Egyptian Journal of Surgery Vol. (20), No. (4), Oct., 2001

PRIMARY GASTROINTESTINAL TRACT LYMPHOMA: MANAGEMENT AND OUTCOME

By
Samy Osman MD, Mansour M Kabash* MD, Hamdy Hussien* MD, Mohamed A Sayed* MD, Alaa-Eldin H Mohamed* MD, Nabil Y Abouldahab M.D.*, Ali Abd El-Rahman Abd-Allah** MD, Ashraf Ziedan***, Etemad H. Yassien*****
*,** Surgery and Clinical Oncology Departments, South Valley University
, * Radiotherapy and Pathology Department, Assiut University

Background: *The optimal management of primary gastrointestinal tract lymphoma (GIT lymphoma) has not been clearly defined. The role of surgery in these cases remains controversial. The aim of this work is to analyze the clinicopathological properties of primary GIT lymphoma, define lines of treatment and to detect outcome and variables affecting overall survival.*

Patients and methods: *64 patients with primary GIT lymphoma presented to Sohag University Hospital and Assiut University Hospital from July 1994 to January 2000. This study outlines clinicopathological features, modalities of diagnosis and treatment, outcome and variables affecting overall survival.*

Results: *The median age of patients was 38 years, including 40 males and 24 females. The stomach was involved in 36 cases (56.3%) and intestinal lymphoma was implicated in 28 cases (43.7%). Stage IIE was the commonest stage (62.5%). The predominant histologic type was high-grade. Overall survival in all cases was 63% at 30 months according to the Kaplan-Meier method. Stage of disease, extension of resection, site of the lesion whether gastric or intestinal and achievement of complete remission (CR) were found to affect overall survival.*

Conclusion: *This study outlined clinicopathological features, modalities of diagnosis and treatment, outcome and variables affecting overall survival of primary GIT lymphoma. Earlier detection, optimal resection and chemotherapy plus efforts to achieve complete remission stand behind the success in management of GIT lymphoma.*

Keywords: *Lymphoma – Non-Hodgkin's lymphoma – Gastrointestinal tract lymphoma.*

INTRODUCTION

Primary lymphoma of the gastrointestinal tract (GIT) is an unusual disease in which the optimal management strategy has not been clearly defined [1]. Primary GIT lymphoma accounts for 2-5% of all GIT malignancies. The GIT is the most frequent site of extranodal lymphoma and the stomach is the most frequently involved site [2]. Most of these lymphomas arise from mucosa associated lymphoid tissue (MALT) [3]. The association of primary gastric lymphoma and Helicobacter pylori (H. pylori) infection has been reported, specially in cases of low-grade lymphoma of MALT type [4].

In these individuals with apparently localized GIT lymphoma, resection of the involved GIT segment may be considered the primary treatment and is potentially curative [5,6]. Surgical resection and/or debulking in patients with more extensive disease may reduce the risk of

bleeding or perforation during the administration of chemotherapy and/or radiation therapy [1].

The aim of this study is to analyze the clinicopathological properties of primary GIT lymphoma and define modalities of diagnosis, lines of treatment, response to treatment, outcome and variables affecting it, which are helpful in the management of these cases.

PATIENTS AND METHODS

This study included 64 patients with primary GIT lymphoma who presented to the South Valley University Hospital and Assiut University Hospital in the period from July 1994 to January 2000. Criteria of selection of patients with primary GIT lymphoma were done according to Dawson et al, (1961) [7] (GIT lymphoma without involvement of liver, spleen, peripheral or mediastinal lymph nodes or bone marrow) or according to Lewin et al, (1978) [8] (primary lymphoma is that patients presented with GIT symptoms and was confirmed to or was clearly predominates within the GIT).

Diagnosis and staging:

All patients were subjected to complete history, clinical examination, blood picture, blood glucose, blood urea, serum creatinine, liver function tests, LDH, stool and urine examination and bone marrow studies. Abdominal u/s and chest x-ray were done for all patients. Abdominal CT scan, plain x-ray abdomen, barium studies, GIT endoscopy, IVU were performed in selected cases.

Staging was done according to a modification of Ann Arbor system for the non-Hodgkin's lymphoma [9], and was based on clinical findings, laboratory, bone marrow studies, u/s and CT scan. It is important to rule out the presence of systemic lymphoma. Stage IE is tumor confined to GIT, IIE has regional lymph node involvement, IIIE has spread to other organs within the abdomen and IV is spread beyond the abdomen.

Surgical techniques:

Surgical interference included curative resection, palliative resection and bulky residual disease. Curative resection means complete resection of tumor with regional lymph nodes. Palliative resection means resection with minimal residue and with regional lymph nodes < 5 cm were left behind and bulky residual disease when there is no resection or residual lymph nodes > 5 cm.

Pathological studies:

Biopsies were fixed in 10% formalin, embedded in paraffin, cut at 5 microns and stained by Haematoxylin and Eosin (H&E) stain for pathological diagnosis and grading of these lymphomas. Classification and grading was done according to the classification of working formulation for clinical usage [10] which subdivides cases according to morphologic criteria into three histologic grades of prognostic significance; but for the purpose of treatment protocols, the intermediate and high grades are grouped together as high-grade lymphomas. Test for H. pylori was done in cases with gastric lymphoma by histopathological study of resected gastric specimen using Giemsa stain.

Chemotherapy (CT):

Patients who were eligible for chemotherapy received combination chemotherapy (CHOP regimen) with doses as follows: (1) Cyclophosphamide 750 mg/m^2 IV; (2) Doxorubicin 50 mg/m^2 IV; (3) Vincristine 1.4 mg/m^2, maximum 2 mg/dose IV; (4) Prednisone 40 mg/m^2, PO days 1-5.

Cardiac, renal, liver function tests were performed. Patients with poor functions were excluded. Premedication with antiemetics was given to all patients.

Radiotherapy (RT):

40 Gy over 4 weeks via 6 MV linac were given to patients with residual or initial bulky disease. Planning was tailored according to CT findings. Whole pelvic irradiation via 20-3 fields was applied to cases with rectal disease.

