

## Primary Gastric Lymphoma in North of Iraq (A Study of 34 cases in the surgical departments of Erbil and Mousl hospitals).

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### ABSTRACT:

#### BACKGROUND:

Primary Gastric Lymphoma is an uncommon malignancy among gastric malignancies. Histology of the Primary Gastric Lymphoma is varied and the extranodal marginal zone B-cells lymphoma is especially significant on account of its potential remission with antibiotic therapy.

#### OBJECTIVE:

To study the incidence, staging, clinical presentation, histological and management of Primary Gastric Lymphoma in the North of Iraq.

#### PATIENTS AND METHODS:

From January 1988 to February 2005, A total number of 534 patients operated as gastric tumors, 34 (4%) diagnosed as Primary Gastric Lymphoma. at the surgical departments of Erbil and Mousl teaching hospitals.

#### RESULTS:

Out of 34 Primary Gastric Lymphoma, 24 cases (70.5%) were located in the distal part of the stomach the most common cell type was B-cell type non-Hodgkin's lymphoma,.

Surgery was the main method of treatment and followed by chemotherapy and radiotherapy. Helicobacter pylori were isolated from all 34 Patients.

All patients received antibiotics for eradication for H. Pylori infection for 4-6 weeks.

Long-term remission were induced in the low-grade MALT lymphomas in 73% of cases by the successful eradication of the H. pylori infection Operative mortality rates was 12 %

#### CONCLUSION:

surgical intervention was confined to stage I&II while patients with stage III surgery was indicated mostly for complications like bleeding and perforation

Mucosa-associated lymphoid tissue tumor (MALT) had a better prognosis because it tends to be localized with a long survival period.

**KEY WORD:** gastric lymphoma, primary

### INTRODUCTION:

Primary gastric lymphoma (PGL) is the second most common primary tumor of the stomach<sup>1</sup>. PGL appear to be a rather common condition in countries of the Middle East including Iraq, and several papers had been published describing various aspects of this interesting tumor, <sup>(1, 2)</sup>.

Gastric lymphoma can occur as an isolated neoplasm confined to the stomach or it may be the manifestation of wide spread infiltrative disease involving lymphatic and other organ system<sup>(3)</sup>. The lesion may be present as a tumor mass or more commonly as thickening of the epithelial folds secondary to lymphocytic infiltration within the submucosa in the early stages of the disease<sup>(4)</sup>. Abdominal pain and weight losses are the most common presenting complaints. PGL merits special attention since most published reports

emphasize its favorable prognosis and better survival as compared with carcinoma of the stomach. At the time of diagnosis they tend to be large, may be multiple, and affect any part of the stomach although the prepyloric region is most commonly involved <sup>(8)</sup>. Like most alimentary lymphomata they ulcerate and some times perforate, <sup>(8, 9)</sup>. In the literature almost every aspect of this entity is controversial including its definition, neither the staging system nor the histologic classification were uniform and there are many types and subtypes with varying degree of malignancy.

The aim of this study is to study the incidence, staging, clinical presentation, histological subtypes and management of Primary Gastric Lymphoma in the North of Iraq (Mousl and Erbil governorates) and to compare endoscopic and endoscopic response assessment with results of

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histological evaluation in this region of the world in comparison to other similar studies done elsewhere, up to our knowledge this is the first study done in the north of Iraq.

### PATIENTS AND METHODS:

A retrospective study involving 34 patients with the diagnosis of PGL. The study was done in surgical department Erbil teaching hospital and Mousl teaching hospitals, between January 1988 and February 2005.

The data was registered in pre-prepared form and all patients were evaluated regarding the clinical symptoms and signs.

In addition to complete blood cell study and blood chemistry, radiological studies including, chest radiography, computerised axial tomography (CT) scanning, Barium contrast studies performed in suspicious cases which suggested a potentially malignant lesion in approximately 70% of the cases, oesophago-gastro-duodenoscopy (OGD) was performed for all the cases.

All patients underwent Endoscopic biopsy, and serological testing for antibodies against H pylori.

