Med. J. Cair Univ., Vol 62, No. 2, June (Suppl.) : 161-167, 1994.

Primary Gastrointestinal Lymphomas

MAGED B. BARSOUM, M.D. and MOHAMED S. HAFEZ, M.D.

The Department of Surgery, Faculty of Medicine, Cairo University.

Abstract

Nine patients with primary gastrointestinal lymphoma are presented. They were all non-Hodgkin lymphoma; 7 lymphocytic, one immunoblastic and one lymphoblastic. The diagnosis was made preoperatively in five patients, doubted in one patient and missed in three patients. All patients were treated surgically by resection followed by chemotherapy. Six patients received postoperative radiotherapy as well. Morbidity occurred in two patients and two patients died from recurrence 10 months and 2½ years after surgery. The longest period of follow-up is 8 years. Emphasis is laid on criteria to suspect the diagnosis and prove the primary nature of gastrointestinal lymphomas. The optimum lines of management are described.

Introduction

GASTROINTESTINAL lymphomas may be primary or secondary due to involvement in systemic lymphoma. Gastrointestinal lymphomatous involvement in systemic lymphoma may be as high as 32% of cases and even up to 43% at postmortem examination[1]. Primary gastrointestinal lymphoma accounts for about 9% of all cases of lymphoma[2].

The stomach appears to be the most favoured site of primary gut lymphomas world-wide[3]. However in the Middle East small bowel lymphoma is the most common form of extranodal lymphomas, representing 75% of gastrointestinal lymphomas in adults[4]. In view of the difficulty in distinguishing primary from secondary gastrointestinal lymphoma, it is impossible to determine the true incidence of primary lymphomas of gut in the world.

This report presents patients with proved primary gastrointestinal lymphomas encountered in our general surgical practice.

Material and Methods

Nine patients were documented to have primary gastrointestinal lymphoma during the period from May 1984 to December 1991. The minimum criteria for the diagnosis of primary lymphoma were[5] :

1. No palpable superficial lymphadenopathy at presentation. 2. No enlargement of mediastinal lymph nodes detected

by plain X-ray of chest or mediastinal CT scan. 3. The white cell count was normal. 4. Normal bone marrow picture. 5. The liver and spleen were normal, and 6. At laparotomy the bowel lesion predominated and the obviously affected lymph nodes were those immediately related.

The studied patients had a mean age of 36.3 years. They were 5 males and 4 females (Table 1). Two patients presented as an emergency; one by intestinal obstruction and other by upper G.I. haemorrhage. The other seven patients suffered variable chronic gastrointestinal symptoms pointing towards upper or lower gastrointestinal pathology. The preoperative diagnosis of gastrointestinal lymphoma was not suspected in three patients, clinically suspected in one patient and correctly diagnosed with a preoperative histological proof in 5 patients. All patients were HIV negative. The final pathological diagnosis showed non-Hodgkin lymphoma in all the patients. Seven patients had low grade lymphocytic lymphoma. Two patients had high grade lymphoma; one immunoblastic and the other lymphoblastic. The lymphoma affected the stomach in four patients, the ileum in two patients, the rectum in two patients and the duodenum was involved in one patient. Gastric lymphoma was treated by total gastrectomy, rectal lymphoma by abdominoperineal resection and the duodenal lymphoma by pancreaticoduodenectomy. Resection of an obstructed loop of ileum was done in one patient with ileal lymphoma and right hemicolectomy was done in another ileal lymphoma presenting by irreducible ileo-colic intussusception. All patients received postoperative six courses of chemotherapy in three week intervals in the form of «CHOP» : cyclophosphamide, adriamycin, oncovin and prednisone. Postoperative whole abdomen radiotherapy was given to six patients : 3000 cGy over a period of four weeks shielding the kidneys. Complications occurred in two patients; one minor and one major. Two patients died; one with bone deposits at 10 months and the other with local recurrence, $2\frac{1}{2}$ years postoperatively.