Follow-up and statistical studies:

All patients (64) who passed the postoperative period (4 weeks), were followed up regularly every 3 months (12-30 months) by different investigations which covered the following:

(1) Response to treatment was detected as complete remission (CR) with complete disappearance of the lesion from its site and no appearance of new tumour sites; major partial response (MPR) (>50%), minimal response (MR) (<50%) and no response.

(2) Overall survival was done in all cases according to Kaplan-Meier method. Overall survival according to the site, stages of the disease and modalities of treatment was performed. Chi square test was used to detect P value of these variables. P value of less than 0.05 was considered statistically significant.

RESULTS

Clinicopathological features:

This study involved 64 patients with primary GIT lymphoma, including 40 males and 24 females, with age range from 17 to 73 years (mean age 38 years). Gastric lymphoma predominated in the older age than intestinal lymphoma. Tumors were located in the stomach in 36 patients (56.3%) and intestinal lymphoma was involved in 28 patients (46.7%). The latter group was distributed as

small intestine (20 patients), colon (5 patients), rectum (2 patients) and appendix in one patient. Stage IE was confirmed in 10 patients (15.6%), stage IIE in 40 patients (62.5%), stage IIIE in 8 patients (12.5%) and stage IV in 6 patients (9.4%) (Table 1). All cases were B-cell lymphoma, including 10 patients with low-grade (15.7%), 19 cases with intermediate-grade and 35 cases with high-grade, the latter two grades were considered as high-grade and included 54 patients (84.4%). H. pylori was detected in 15 patients with gastric lymphoma (41.7%), distributed as 6 out of 8 patients (75%) with low-grade and 9 out of 28 patients (32%) with high-grade.

Different abdominal manifestations were outlined in these patients (Table 1). Emergency presentation was encountered in 14 patients (21.9%). Emergency presentation and the presence of palpable abdominal mass were more common with intestinal lymphoma, while weight loss and vomiting were common with gastric lymphoma.

Endoscopic diagnosis and surgical role:

Gastric lymphoma:

(1) Gastroscopy and biopsy confirmed diagnosis in 30 patients (83.3%), ulcerative lesion in 12 patients, polypoid lesion in 10 patients and diffuse infiltrative type in 8 patients. Repeated biopsies were recommended in most of these patients to prove the diagnosis and 6 patients (16.7%) were diagnosed on laparotomy only.

(2) Laparotomy was performed in 19 patients (52.8%) (Table 2). Curative gastrectomy was carried out in 10 patients (total in 3 patients, subtotal in 7 patients). Palliative gastrectomy was done in 5 patients. Resection was not carried out in 4 irresectable tumours where only operative biopsy was done. Seventeen patients (47.2%) were not subjected for surgery.

Intestinal lymphoma:

(1) Endoscopic biopsy was done and confirmed the diagnosis in 4 cases with colorectal lymphoma.

(2) Laparotomy was done in 24 patients (85.7%) (Table 2). Curative resection with no residual disease was carried out in 6 patients, palliative resection in 15 patients and resection was not done in 3 irresectable tumours.

Modalities of treatment:

Different therapeutic modalities were performed in these 64 patients (Table 3). Resection alone with treatment of H. pylori was performed in 8 patients with low-grade gastric lymphoma. Resection followed by chemotherapy in 23 patients (36%). Resection, chemotherapy and radiotherapy were indicated in 5 gastric lymphoma patients (7.8%). Chemotherapy alone or in combination with radiotherapy were adopted in the remaining 28 cases (43.8%), who were not subjected to resection.

Role of surgical resection was more common in intestinal lymphoma than gastric lymphoma (75% versus 41.7% respectively). Most patients received chemotherapy (58 cases) while radiotherapy was added to 15 cases (23.4%). Vomiting and cytopenia were the commonest side effects associated with chemotherapy. All patients treated by radiotherapy could tolerate the treatment course without undue toxicity.

Response to treatment:

Response to treatment in all patients according to stage of the disease is outlined in Table 4. Complete remission was obtained in 15 patients (23.4%), all of them were stages I & II after initial treatment. Major partial response was detected in 29 patients (45.3%), minimal response was observed in 16 patients (25%) and lastly no response was detected in 4 patients (6.3%). Relapse occurred in 3 out of 15 patients who achieved with complete remission (20%).

Outcome:

- Outcome of treated primary GIT lymphoma according to different variables is outlined in Table 5. Overall survival at 30 months of all cases was 63% according to the Kaplan-Meier method (Fig. 1).

- The Stage of disease had great impact on prognosis (Fig. 2). Stage IE had the best outcome (80%) followed by stage IIE (73%) and stage IIIE (37%). Stage IV had 33% overall survival at 18 months and 0 at 24 months with poorest prognosis (Fig. 2). The overall survival rate in stage I&II was statistically significant in comparison to stage III&IV (P value 0.01).

- Extension of resection had an effect on the prognosis. Curative resection with no residual disease had 87% overall survival followed by palliative resection with minimal residual disease (75%), while patients without surgical resection (bulky residual) had 43% overall survival (Fig. 3) with statistically significant P value (0.02).

- Gastric lymphoma had a better prognosis than intestinal lymphoma (70% vs 56%) (Fig. 4), as low-grade lymphoma was detected in gastric lymphoma more than intestinal lymphoma.

- Achievement of complete remission had a better outcome than those who failed to achieve complete remission (86% vs 57%) (Fig. 5) with statistically significant P value (0.001).

