressure 110/60 mm Hg. The chest was clinically clear. The abdomen was soft; there was slight tenderness in the Left Iliac Fossa. Slightly enlarged, discrete, non-tender lymph nodes were noted in the groins.

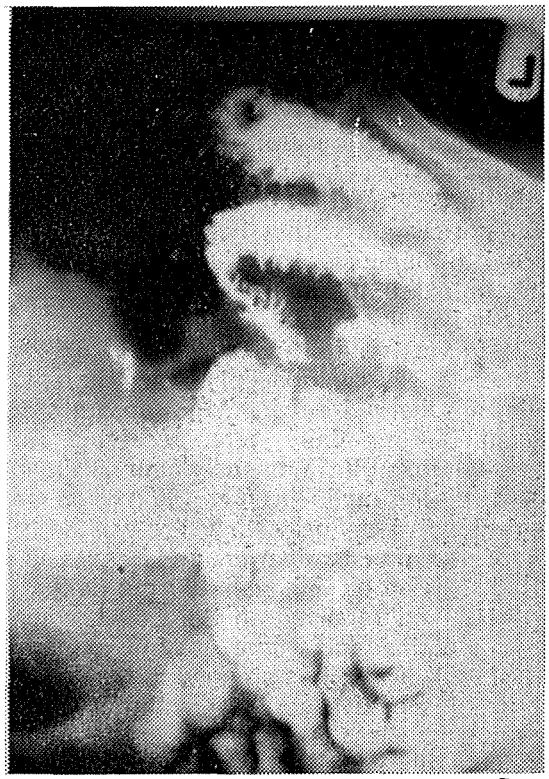
Investigations: haemoglobin 98%; white cells 4,000; urinalysis: negative; blood urea: 26 mg%; faecal occult blood was positive. Barium enema on the 22.5.62 showed an irregular filling defect of the caecum.

Laparotomy (J.A.M.) was performed on 25.5.62. There was a large growth affecting the ileocaecal region of the bowel, tgether with diffuse mesenteric lymphadenopathy. Right hemicolectomy was performed. Post-operative recovery was satisfactory, the wound healed, and normal motions were passed on the 6.6.62. He was discharged to Surgical Outpatients on the 10.6.62.

The histological report (Prof. G. P. Xuereb) was as follows: A portion of distal ileum, ileo-caecal junction, appendix and colon, measuring 40cm in length, and 6.5cm in diameter at the ileo-caecal junction. Numerous enlarged lymph nodes are embedded in fat and in omentum, the largest of these measures 3.4 x 2.7 x 2.5cm, and on section it presents a grey surface with several haemorrhagic areas. The smaller lymph nodes show replacement of their normal architecture by glistening translucent tissue. Transverse section through ileum and caecum shows greyish-white tumour tissue growing into the lumen of the intestine and reducing it to slit-like dimensions. The tumour occupies 7cm length of the caecum and extends proximally into ileum for 6.8 cm. Microscopical examination shows a lymphosarcoma arising in the caecum and extending to the terminal portion of the ileum. The tumour consists largely of well differentiated lymphocytes, compactly arranged with scanty connective tissue support. The sarcoma cells are within the submucosa, and have produced atrophy and replacement of the mucosal lining. There is little evidence of muscle infiltration. Mitotic divisions are not abundant; cellular pleomorphism is not a feature. There is diffuse metastasis of lymphosarcoma within lymph nodes. Histological diagnosis: Lymphosarcoma of the caecum extending into ileum and metastatning in lymphy nodes.

He was readmitted on the 18.6.62 for a course of cyclophosphamide therapy, being discharged on the 2.7.62 on oral endoxan 100 mg daily, after receiving 1.5 gm of endoxan intravenously over 11 days. He was seen again in July 1962 when he said he was keeping well. There was nothing of note on examination, and he was advised to keep on endoxan 100 mg daily.

He next reported on the 4.8.62, when he complained of vague abdominal pain. He stated that he had stopped taking endoxan of his own accord some three weeks previously. On the 29.9.62 he was found to have developed gross enlargement of the cervical lymphnodes, and notable enlargement of the glands in both groins. He complained of sore throat, and his voice was nasal in character. He was readmitted to hospital. Further treatment with cyclophosphamide resulted in marked subsidence in the size of the cervical nodes. A chest X-ray in this period showed the presence of a mass in the right hilum (5.10.62). He was discharged to outpatients on the 3.11.62. He kept reasonably well till the 15.12.62 when he complained of sore throat, hoarseness, and renewed enlargement of the cervical nodes. A severe bilateral conjunctivitis was also observed. On the 16.12.62 he was put on intravenous cyclophosphamide for the third time. His subsequent course was gradually downhill, though a chest X-ray on the 24.11.62 was reported 'Lungs are clear'. On the 28.1.63 he was noted to have stridor. His tonsils were enlarged and his fauces inflamed. The cervical nodes were again enlarging. On the 31.1.63 tracheostomy was performed under local anaesthesia. In spite of further chemotherapy with leukeran and cyclophosphamide, his decline was not arrested, and he died on the 15.2.63.