All patients underwent surgical exploration, and surgical excision had been the mainstay of treatment the aim of surgery was to excise the entire tumor with negative margins, but this goal balanced against the morbidity of the operation and the resulting quality of life.

In individuals with evidence of invasion and a definitive biopsy diagnosis by endoscopy and barium

contrast study, chemotherapy had been considered prior to surgery while in those patients with non-diagnostic biopsies; surgical exploration and resection were needed.

### RESULTS:

The results were analyzed as follows: a total of 34 patients with PGL, 24 (70.5%) were males and 10(29.5%) females, a sex ratio 2.4:1. Their ages ranged from 16 to 68 years, with a mean age of 39.5 years, 24 patients were under 40 years.

Physical examination was non-specific and most of them had more than one signs and symptoms (Table 1).

The duration of symptoms ranged from 2 to 26 months, with a mean of 13 months. The most common presenting symptoms were abdominal pain; weight loss was present in most of the patients (90.4%). Other important symptoms and signs are summarized in table 1.

Abdominal emergencies were seen in 8 patients [23.5 %] at presentation; exploration revealed 4 patients with perforation and generalized peritonitis, 2 patients presented with intestinal obstruction, and the other 2 with bleeding.

Table 1-Clinical signs and symptoms\*

Clinical presentation	No. of patients	Percentage %
1.weight loss	32	94.1
2. abdominal tenderness	30	88.2
3. abdominal pain	30	88.2
4. cachexia	20	58.8
5. anemia	18	52.9
6. nausea-vomiting	18	52.9
7. fever	16	40
8. raised ESR	16	47
9. abdominal mass	10	29.4
10.haematamesis	10	29.4
11. hepatomegaly	9	26.4
12. lymphadenopathy	9	26.4
13.diarrhea	8	23.5
14. melena	7	20.5
15. splenomegaly	2	5.8
16.jaundice	2	5.8

\* The overlap occurred in the No. of patents and percentage because most of the patients had more than one symptom and signs during their consultations.

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### Endoscopic and histological findings;

No specific pathognomic finding on endoscopy. The sensitivity of multiple endoscopic biopsies was 80% comparing with 100% open biopsies probably because of inadequate tissue obtaining and technical errors.

Histopathological Finding in 26 patients[ 76.4%] of diffuse large cell lymphoma ,and 4 patients with

diffuse small cell type [11.7 %] ,and 4 patients had diffuse lymphoplasmacytic infiltrative type of lymphoma [11.7 %].(figure 6,7). All the cases were of non-Hodgkin's lymphoma, 14 were poorly differentiated lymphocytic, 6 histiocytic and 14 mixed lymphomas. On microscopic examination there was little doubt as to their nature

**Table 2:Shows endoscopic findings**

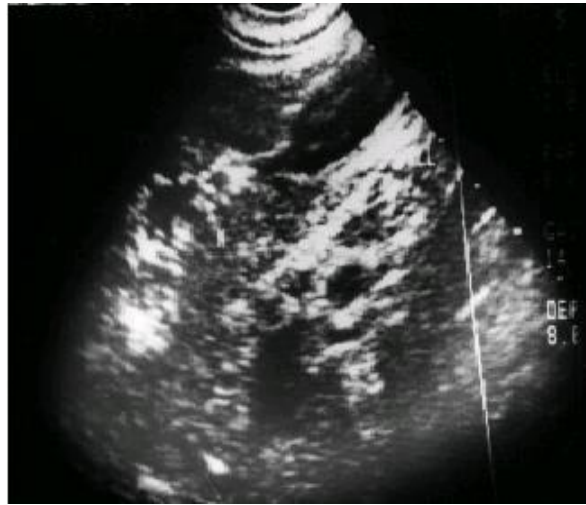
Endoscopic findings	No. of patients	Percent.
erosions and ulceration's	12	35.29
friability and patchy redness	10	29.41
Diffuse and atypical ulcerative lesions	6	17.64
narrow lumen and spot bleeding	4	11.76
Complete pyloric obstruction	2	5.88
total	34	100