Table (1): *Clinicopathological features of primary GIT lymphoma.*

Findings	*All patients (64)*	*Gastric (36)*	*Intestinal (28)*
Age:			
Range (years)	(17-73)	(37-73)	(17-61)
Mean (years)	(38)	(44)	(22)
Sex:			
Male to females	40:24	23:13	17:11
Grade:			
Low-grade	10 (15.7%)	8 (22.2%)	2 (7.1%)
High-grade	54 (84.4%)	28 (77.8%)	26 (92.9%)
Stage:			
Stage IE	10 (15.6%)	7 (19.4%)	3 (10.7%)
Stage IIE	40 (62.5%)	23 (63.9%)	17 (60.7%)
Stage IIIE	8 (12.5%)	3 (8.3%)	5 (17.9%)
Stage IVE	6 (9.4%)	3 (8.3%)	3 (10.7%)
Clinical features:			
Abdominal pain	57 (89.1%)	33 (91.7%)	24 (85.7%)
Weight loss	43 (67.2%)	29 (80.5%)	14 (50%)
Vomiting	34 (53.1%)	22 (61%)	12 (42.8%)
Anorexia	25 (39.1%)	19 (52.8%)	6 (21.4%)
Palpable abdominal mass	27 (42.2%)	11 (30.5%)	16 (44.4%)
Altered bowel habit	12 (18.8%)	3 (8.3%)	9 (32.1%)
Bleeding	6 (9.4%)	3 (8.3%)	3 (10.7%)
Obstruction	17 (26.6%)	5 (13.9%)	12 (42.8%)
Perforation	2 (3.1%)	1 (2.8%)	1 (3.6%)
Fever	20 (31.3%)	9 (45%)	11 (55%)

Table (2): ***Diagnosis and surgical role.***

Procedure	All cases	Gastric	Intestinal
Laparotomy:	43 (67.2%)	19 (52.8%)	24 (85.7%)
Curative resection	16 (25%)	10 (27.8%)	6 (16.7%)
Palliative resection	20 (31.3%)	5 (13.9%)	15 (53.6%)
Biopsy only	7 (10.9%)	4 (11.1%)	3 (10.7%)
Endoscopic biopsy only	21 (32.8%)	17 (47.2%)	4 (14.3%)
Total	64	36	28

Table (3): *Modalities of therapy in primary GIT lymphoma.*

Modalities of treatment	*All cases*	*Gastric*	*Intestinal*
Resection:			
Resection *	8 (12.5%)	8 (16.7%)	-
Resection and CT	23 (36%)	2 (5.6%)	21 (75%)
Resection, CT and RT	5 (7.8%)	5 (13.9%)	-
No resection:			
CT	18 (28.1%)	13 (36.1%)	5 (17.9%)
CT and RT	10 (15.6%)	8 (22.2%)	2 (5.6%)
Total	64	36	28

* 8 cases with low-grade gastric lymphoma received treatment for H. pylori.

Table (4): *Response to treatment.*

Response to treatment	*CR **	*MPR ***	*Minimal response*	*No response*
Stage (No. of patients):				
Stage I (10)	8 (80%)	2 (20%)	-	-
Stage II (40)	7 (17.5%)	22 (55%)	11 (27.5%)	-
Stage III (8)	-	4 (50%)	3 (37.5%)	1 (12.5%)
Stage IV (6)	-	1 (16.7%)	2 (33.3%)	3 (50%)
Total (64)	15 (23.4%)	29 (45.3%)	16 (25%)	4 (6.3%)

**** CR : Complete remission.***
***** MPR : Magor Parial Resperse.***

Table (5): *Overall survival rates of variables affecting outcome in primary GIT lymphoma at 30 months.*

Variable	*All cases*	*Overall survival rate*	*P value*
Stage:			
Stage IE	10	80	P<0.01 in favour of stages I&II
Stage IIE	40	73	
Stage IIIE	8	37	
Stage IVE	6	00 *	
Resection:			
Curative	16	87	P=0.02 in favour of resection
Palliative	20	75	
No resection or bulky residual disease	28	43	
Site:			
Gastric	36	70	P<0.01 in favour of gastric
Intestinal	28	56	
Complete remission (CR):			
Achieved	15	86	P=0.001 in favour of achieved remission
Not achieved	49	57	

* Stage IV E had 33% overall survival at 18 months and zero at 24 months.

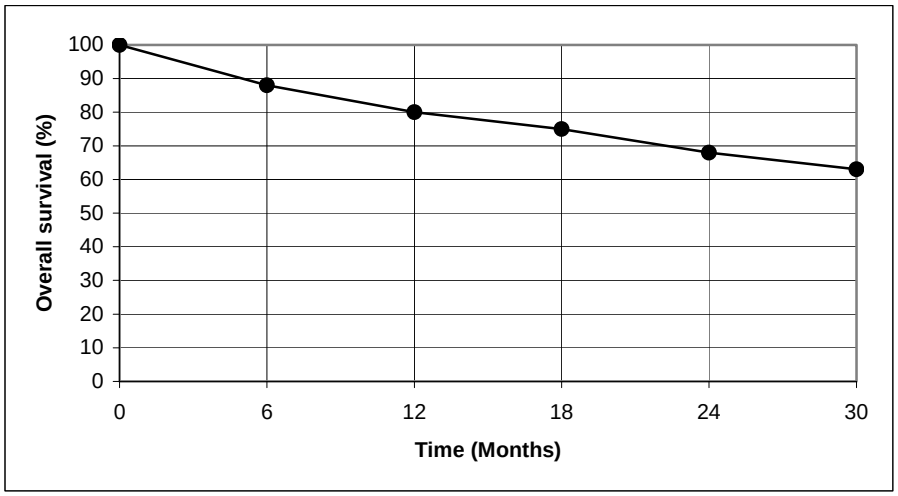

Fig. (1): Overall survival at 30 months in all patients.