Case 3. — Barium study of small intesting showing a narrowed segment.

Case 3. Female aged 62 years, presented in January 1970 with a history of low grade pyrexia and intermittent abdominal pain since April 1969. In October 1969 she had a bout of vomiting lasting one week. She was anorexic, but her bowels were said to be regular. There was no diarrhoea, some weigth loss, and no dysuria. She had a past history of Undulent Fever in 1927, and haemorrhoidectomy in 1956.

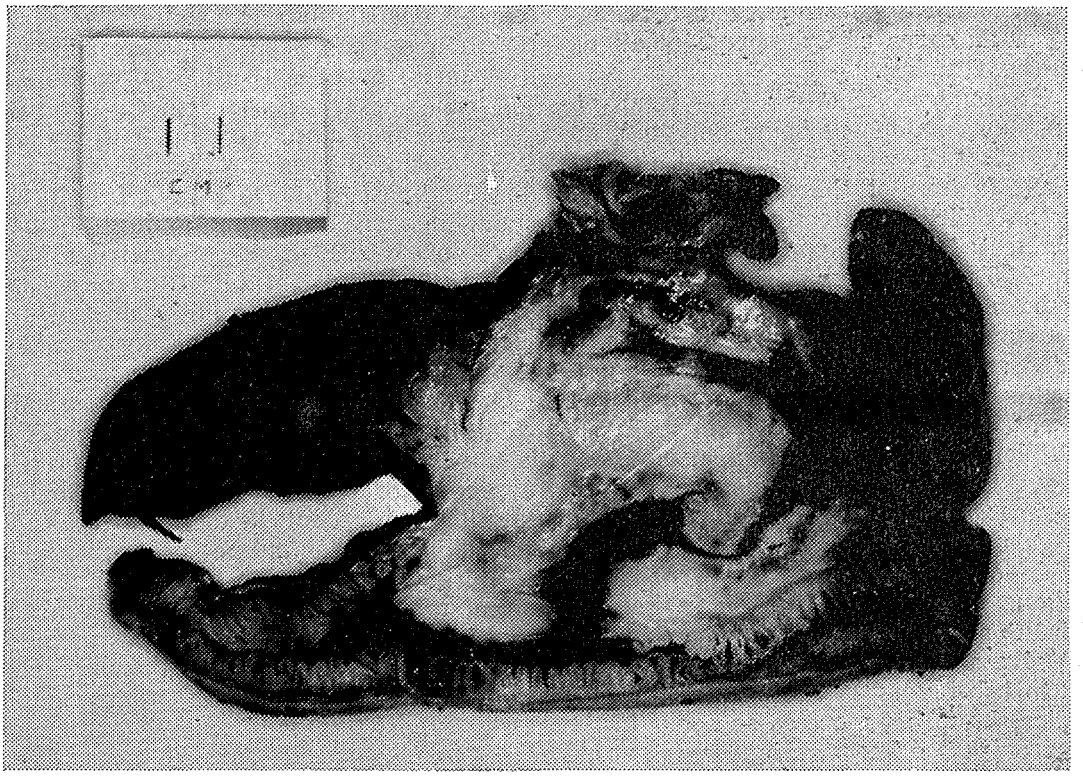
On examination, she was found to be pale and listless. Her pulse rate was 80 per minute, and blood pressure 140/90mm Hg. Abdominal examination revealed an ill defined mass in the left lumbar region.

Investigations: on the 31.5.69: haemoglobin 72%; white cells 8,000: Polymorphs 67%; Lymphocytes 28%; Monocytes 4%; Eosinophils 1%. There were no immature or abnormal white cells. ESR: 31 mm in the first hour. On the 19/5/69, tests for Brucella melitensis, Salmonella typhi, and Proteus OX19 were negative. On the 12.9.69, faecal occult-blood was negative.

Radiological investigations: Chest X-ray on the 3.6.69 showed slight linear atelectasis in the right mid zone. No evidence of active lesions. Heart not enlarged. Barium meal and follow through on the 12.11.69: Oesophagus normal; stomach and duodenum: no lesions seen. Small intestine: there is a narrowing about one inch in length in jejunum, which shows in many but not all films. As it is not persistently present, we have to assume that it is spastic, possibly inflammatory. If clinical signs of obstruction supervene, one has to repeat examination of the small bowel. Cholecystography on the 10/1/70: no opaque calculi seen. Good concentration of the dye by the gallbladder, very little contraction after a fatty meal. Intravenous pyelogram on the 26.1.70: Preliminary film: no opaque calculi seen. Excretion urography: good concentration of the dye on both ces of the rikht kidney are dilated — varsize, shape and position. Some of the calyces of the right kidney are dilated — variation of the normal. The left kidney, ureter and bladder show no abnormality.

Laparotomy (J.A.M.) was carried out on the 29.1.70, through a right paramedian incision. This revealed a tumour mass involving three dilated loops of ileum, and omentum. There were numerous enlarged nodes in the mesentery. No free fluid. The liver and spleen were normal. The three affected loops of small bowel and omentum were resected, and continuity restored by three end-to-end anastomoses. The post-operative recovery was uninterrupted, and the patient was discharged home on the 9.2.70.