Case 1 : The patient presented with dyspepsia and progressive anaemia of 10 months duration. An ulcerated filling defect with localized thickening of the posterior wall of the pyloric antrum was seen on contrast studies and CT examination. Upper G.I. endoscopy revealed an ulcer $3\frac{1}{2}$ cm in size with necrotic floor. Preoperative biopsy showed anaplastic carcinoma. On exploration the wall of the pyloric antrum was diffusely thickened encroaching on the region of the body of the stomach. Total radical gastrectomy was done. Pathologic examination revealed diffuse submucosal thickening and infiltration of muscularis propria. Atypical lymphoid cells with hyperchromatism, disorderly arranged and occasional notching were seen. The retropyloric lymph node was infiltrated. The patient is free for 8 years after receiving combined radiotherapy and chemotherapy.

Case 2 : The patient presented with bleeding per rectum of one year duration. An extensively ulcerated shaggy and friable growth was seen on sigmoidoscopy to occupy the whole circumference of the lower two thirds of the rectum

encroaching on the anal sphincters. Despite the bulky infiltrating character of the lesion, the rectum was mobile without pararectal invasion on CT examination. Biopsy revealed lymphocytic lymphoma. Abdominoperineal resection was done and pathologic examination verified the diagnosis with infiltration of the pararectal lymph nodes of Gerota. This patient died $2\frac{1}{2}$ years later with extensive local recurrence although he had received radiotherapy in addition to the chemotherapy.

Case 3 : Epigastric pain and swelling were the presenting symptoms. An ulcerated bulky growth infiltrating the region of the greater curvature of the stomach was seen on contrast studies. Endoscopy showed an excavating 4 cm ulcer overlying diffusely infiltrating lesion. Biopsy showed anaplastic carcinoma. Exploration revealed a large infiltrating growth of the body of the stomach. Total radical gastrectomy was done. Pathologic examination showed lymphocytic lymphoma with infiltration of the left gastroepiploic lymph nodes. This patient received radiotherapy in addition to chemotherapy and he is well for 6 years.

Case 4 : Repeated vomiting and loss of weight were prominent for 8 months. An extensively infiltrating thickening was seen to involve the distal two thirds of the stomach resembling linitis plastica on contrast and CT examination. Endoscopy revealed nodular mucosa with hypertrophic rugae and multiple superficial ulcers. Biopsy correctly diagnosed lymphocytic lymphoma. Exploration revealed a bulky growth for which total gastrectomy and splenectomy were done. Pathologic examination confirmed the diagnosis and no lymph nodes were involved. Radiotherapy was not given and the patient is alive for 6 years.

Case 5 : The patient presented with protracted dysenteric symptoms for 14 months. Sigmoidoscopy revealed diffusely infiltrating growth of the lower third of rectum. Multiple superficial ulcers and hyperaemic mucosa were seen. Biopsy revealed lymphocytic lymphoma. Exploration showed bulky rectal growth with no lymph node affection. Abdominoperineal resection was done. Pathologic examination confirmed the diagnosis of this transmural infiltrating extensive lesion. Transient perineal wound infection developed that resolved within 6 weeks. Radiotherapy was not given and the patient is alive for 5 years.

Case 6 : The patient presented with epigastric mass of 3 months duration. CT and contrast study examination showed a bulky infiltration mass occupying the distal two thirds of the stomach and irregular filling defects. Endoscopy revealed giant gastric rugae mucosal thickening and extensive superficial ulceration. Biopsy revealed non-Hodgkin lymphoma. Exploration revealed nodular dusky red diffuse gastric mass for which total gastrectomy with splenectomy was done. Pathologic examination revealed marked destruction of the muscularis propria. Multiple fissures and ulcerations were seen and the clusters of immunoblasts were multiple and sharply circumscribed. The paracardiac and right gastric lymph nodes were involved. This patient developed a left subphrenic abscess that was drained 4 weeks postoperatively.

Table (1) : Analysis of Patients with Primary Gastrointestinal Lymphoma.