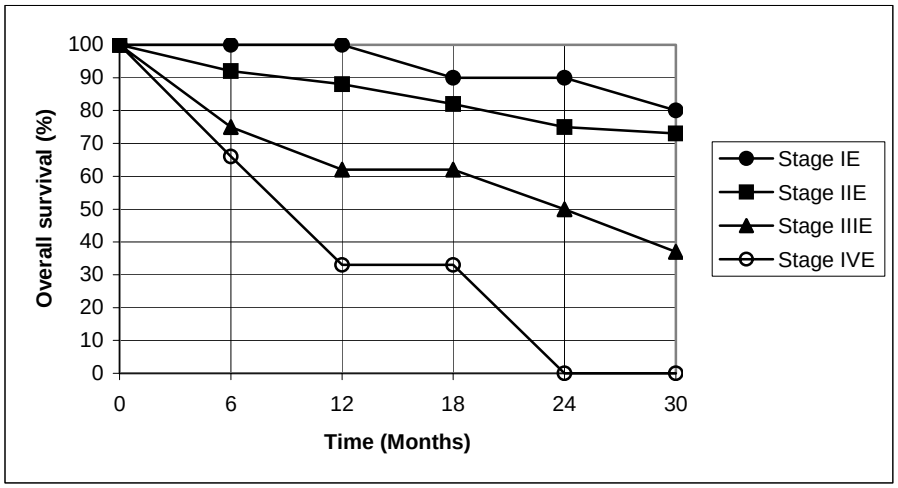

Fig. (2): *Overall survival at 30 months in different stages.*

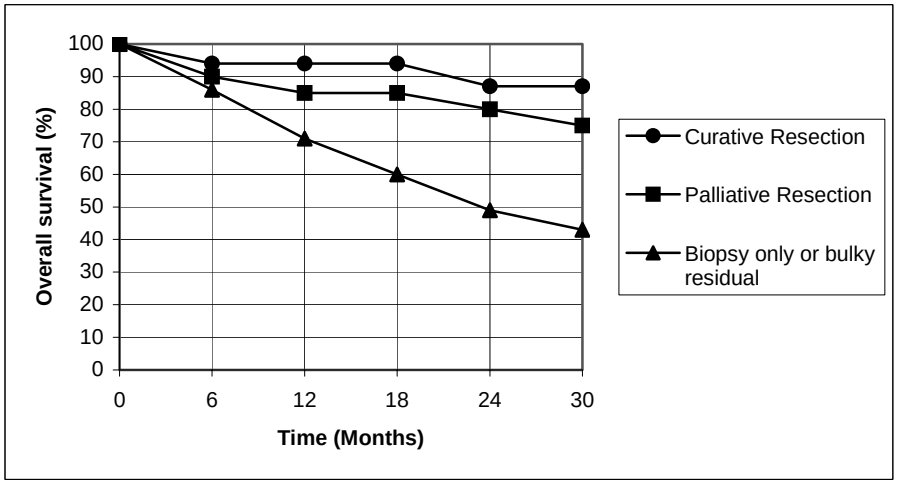

Fig. (3): *Overall survival according to the surgical resection.*

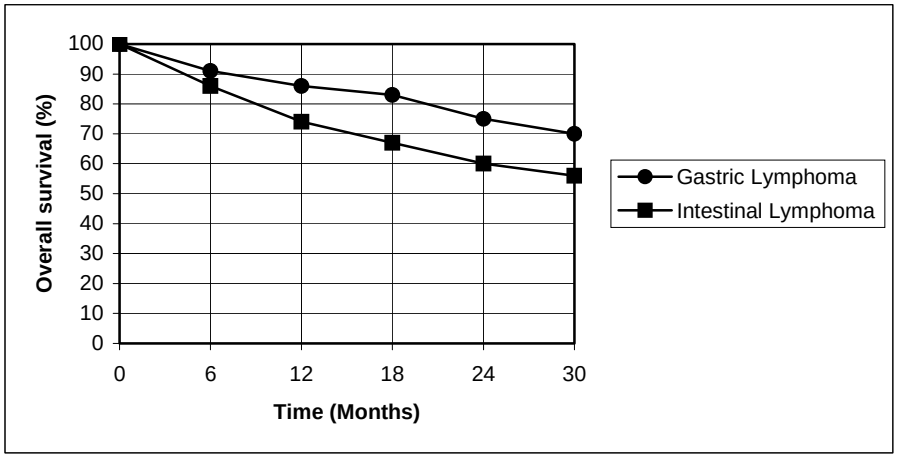

Fig. (4): *Overall survival in gastric and intestinal lymphoma.*

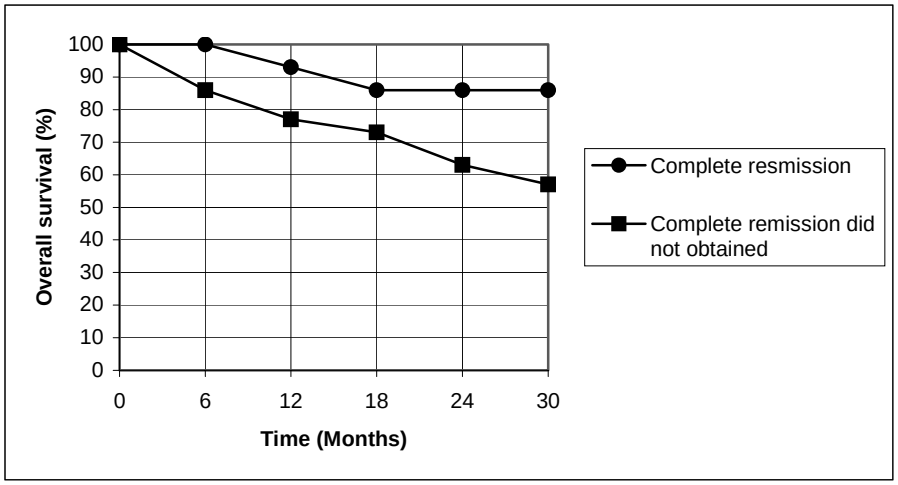

Fig. (5): *Overall survival according to response to treatment.*

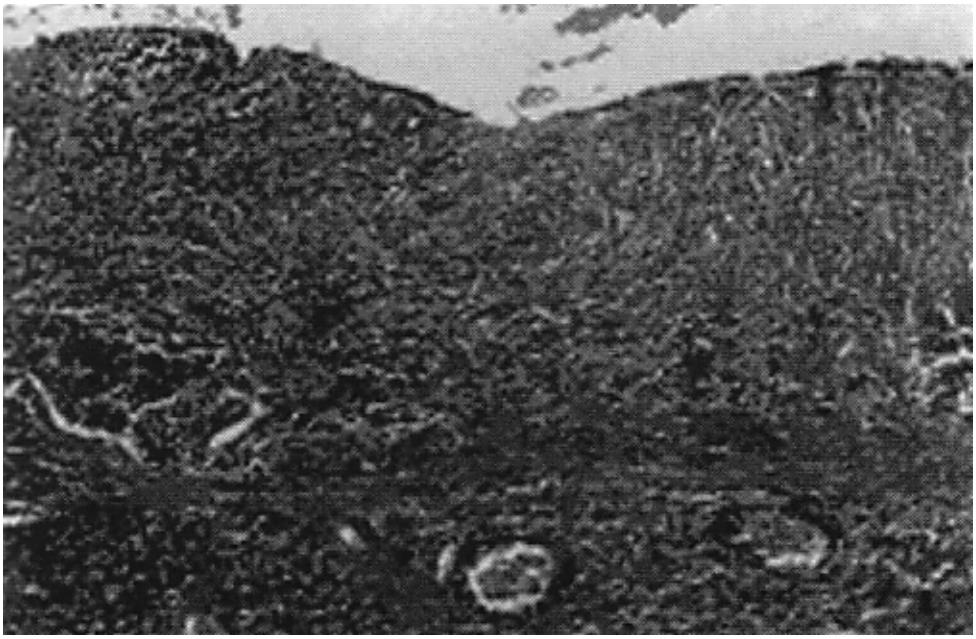

Fig. (I): MALT lymphoma of the stomach showing marked lymphoid follicle proliferation with ulceration of the surface epithelium (H&E stain X 40).