Biopsy report was as follows: "When sectioned the tumour is seen to extend over an area 8 × 7 cm involving the wall of both excised segments of upper ileum. A fistulous track containing bile stained faecal material lies in the tumour mass. The small loop of lower ileum is adherent but not infiltrated by tumour. Lymph nodes in the mesentery are enlarged. Microscopy shows Lymphosarcoma permeating ileum. Lymphnodes show sinus catarrh. There is no evidence of metastasis.



Specimen from Case 3. — Three loops of small bowel resected. Tumour mass involving the two lower loops with a fistula connecting the two loops.

Discussion

By 1932, when Ullman and Abeshouse published their classical paper on this disease, some 440 cases had been reported in the literature; this number rose to some 600 cases by 1961. Since 1932 no striking advance has been made in the study of its pathology, diagnosis, or treatment, however certain facts have emerged from the study of the mounting number of cases reported. The method of selection of cases for study has varied with the author. Dawson, Cornes and Morson have been the most specific in this respect, and exclude from their study, all those cases in which lymphomatous change was present at any site other than the intestine and regional lymphnodes. We have considered it more useful from the clinical standpoint to select these three cases on the basis adopted by Burman and Van Wyk, who included in their series all those cases in which the symtom producing lesion was situated in the small bowel or caecum, and excluded those in which generalised lymphoid sarcomatosis happened incidentally to involve the lymphoid tissues of the small intestine. We agree with these authors in including caecal growths along with those affecting the terminal ileum, as it is often impossible to determine the exact site of origin of a tumour that affects both caecum and terminal ileum.

All our three cases were diagnosed histologically as Lymphosarcoma. It is interesting to note that in published series, Lymphosarcomas and Reticulum Cell Sarcomas have been about equally represented, and together accounted for the vast majority of cases. Hodgkin's Lymphoma and Giant Follicular Lymphoma have been very rare as primary intestinal pathological changes. This contrasts sharply with the high overall incidence of Hodgkin's Lym-

phoma, which is said to account for about 50% of all cases of Lymphoma in all tissues (De Gruchy).

Various gross features have been reported, the commonest being polypoid, annular, ulcerative and aneurismal. An important feature of these tumours is that they have little connective tissue stroma, as indicated in the biopsy report of our Case 2. This, together with infiltration of the muscle coat, is said to account for the aneurismal varieties of the growth. (Azzopardi and Menzies, 1960). Polypoid growths have shown a tendency to intussuscept. (Faulkner and Dockerty, 1953). Multiple growth, as occurred in our Case 1, have frequently been reported. The occurrence of fistulous tracks, as in our Case 3, seems to be rare.

Of our three cases, two were males and one was female. This is in keeping with the sex incidence in published series, that give a sex ratio varying from 3 to 2, to 3 to 1 in favour of males. Age incidence studies show that most cases occur in the age group 45 to 60 years, but no age group is exempt.

As for signs and symptoms, it is true to say that no definite syndrome is produced by this disease. In general, it may be said that cases have presented either as surgical emergencies or insidiously. In the former group, the picture has been that of acute, or acute on chronic intestinal obstruction, or of perforation with peritonitis. A few cases have presented with massive bleeding per rectum. As for those cases presenting insidiously, the picture has been that of vague malaise, anorexia, mild abdominal pain that was usually colicky, some disturbance of bowel habit, anaemia and weight loss. On examination, there has often been noted some indication of partial obstruction. The finding of a palpable mass has been frequent. This was present in our Case 3. It occurred in half the cases described by Allen *et al.*, 19 of the 25 cases described by Burman and Van Wyk, and 19 of the 33 cases described by Faulkner and Dockerty. Irvine and Johnstone mention this finding in only three of their 17 cases, and attribute this low incidence to the fact that a sizeable proportion of their cases presented as surgical emergencies with perforation and peritonitis.

The sheet anchor of therapy remains what it was in 1932 when Ullman and Abeshouse wrote "Surgery in the form of resection of involved gut offers the best results from a curative or palliative standpoint. These results are still such as to 'inspire widespread pessimism'. The long term survivals are the exceptions, and this despite the advances in the fields of radio- and chemo- theraphy. Case 2 was given a course of deep X-rays and the isotope P_{32} He survived two and a half years.

Even in the presence of marked and widespread enlargment of the mesenteric nodes, surgical extirpation of the intestinal lesion or lesions is the best course. Enlarged nodes may not necessarily be the seat of metastasis, as in our Case 3. This latter consideration has lead Azzopardi and Menzies to recommend that in the face of a non-resectable growth, a biopsy of the actual neoplasm is essential to establish the diagnosis and submit the patient to radiotheraphy if necessary. There is general consensus regarding the value of post-operative radiotherapy in unresectable growths, and in those with regional lymph node metastasis. What is uncertain is the value of radiotherapy where no evidence of lymph node spread is present.