**Figure 1–Malignant ulcerative type of primary gastric lymphoma (endoscopic view).**



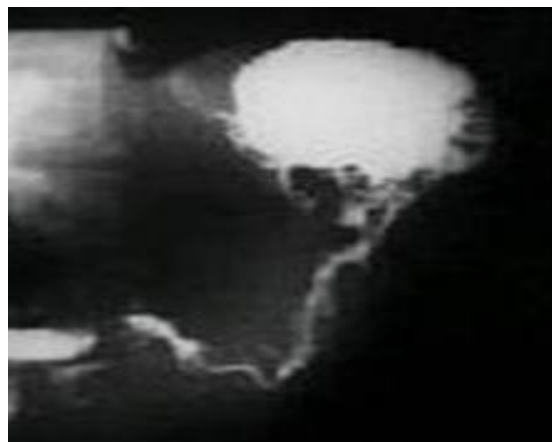
**Figure 2- primary gastric lymphoma of the distal half of the stomach showing narrowing rigid segment.**



**Figure 3. Sonogram of the fluid filled stomach showing an intraluminal mass with disruption of wall layering - lymphoma antrum.**



**Figure 4. Barium meal UGI of the same patient showing abrupt narrowing and shouldering in the antrum - lymphoma antrum.**



**Figure 5. Barium UGI showing decreased distensibility of the body with mucosal ulcerations.**



Figure 6: Ultrasound showing gross hypoechoic wall thickening with luminal narrowing in the region of the body. Serosa appears intact-lymphoma- body



Figure 7: Barium study of UG of the same patient showing decreased distensibility of the body with mucosal ulcerations.

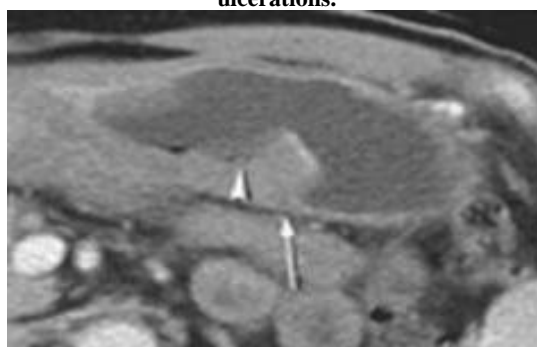
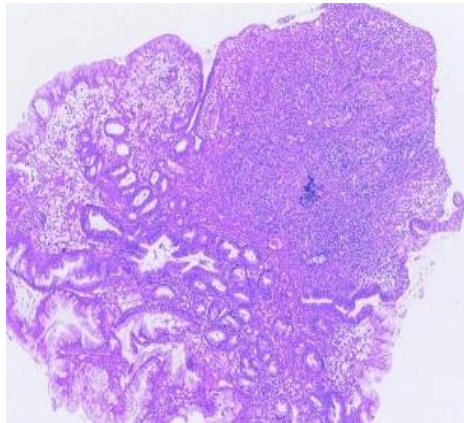
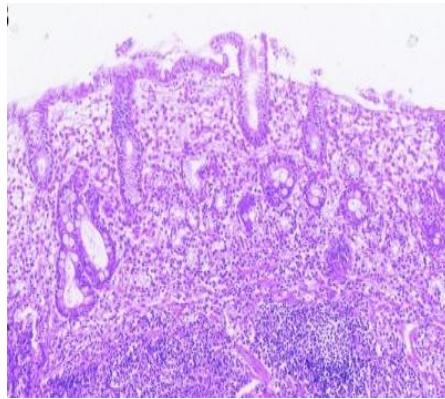


Figure 8: —46-year-old man with high-grade gastric mucosa-associated lymphoid tissue (MALT) lymphoma. Axial helical CT scan obtained through stomach shows segmental and moderate wall thickening (arrows) in gastric antrum. No normal mucosa is overlying lesion, and deep ulcer (arrowhead) is note



**Figure 9:** Endoscopic biopsy from a patient with primary gastric lymphoma. There is massive substitution of the gastric glands by a lymphoid infiltrate (right) and focal intestinal metaplasia of the epithelium (left) (hematoxylin-eosin, original magnification  $\times 50$ ).