Fig. (II): MALT lymphoma of the stomach showing diffuse infiltration of the muscularis mucosa and submucosa (H&E stain X 100).

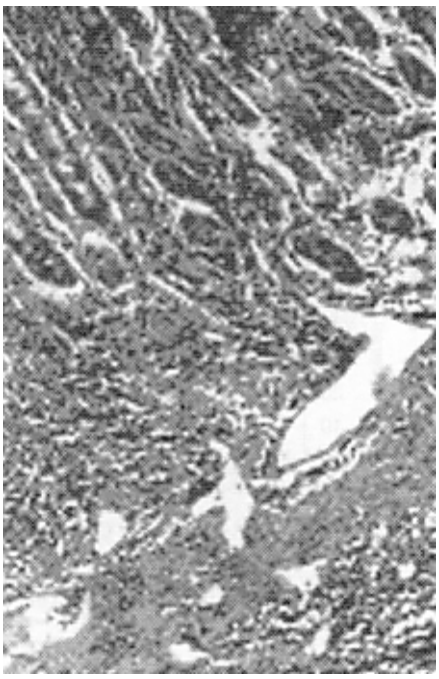

Fig. (III): Gastric gland showing the typical spiral shape of H. pylori within the lumen and attached to the surface epithelium (arrow) (Giemsa stain X 1000).

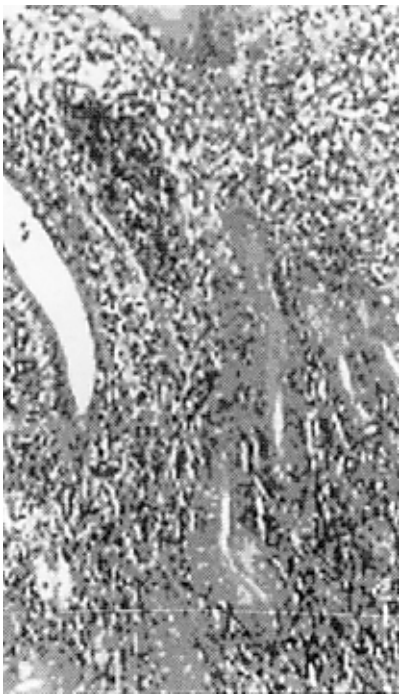

Fig. (IV): High-grade intestinal lymphoma, the tumour diffusely infiltrates the submucosa and the lamina propria (H&E stain X *200).*

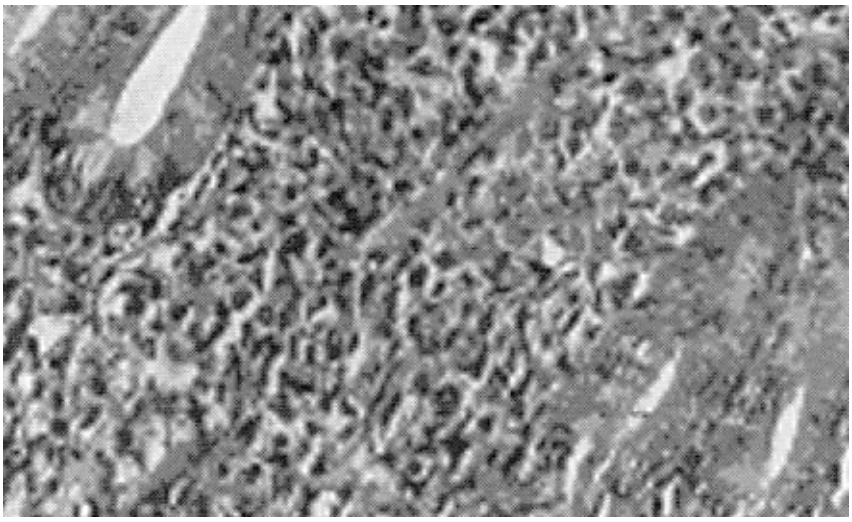

Fig. (V): High-power of the previous case to show large size and pleomorphism of the tumour cells (H&E stain X 400).

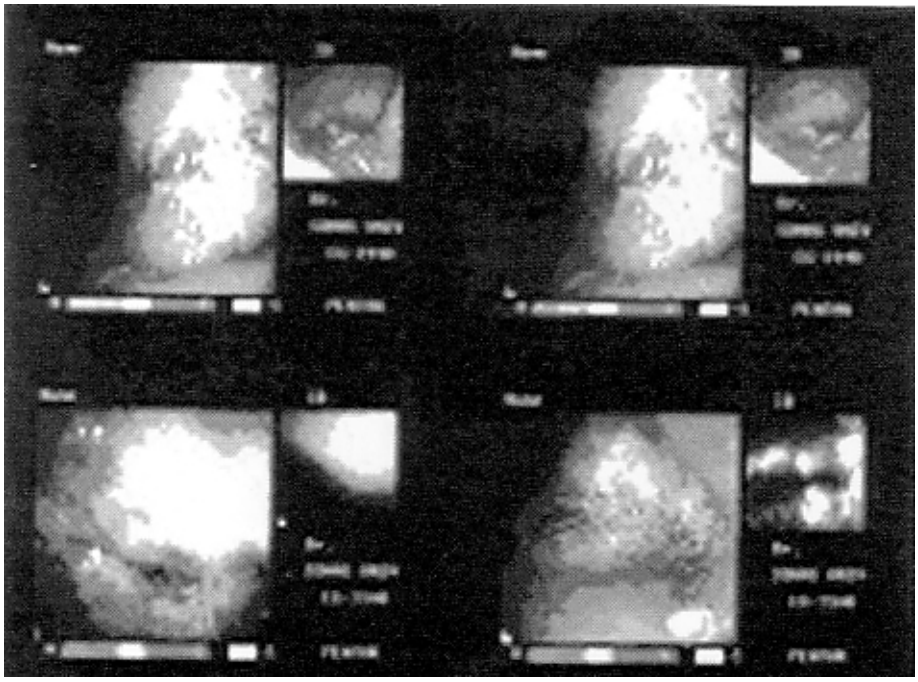

Fig. (VI): Antral gastric lymphoma: Endoscopic picture shows localized antral mass with areas of ulceration.