Patient No.	Age yrs.	Sex	Presentation	Preop. Diagnosis	Operative procedure	Final Diagnosis	Morb.	Mort.
1	54	M	Dyspepsia and anaemia	Cancer Stomach	Total gastrectomy	NHL Lc.	—	—
2	60	M	Bleeding per rectum	Lymphoma of rectum	Abdomino-perineal resection	NHL Lc.	—	+
3	31	F	Abdominal mass	Cancer Stomach	Total gastrectomy	NHL Lc.	—	—
4	51	F	Vomiting loss of weight	Lymphoma of Stomach	Total gastrectomy	NHL Lc.	—	—
5	42	F	Dysenteric symptoms	Lymphoma of rectum	Abdomino-perineal resection	NHL Lc.	+	—
6	29	M	Abdominal mass	Lymphoma of Stomach	Total gastrectomy	NHL Imm.	+	+
7	43	F	Intestinal obstruction	Intestinal obstruction	Ileal resection	NHL Lc.	—	—
8	9	M	Upper G.I. bleeding	Lymphoma of duodenum	Pancreatico-duodenectomy	NHL Lb.	—	—
9	8	M	Recurrent abdominal colic	Ileocolic intussus-ception	Right hemicolectomy	Lc.	—	—

NHL = Non-Hodgkin Lymphoma Lb = Lymphoblastic Imm = Immunoblastic
Lc. = Lymphocytic Morb. = Morbidity Mort. = Mortality

Combined radiotherapy and chemotherapy were given. The patient died ten months after surgery with bone deposits.

Case 7 : This patient presented by acute small bowel obstruction following a four months period of diarrhea and loss of weight. Having no previous abdominal operations, the possibility of Crohn's disease or a neoplasm probably a lymphoma of the small gut was raised. Exploration revealed a rigid 12 cm long segment of distal ileum with obstructed lumen. The serosal surface was nodular and pearly white. The mesentry was normal apart from few slightly enlarged lymph nodes. Resection of the ileal loop with end-to-end anastomosis was done. Pathologic examination revealed diffuse ulcerating polypoid mucosal and submucosal growth with transmural infiltration. Microscopic examination showed lymphocytic lymphoma. The patient is recurrence free for $3\frac{1}{2}$ years.

Case 8 : This boy presented with recurrent alarming upper gastrointestinal bleeding following a short period of vomiting and loss of weight. Upper G.I. endoscopy revealed an ulcerating necrotic friable ilfiltrating mucosal lesion extending from below the region of the ampulla of Vater to the junction of the second and third parts of duodenum. Biopsy showed non-Hodgkin lymphoma. ERCP, and barium follow-through showed normal biliary system and small gut respectively. Pancreatico-duodenectomy was done. Pathologic examination revealed lymphoblastic lymphoma deeply invading and widely permeating the muscularis propria. The lymph nodes were not involved. Combined radiotherapy and chemotherapy were given. The patient is alive 20 months after surgery.

Case 9 : This patient presented with recurrent attacks of abdominal colic for the last six months. No masses could be felt. It is interesting that the possibility of ileo-colic intussusception was first raised on colonoscopy where a bulky rounded ulcerated advancing mucosal growth was seen to occupy most of the lumen of the ascending colon. Barium enema proved the diagnosis. Exploration revealed irreducible ileocolic intussusception. Right hemicolectomy was done. Pathologic examination showed the head of the intussusception to be big tumour 5 × 3 cms in size which proved to be lymphocytic lymphoma. The ileocoecal lymph nodes were enlarged but showed reactive hyperplasia. Combined radiotherapy and chemotherapy was given and the patient is alive 14 months after surgery.

Discussion

Primary gastrointestinal lymphomas are most frequent in the ileum, coinciding with the large number of normal lymphoid follicles in this region[6]. Primary lymphoma is still less common than primary carcinoma to affect the small gut. The same holds true for the stomach, duodenum and rectum. The incidence of gastrointestinal lymphomas may be increased because of the increasing number of HIV positive patients. There is no sex predominance among lymphomas of all portions of the gastrointestinal tract[7]. However,

there is slight male to female predominance among small gut 3 : 1[4] and gastric 1.7 : 1 lymphomas[7]. Small gut lymphomas affect younger age groups < 20 years whereas gastric and rectal lymphomas occur in elderly patients[4].

Gastrointestinal lymphomas should always be born in mind in the differential diagnosis of tumours affecting the alimentary tract. They are suspected whenever a bulky growth with deep and extensive infiltration is seen with unexpectedly few symptoms, i.e., the signs far exceed the symptoms. Endoscopy and barium studies only disclose luminal and mucosal abnormalities. Contrast computerized tomographic scanning of the alimentary tract with guided biopsy are crucial in their accurate preoperative diagnosis. Gastrointestinal lymphomas are only considered to be primary if they fulfill Dawson's criteria described in 1961[5]. To these we add that they should show a negative skeletal survey including an isotope bone scan.

