PRIMARY GASTRIC LYMPHOMA

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ABSTRACT

Primary gastric lymphoma is a rare gastrointestinal lymphoma. The treatment of this condition remains controversial, especially the extent of surgical resection. Ten cases were operated on over a five-year period at our institution and the outcome was reviewed. Early results suggest no difference in survival whether the margin of resection was clear or not so long as postoperative chemotherapy was given. The outcome appear to depend more on the extent of the disease at the time of surgery. Full thickness involvement of the stomach wall with lymph node involvement were bad prognostic indicators.

Keywords: primary gastric lymphoma, treatment, survival, surgery.

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INTRODUCTION

Lymphomas of the gastrointestinal tract are uncommon. The stomach is the most common organ involved, comprising about 50% of all cases. Taken as a whole, however, primary gastrointestinal lymphomas only make up 2-3% of all malignancies in the gastrointestinal tract (GIT).

Primary gastric lymphoma is defined as lymphomatous involvement of the stomach without any evidence of lymphomatous disease outside the stomach and its immediate vicinity. The diagnosis must be confirmed histologically[1]. It is important to differentiate between primary gastric lymphoma and late involvement of the stomach by lymphoma which has disseminated throughout the body. The latter, of course, holds a very grave prognosis and the eventual involvement of the GIT is a terminal event.

The role of surgery in this disease remains controversial, especially since potent chemotherapeutic agents are now available. The importance of clear margins and the extent of surgery remain unclear. This problem is compounded by the rarity of the disease, making controlled clinical trials impossible.

We have analysed the results of the 10 cases managed in our institution over the last five years. All case records were traced and the epidemiological data, treatment given, stage of the disease at the time of surgery and outcome were looked at.

RESULTS

There were 10 patients in all. Six of them were male and four were female. The age range was between 27 to 69 years. All of them were Chinese.

Epigastric pain was the most common symptom, this being the presenting complaint in 9 patients. One had an upper GI bleed as the predominant symptom. Fever was only present in one of them and loss of weight in two.

The diagnostic investigations were upper GI endoscopy and barium meal studies. All patients had their diagnosis made or at least suspected preoperatively.

The most common site of involvement was the gastric antrum, this being the case in eight of the patients (see Table II). One had predominant involvement of the lesser curve and the last had total gastric involvement.

At the time of the operation, there was no evidence of lymphomatous disease outside of the stomach or its immediate vicinity as ascertained by radiological studies and bone marrow examination.

Frozen section control for clearance of the margin of resection was not used at the time of the surgery, our pathologists being on the whole pessimistic about its value.

One patient did not have any resection performed as the tumour was too extensive. She only had a palliative gastrojejunostomy to obviate future obstruction of the pyloric outlet. Three had total gastrectomy and the rest[6] had subtotal gastrectomy (R_2 resection). One of the three who had total gastrectomy had extensive involvement of the stomach. The other two had total gastrectomy done because of the difficulty in determining freedom of tumour involvement of the resection margin at the time of surgery.

The resection margin was free of tumour involvement in six of the nine who had resection. Two had tumour at the resection margin and one did not show any evidence of tumour in the resected specimen, even though preoperative gastric biopsies were positive for lymphoma.

Three of the patients had advanced disease as evidenced by lymph node involvement. The rest had disease confined only to the stomach.

Eight of the patients were subjected to postoperative chemotherapy. Two were not: one because he refused chemotherapy and the other because no tumour could be found in the specimen. This was in the form of the CHOP (cyclophosphamide, adriamycin, vincristine, prednisolone) regimen. One of the eight had in addition a second course of MACOP-B (methotrexate, adriamycin, cyclophosphamide, vincristine, prednisolone, bleomycin) chemotherapy and another had postoperative irradiation as well. These two had advanced disease.

At the time of review, three of the patients were dead, two from their disease and one probably from an unrelated cause. The rest were still alive with no evidence of recurrence.

A summary of the clinico-pathological features, treatment and current status of the patients are presented in Tables I and II.

DISCUSSION

Malignant lymphoma of the gastrointestinal tract is the most common extranodal site of lymphoma, accounting for between 30-37% of such cases[2]. The stomach is the most common organ involved in the gastrointestinal tract, accounting for half of the cases. It is also the site showing the most favourable prognosis with a 40-59% five-year survival rate for palliative and curative resection. This contrasts sharply with a 21-26% five-year survival for gastric carcinoma after "curative resection"[3,4].