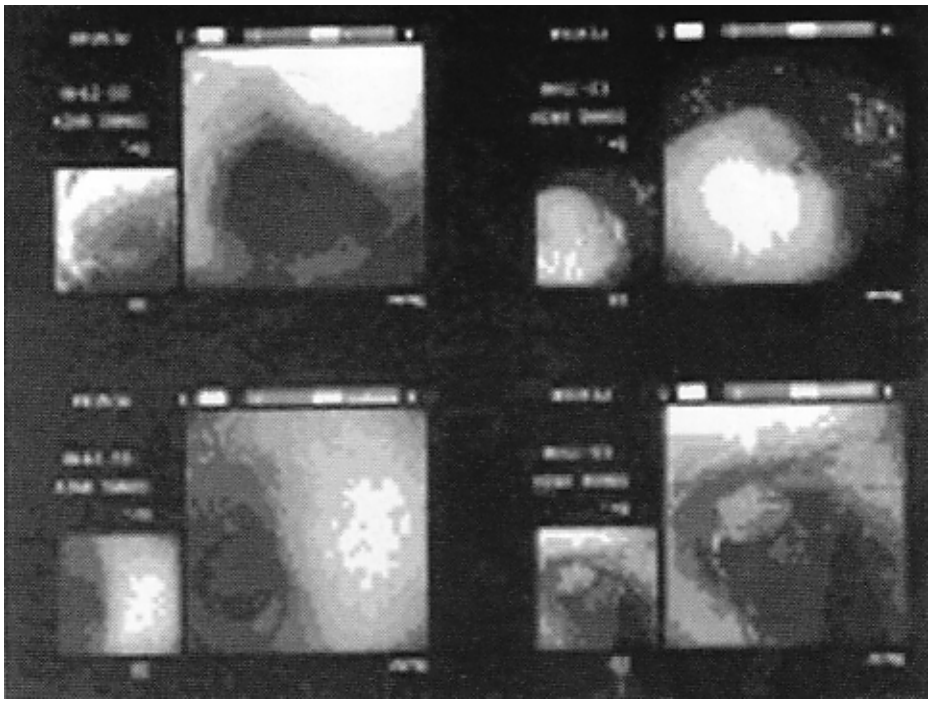

Fig. (VII): Fundic gastric mass (Localized type): Endoscopic picture shows localized lymphoma (mass) at region of fundus of stomach.

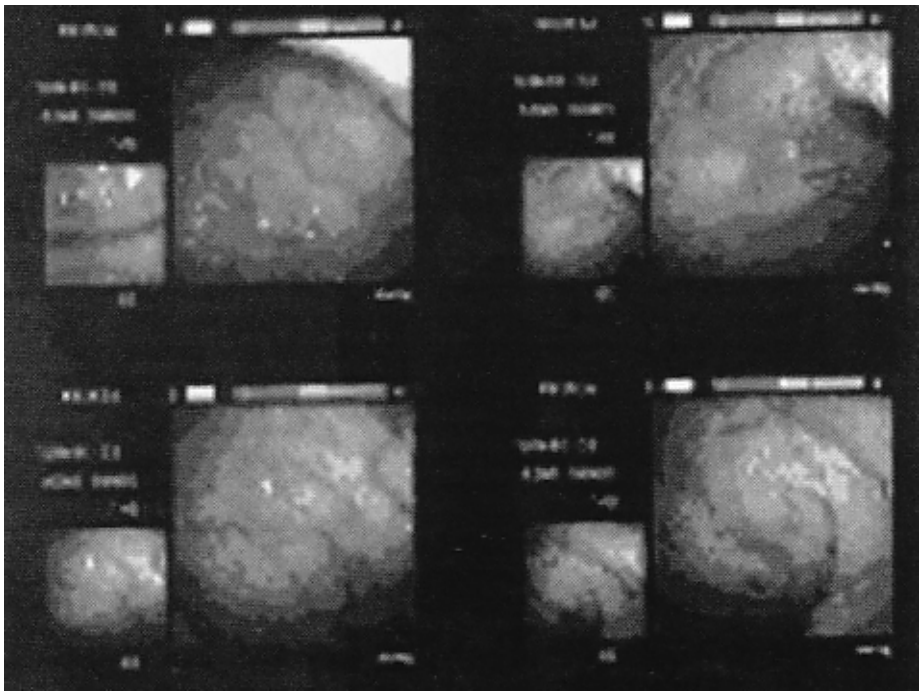

Fig. (VIII): Diffuse gastric lymphoma: Endoscopic picture shows diffuse gastric lymphoma affecting most of stomach wall mucosa.