**Figure 10** -High-grade mucosa-associated lymphoid tissue (MALT)-type lymphoma is observed (hematoxylin-eosin, original magnification  $\times 1000$ ). Tissue fragment



**Figure 11**-gross pathological appearance of a group of lymph nodes around the stomach in a patient with PGL.

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Staging classification was a modification of the Ann Arbor system used for Hodgkin's lymphoma (Table 2). This system was challenged at the Fifth International Conference on Malignant Lymphoma in 1993, and a new proposal has been done.<sup>14</sup>

**Table 3- Staging classification of primary gastric lymphoma<sup>10</sup>**

Stage	Definition
IE	lymphoma limited to the stomach
II E1	Involvement of stomach and contiguous lymph nodes
II E2	Involvement of stomach and sub-diaphragmatic lymph nodes
III	Involvement of stomach and lymph nodes ON both sides of diaphragmatic
IV	Hematogenous spread ( stomach and one or more extra lymphatic organs or tissues
The following subscripts may be added: E: Extranodal, S: Splenic, A: Asymptomatic S: Symptomatic.	

**Table 4 –Histological types of primary gastric lymphoma.**

Histology	No. of patients	Percentage %
Diffuse large cell type	26	76.47
Diffuse small cell type	4	11.76
Diffuse lymphoplasmacytic infiltrative type	4	11.76
Total	34	100 %

**Table 5 :Staging of [PGL] according to the Ann Arbor system**

No. of patients	Stage [Ann Arbor system]	Percentage %
8	IE <sup>1</sup>	23.5
18	II E <sup>2</sup>	52.9
8	III	23.5
Total 34		100%

<sup>1</sup>. Tumor localized to the stomach and regional lymph nodes free histologically.

<sup>2</sup>. Tumor in stomach with histological involvement of regional lymph nodes.

### DISCUSSION:

Among a total number of 534 patients operated on with primary gastric tumors, 34 patients (4 %) diagnosed as Primary Gastric Lymphoma (PGL).

The average age at diagnosis of PGL was 39 years, considerably younger comparing with the average age of the patients in four series reported from North America; the age is mainly between 55 and 60 years<sup>(7, 11)</sup>. The sex preponderance and other features of the disease which mentioned in this study were similar to those reported studies done by other workers in Japan and India<sup>(8, 12)</sup>.

The sensitivity of Endoscopic biopsy were varied because most of the lesions were submucosa, it was 80% compared with other similar reports by Maor et al, (88%) of 24 patients and Seifert et al (98.5%) of 34 patients<sup>(9,12,13)</sup>.

Barium meal on the other hand, was suggestive a potentially malignant lesion in approximately 75%

of cases, comparing with a similar study done in Japan which was 91 % accuracy<sup>14</sup>, the most common finding were enlarged configured gastric folds.

CT scan of the abdomen showed the extent of the lesion and ruled out other metastatic lesions, but it didn't differentiate reliably between metastatic lymphadenopathy and reactive lymphoid hyperplasia. In a report by Doyle and Dixon describing the CT features of 19 patients with primary gastric lymphoma showed the extent of the lesion in 17 patients (90%) comparing with this study only 25 patients (73%) showed the extent of the lesion<sup>(9, 11,14)</sup>, the most common and interesting findings in our study were clefts and tracks that have been suggested to be specific and peculiar to these lesions<sup>(14,15)</sup> were seen in nine scans(26.4%).

In this study other features of PGL was seen in 19

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cases (55.8), a diffuse wall thickening lymphadenopathy rugal prominence and intraluminal mass.

At operation most of the tumors grossly were indistinguishable from carcinoma in most cases, the cut sections was typically of fish-flesh appearance tended to be large, usually multiple, the prepyloric region was the most commonly involved (82.3%).

The tumor was localized to the stomach and regional lymph nodes in 24 cases, 14 in the antrum, 8 in the body, and 2 in the cardia. Involvement of stomach and lymph nodes ON both sides of diaphragmatic in 10 patients (23.5%).