These peculiar lymphomas are considered to be of B-cell lymphocyte origin[2]. They could be quite innocent low grade growths or may turn to be rapidly fatal aggressive high grade tumours[8]. Two of our patients had high grade lymphomas, one immunoblastic with plasmacytoid differentiation who died and the other lymphoblastic type. These tumours have a tendency to infiltrate deeply across the muscle coat of gut with variable degree of destruction, resulting in perforation[4]. Among the nine presented patients however, perforation did not occur.

All patients with presumptive preoperative diagnosis of gastrointestinal lymphoma should undergo exploratory laparotomy unless there is evidence of diffuse systemic involvement or unless there are strong medical contraindications[2]. An abnormal liver ultrasound or an abdominal mass should not exclude exploration. At laparotomy all intra-abdominal viscera are thoroughly examined for the presence of metastases. Resection with safety margin is designed according to the usual oncologic surgical principles. Frozen section examination of the resection margins is mandatory. The spleen should be removed in all cases of primary gastric lymphomas. However, enbloc dissection of regional lymph nodes is not required since these groups of lymph nodes should not be involved in primary lymphomas, otherwise they are considered secondary gastrointestinal lymphomas which should not be surgically treated.

Resection of primary lymphoma is better than radiation therapy. The use of postoperative irradiation after resection is debatable. If recurrence occurs, irradiation should probably be employed and if there is invasion of the line of resection, irradiation is indicated. Lymphocytic lymphomas are highly radiosensitive but the reticulum cell lymphosarcoma is relatively radioresistant. Chemotherapy is preferably given to all cases after resection. This is particularly important if the lymph nodes are positive or if there is evidence of a systemic disease. Complete response rates for chemotherapy vary from 13 - 69% [2].

The 5 year survival for gastric lymphomas varies from 34% for resection alone[**9**] to 40 - 50% if postoperative radiotherapy is added and to 73.4% for node-negative patients.

The 5-year survival for intestinal and rectal lymphomas is about 30% after resection, radiotherapy and chemotherapy. Radiotherapy alone has been found to be as effective as resection if the disease is localized[**10**].

References

1. HERRMANN, R.; PANATRON, A.M. et al. : Gastrointestinal involvement in non-Hodgkin's lymphoma. Cancer, 46 : 215, 1980.
2. ROSIN, R.D. : Tumours of the stomach in Maingot's abdominal operation. Schwartz S.I., Ellis H., editors, Appleton and Lange, pp. 679-699. 1990.
3. LIM, F.E.; HARTMAN, A.S. et al. : Factors in the prognosis of gastric lymphoma. Cancer, 39 : 1715, 1977.
4. LEAPER, D.J. : Tumours of the small intestine in Maingot abdominal operations. Schwartz S.I., Ellis H., editors Appleton and Lange, pp. 871-883, 1990.
5. DAWSON, IMP.; CORNES, J.S. and MORSON, B.C. : Primary malignant lymphoid tumours of the gastrointestinal tract. Br. J. Surg., 49 : 80, 1961.
6. GRAY, G.M.; ROSENBERG, S.A. et al.: Lymphomas involving the gastrointestinal tract. Gastroenterology, 82 : 143, 1982.
7. ROSENBERG, S.A.; DIAMOND, H.D.; et al. : Lymphosarcoma. A review of 1269 cases. Medicine, 40 : 31, 1961.
8. STOBBE, J.A.; DOCKERTY, M.B.; et al. : Primary gastric lymphoma and its grades of malignancy. Am. J. Surg. 122 : 10, 1966.
9. HOCKEY, M.S.; POWELL, J.; et al. : Primary gastric lymphoma. Br. J. Surg. 74 : 483, 1987.
10. SKUDDER, P.A. and SCHWARTZ, S.I.: Primary lymphoma of the gastrointestinal tract. Surg. Gynoecol. Obstet., 160 : 5, 1985.