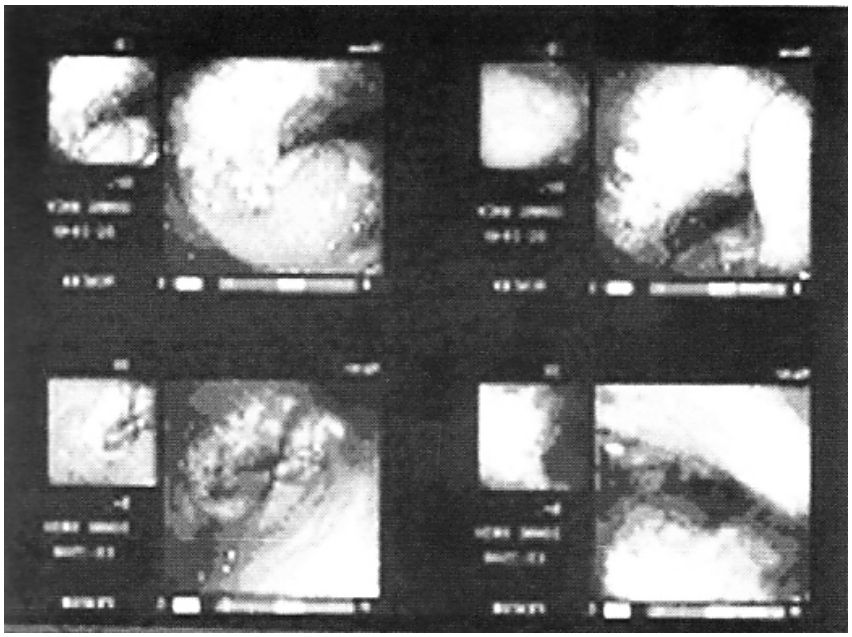

Fig. (IX): Antral gastric lymphoma: Endoscopic picture shows localized antral mass which showing areas of ulceration.

DISCUSSION

The gastrointestinal tract is the most common site of primary extranodal lymphoma. It is usually of NHL where HD very rarely primarily affects the GIT. National Cancer Institute, Cairo, studies shows that high-grade lymphomas predominate and the patients present at a late stage with large tumour [11]. Our results were concordant with other series and concluded that gastric lymphoma has a higher incidence than intestinal lymphoma [12,13]. In our study, males were affected more than females; gastric lymphoma was encountered in older patients than intestinal lymphoma[14].

The stomach is the commonest site of extranodal lymphoma. B-cells lymphoma of MALT type are the commonest lymphoma and may be low-grade or high-grade [15,16]. Low-grade lymphoma was encountered in 32% of gastric MALT lymphoma and high-grade in 68% of these cases [4], while in our cases, low-grade constituted 22% and high-grade 78% of cases. The prevalence of H. pylori infection varies worldwide between 20% and 100% of the general population, depending mostly on socioeconomic conditions. H. pylori has been reported between 42-59% in gastric MALT lymphoma, so that not all cases are H. pylori dependent. H. pylori infection may play a promotor role in the development of MALT lymphoma [16]. Intestinal lymphoma is divided into western type lymphoma similar to that seen in the developed countries and Mediterranean type lymphoma characterized by secretion of alpha heavy chains disease. The latter is a predominant in the poor risk socioeconomic conditions, second and third decades of life, associated with malabsorption and diagnosed by intestinal biopsy with or without detection of alpha heavy chain immunoglobulin [17].

The clinical features of primary GIT lymphoma have a wide variation. Abdominal pain and weight loss were the commonest manifestations (89% & 67.2% respectively) while palpable abdominal mass was found in 42.2%. Weight loss, anorexia and vomiting were common with gastric lymphoma while obstruction and palpable abdominal mass predominated in intestinal lymphoma. These findings with some difference were reported in other studies [1, 8,19].

Endoscopy has great role in the diagnosis of GIT lymphoma especially gastric lymphoma. It clarifies morphological features of the tumour whether ulcerative, infiltrative or polypoid lesion. Endoscopic biopsy proved diagnosis in 83.3% of gastric cases and 100% of rectal tumours of our cases. The reported range of accuracy of preoperative endoscopic diagnosis of gastric lymphoma ranged from 30 to 96%. This wide range is mainly due to submucosal development of lesion and vague surface qualities, therefore many specimens may be required for accurate diagnosis [20]. Preoperative accuracy of CT scan for evaluation for nodal extension has been questionable with false negative results [21]. Endoscopic ultrasound has a more accurate detection of depth of tumour invasion and regional lymph nodes involvement [22].

Management of GIT lymphoma may be accomplished in cases amenable for curative or palliative resection, in combination with chemotherapy while radiotherapy was adopted in selected cases. Chemotherapy with or without radiotherapy was done for cases not amenable for surgical resection. Many studies adopted surgery in these cases and considered it as the first line of treatment. It provides a reliable histologic diagnosis, accurate pathology and staging. Resection of tumour results in improved survival and avoids the risk of life threatening hemorrhage or perforation developed on treating unresected tumour with chemotherapy or radiotherapy [14, 18]. Most cases with gastric lymphoma may be subjected to surgery [23]. Resection in patients with advanced disease followed by chemotherapy, with or without radiotherapy decreases the risk of distant failure or local recurrence [24]. In contrast, many studies did not consider surgery as the first optimal treatment and resection rate was decreased in cases with gastric lymphoma [25]. The policy of debulking large tumour prior to chemotherapy is unwarranted. The surgical morbidity and mortality rates were considerable and argue for careful evaluation of surgical risk of this frequently debilitated group of patients [1]. Laparotomy was done in 67.2% of our cases and surgical resection was performed in 56.3% including curative resection in 25% and palliative resection in 31.3%. Surgery and chemotherapy treated 65.4% of cases of one study [26], and surgery was performed in 69% in other study [18].

H. pylori is usually associated with low-grade lymphoma. Medication of H. pylori is a promising therapeutic approach for localized low-grade lymphoma [27]. Eradication of H. pylori is harmless and inexpensive and should be given for localized gastric MALT lymphoma specially cases with H. pylori positive cases, superficial and low-grade tumours [15].

Complete remission was achieved in 23.4% of our cases, all of them included in stages IE & IIE. Major partial response was encountered in 45.3% while minimal and no response were found in 31.3%. Other series reported that complete remission was achieved in 58%, major partial response in 19% and 23% without response [28] while in another study, complete remission was reported in 65.4%[26].

Overall survival of our cases was 63% at 30 months. Stages IE and IIE, curative resection, achievement of complete remission and gastric lymphoma showed statistically significant outcome with P values of 0.01, 0.02, 0.001 and 0.01 respectively. From our study and other series, we found that the prognostic factors affecting overall survival and outcome are related to the underlying pathology, its extension and site. Consequently the effects of therapeutic modalities will be different in individual cases. The early stages and localized disease are amenable for curative resection and the benefit of chemotherapy and radiotherapy will be more effective with achievement of complete remission and better prognosis. In contrast late stages with disseminated disease are not amenable for resection and consequently chemotherapy or radiotherapy will not be effective enough and complete remission will not be achieved and outcome will be less than early stages.