Eight patients in stage IE and 4 patients in stage IIE underwent radical gastrectomy, the remains , 5 had partial palliative resections, 12 patients with locally advanced disease, distant metastasis underwent bypass operations, and 7 with poor general conditions had biopsy alone. In developed countries (East Europe) more than 75% of the patients underwent radical and partial gastrectomies because the tumor was diagnosed in its early stages<sup>(22)</sup>

Eight patients (23.5%) presented with acute abdominal complications in comparison with similar studies done in North America, Japan and Australia in which the acute abdominal presentation were 5%, 7%, and 6.5 respectively this deference in higher incidence of completions in our study probably because of late presentation of patients , late diagnosis and more aggressive nature of the tumor<sup>(21)</sup>. In this study 4 patients (11.7%) presented with perforation and generalized peritonitis, 2 patients (5.8%) with gastric outlet obstruction, and 2 patients (5.8%) with ulceration and bleeding.

All patients received eradication therapy for H pylori infection which was successful in 85% of patients while in 15% of patients no regressing occurred after eradication therapy within one year. In patients with disease advanced beyond the submucosa were treated additionally with chemotherapy and/or radiotherapy.

Endoscopic and open biopsy revealed that lymphomas that likely responded to the H. pylori eradication were those that are located superficially within the gastric mucosa in 83% of cases.

Stage of the disease and grade of the lesion were the most significant prognostic factors that consistently and independently influence outcome and survival in gastric lymphoma<sup>(15, 16, 17)</sup>. In our series most recurrences appeared locally and distally within 12 months of surgery and they had

received postoperative chemotherapy and/or radiotherapy in the form of cyclophosphamide-doxorubicin-vincristine-prednisolone

In our study 5-year survival rate in stage I and stage II lymphoma were 68 % and 28 %respectively while in low grade and high grade lymphoma were 54 % and 31 % respectively, comparing with other similar studies done in North America and Japan stage I stage II was 87-83% 36-32% respectively and for low grade and high grade was 78-69% 46-41% respectively<sup>(18,19)</sup>.

Regarding 5-year survival rate, with higher mortality in this study comparing with other similar studies done in North America and Japan<sup>(16, 17)</sup>.

These significant differences in higher mortality between this study and other similar studies in spite of younger patients in our series compared with elderly patients in other studies in the same stage of the disease might be related to late presentations of the patients, delay in the diagnosis and limited medical facilities in our locality.

The two-year remission were induced in the low-grade MALT lymphomas in this study was 73% of cases by the successful eradication of the H. pylori infection comparing with other similar study done in England and India which<sup>(20)</sup> was 86%,81% respectively .This remission induced because low-grade B-cell lymphomas of mucosa-associated lymphoid tissue (MALT) has a better prognosis because it tends to be localized for a long period of time.<sup>(21)</sup> This has been attributed to its homing phenomenon in which the neoplastic cell tends to return to its original mucosal site rather than disseminate elsewhere.<sup>(15,18)</sup>

Complete resections had five-year survival rates of 68 % while palliative resection or bypass and biopsy five-year survival rates of 4-6 % compared with a similar study done in South Africa with a 87% five-year survival rates with complete resections and 24% palliative resection or bypass and biopsy<sup>(19,21,23)</sup>.

Operative mortality rates was 12 % in comparison with studies done in Japan and North America ranged from 2.3% to 6 % for cases with radical resections because of late diagnosis and limited facilities in our locality, and were generally higher for palliative procedures which have traditionally been performed not only for symptomatic relief but to remove tumor mass and avoid hemorrhage or perforation<sup>(17, 18, 19, 24)</sup>. Follow-up of the patients ranged from 18 months to 7 years for 82% of patients.



### CONCLUSION:

North of Iraq is of higher prevalence for PGL 4% compared with 2.5% in Western countries and States and of less prevalence than Japan 7%, and the average age at diagnosis of PGL in our patients were younger in comparing with Western countries. *Helicobacter pylori* were isolated from all patients with PGL by endoscopic biopsy and serum agglutination testes.

Surgical excision was the mainstay of treatment for stage I and II, and complication of advanced cases. MALT-type lymphoma had a better prognosis than other types of PGL because it tends to be localized for a long period of time. This has been attributed to its homing phenomenon in which the neoplastic cell tends to return to its original mucosal site rather than disseminate elsewhere.

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