In conclusion primary GIT lymphoma has a wide range of clinical behavior. Multimodality treatment is recommended in most cases. Surgical resection is considered for patients amenable for surgery. Surgical treatment provides local control and allows for proper staging. Chemotherapy was given for most cases. Radiotherapy adopted for residual or unresectable disease. Eradication of H. Pylori has nowadays been proposed as the first line approach in low-grade lymphoma before conventional treatment especially gastrectomy. Results of treatment are comparable. The prognostic factors affecting overall survival are stage of the disease, curative resection, achievement of complete remission and gastric lymphoma which are statistically significant affecting outcome. Early diagnosis of the disease with multimodality treatment may lead to favourable prognosis in these patients.

REFERENCES

1. Low M, Williams S B, Wong J H: Role of surgery in the management of primary lymphoma of GIT. Journal of surgical oncology, 1996; 61:199-204.

2. Gossios K, Katsimbri P, Tsianos E: CT features of gastric lymphoma. Eur Radiol 2000; 10(3):425-30.

3. Pandey M, Wadhwa M K, Patel H P, et al: Malignant lymphoma of the GIT. Eur J Surg Oncol, 1999; 25(2):164-7.

4. Bouzourene H, Haefliger T, Delacretaz F, et al: The role of H. pylori in primary gastric MALT lymphoma. Histopathology, 1999; 34:118-123.

5. Talamonti M, Dewesl, Joehl R, et al: Gastrointestinal lymphoma, a case for primary surgical resection. Arch Surg, 1999; 125:972-977.

6. Rackner V, Thrilby R, Ryan J: Role of surgery in multimodality therapy for gastrointestinal lymphoma. Am J Surg 1999; 161:570-575.

7. Dwason JMP, Cornes J S, Morson B C: Primary malignant lymphoid tumours of the intestinal tract, report of 37 cases with a study of factors influencing prognosis. Br J Surg 1961; 49:80-89.

8. Lewin K J, Ranchod M, Dorfman R F: Lymphoma of the gastrointestinal tract. A study of 117 cases presenting with gastrointestinal disease. Cancer, 1978; 42:693-707.

9. Rosenberg S A: Validity of the Ann Arbor staging classification for the non-Hodgkin's lymphomas. Cancer Treat Rev, 1977;61:1023-1027.

10. The Non-Hodgkin's lymphoma: Pathologic classification project. National Cancer Institute sponsored study of classification of non-Hodgkin's lymphoma summary and description of a working formulation for clinical usage. Cancer, 1982; 49:2112-2135.

11. El-Bolkainy M N, Gad El-Mawla N, Magrath I: present report epidmiology, immunology and clinical studies on lymphomas and leukemias in Egypt, Published by NCI, Cairo University; 1994:p1.

12. Dragosics B, Bauer P, Radaszkiewicz T: Primary gastrointestinal non-Hodgkin's lymphoma; a retrospective clinico-pathological study of 190 cases. Cancer 1985,55:1060-1073.

13. Amer M H, El-Akkad S: Gastrointestinal lymphoma in adults; clinical features and management of 300 cases. Gastroenterology, 1994; 106(4):846-58.

14. Sanchez-Bueno F, Gracia-Marcello J A, Alonso J D, et al: Prognostic factors in primary gastrointestinal non-Hodgkin's lymphoma; a multivariate analysis of 76 cases. Eur J Surg 1998; 164(5):385-92.

15. Isaacson PG: Gastrointestinal lymphoma. Human Pathology, 1994; 25(10):1020-1028.

16. Ohashi S, Segawa K, Okamura S, et al: Clinicopathologic study of gastric mucosa associated lymphoid tissue lymphoma. Cancer, 2000; 88(10):2210-2219.

17. Mortin I G, Aldoori M I: Immunoproliferative small intestinal disease; Mediterranean lymphoma and alpha heavy chain disease. Br J Surg 1994; 81(1):20-4.

18. Chandran R R, Raz H, Chaturvedi H K: Primary gastrointestinal lymphoma; 30 year experience at the cancer institute, Madras, India. Journal of Surgical Oncology, 1995,60:41-49.

19. Economopoulas T, Alexopoulos C, Stathakis N, et al: Primary gastric lymphoma, the experience of a general hospital. Br J Cancer, 1985; 52:391-397.

20. Frazee RC, Roberts J: Gastric lymphoma treatment: medical versus surgical. Surg Clin North Am, 1992; 72:423-31.

21. Burgers J M H, Taal B G, Vantteerde P, et al: Treatment results of primary stage I and II non-Hodgkin's lymphoma of the stomach. Radiother Oncol, 1988, 11:319-25.

22. Schuder G, Hildebrandt U, Kreissler H D, et al: Role of endosonography in the surgical management of NHL of the stomach. Endoscopy Oct; 25(8):509-512.

23. Cattedra ES, Luca OC: Combined surgery and chemotherapy in primary gastric NHL. Leuc. Lymphoma, 1994; 14(5-6):483-489.

24. Tedeschi L, Romanell A, Dallavalle G, et al: Stages I & II non-Hodgkin's lymphoma of the gastrointestinal tract; Retrospective study analysis of 79 patients and review of the literature. J Clin-Gastroenterol, 1994; 18(2):99-104.

25. Taal B G, Buergers J M, Van H P, et al: The clinical spectrum and treatment of primary NHL of the stomach. Ann Oncol, 1993; 4(10):839-846.

26. Hernandez J A, Ribera J M, Oriol-A, et al: Primary gastrointestinal lymphomas; response to eradicative therapy and prognostic factors in 52 patients. Med Clin Barc 1998, 24;110(2):45-50.

27. Roher HD, Verreet PR, Wormer O, et al: Helicobacter pylori in the upper gastrointestinal tract: medical or surgical treatment of gastric lymphoma? Langenbecks Arch Surg 2000; 385(2):97-105

28. Hansen P B, Vogt K C, Skov R L, et al: Primary gastrointestinal NHL in adults; a population based clinical and histopathological study. J Intern Med; 1998 Jul; 244(1): 71-8.