The main form of treatment for non-Hodgkin's gastric

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Table I - Epidemiological date - gastric lymphoma cases

Case	Age	Sex	Race	Presenting complaints	Diagnostic investigations	Site of tumour	Operation	Resection margin/LN	Adjuvant therapy	Status
1	65	F	C	Epi Pain Low	Upper GI Scope	Lesser Curve	G-J	No resection	CHOP-B DXT	Dead 7 mths
2	53	M	C	Bleeding GIT	Upper GI Scope	Antrum	STG	Free	CHOP 39 mths	Alive
3	27	F	C	Epi Pain	Upper GI Scope	Whole Stomach	TG	Free/LN involved	CHOP MACOP-B 17 mths	Dead
4	59	M	C	Epi Pain	Ba meal Up GI scope	Antrum	STG	Involved LN free	CHOP 31 mths	Alive
5	69	M	C	Epi Pain	Ba meal Up GI scope	Antrum	STG	Involved LN free	CHOP 23 mths	Alive
6	56	F	C	Epi Pain Fever	Ba meal	Antrum	STG	Free/LN free	CHOP	Alive 22 mths
7	57	M	C	Epi Pain	Upper GI Scope	Antrum	TG	Free/LN involved	CHOP	Alive 20 mths
8	59	F	C	Epi Pain	Ba meal Up GI scope	Antrum	TG	Free/LN free	CHOP	Alive 15 mths
9	63	M	C	Epi Pain Low	Upper GI Scope	Antrum	STG	Free/LN free	one	Dead 15 mths (cause not related to disease)
10	36	M	C	Epi Pain	Upper GI Scope	Antrum	STG	No tumour in spec	one	Alive 8 mths

G-J : gastrojejunostomy
STG : subtotal gastrectomy
TG : total gastrectomy
CHOP : cyclophosphamide, adriamycin, vincristine, prednisolone.
DXT : Radiotherapy
LN : Lymph node
MACOP-B : methotrexate, adriamycin, cyclophosphamide, vincristine, prednisolone, bleomycin.

Table II - Pathological features - gastric lymphoma

Case	Operation	Size of lesion	Cell type	Depth of penetration	Lymph Node involvement	Grade	Survival
1	G-J	"large"	B-cell	Through serosa	Distant	High	Dead 7 mths
2	STG	Unknown	B-cell	Submucosa	None	Low	Alive 39 mths
3	TG	Whole stomach	B-cell	Through serosa	Distant	High	Dead 17 mths
4	STG	4.2cm	B-cell	Submucosa	None	Inter	Alive 31 mths
5	STG	2 cm	T-cell	Submucosa	None	Inter	Alive 23 mths
6	STG	2.5cm	B-cell	Muscle	None	High	Alive 22 mths
7	TG	5cm	T-cell	Unknown	Perigastric	Inter	Alive 20 mths
8	TG	3cm	B-cell	Submucosa	None	Inter	Alive 15 mths
9	STG	5cm	B-cell	Muscle	None	Unknown	Dead 15 mths (cause not related to disease)
10	STG	1cm	Unknown	Submucosa	None	Unknown	Alive 8 mths

GJ : gastro-jejunostomy
STG : sub-total gastrectomy
TG : total gastrectomy

lymphomas before the advent of chemotherapy was gastric resection[5-7]. The importance of resection was underlined by the increased incidence of gastric bleeding and perforation that occurred when radiotherapy was used as the primary form of treatment[3,8]. With the advent of potent chemotherapeutic drugs, these two complications remain worrisome and most clinicians still subject their patients to surgical resection first before using chemotherapy on them.

Most people favour subtotal gastrectomy as opposed to total gastrectomy with its higher morbidity[9,10]. Proponents of total gastrectomy argue that present day anaesthesia and technical capability have rendered total gastrectomy as safe as subtotal resection. They also highlight the point that resection with clear margins render unnecessary postoperative chemotherapy with all its attendant morbidity and side effects. Crucial to the debate is the importance of clear margins. With potent chemotherapy and the responsiveness of the tumour to these drugs, the importance of clear margins has decreased significantly[11]. There has been no studies however that has managed to elucidate this point. Part of the problem has been the difficulty with numbers, this being a rare tumour. Another difficulty has been that frozen section has not always been able to confirm the presence or absence of tumour cells at the margins.

Although two of our patients have involvement of the margins, they are still alive (23 months, 31 months) after surgery. Part of the reason for this may be that they have early disease as evidenced by the fact that the lymph nodes were free of tumour. Chemotherapy also probably helped.

It would appear from our short follow-up that clear margins microscopically, although desirable, are not absolutely necessary. If the tumour is removable macroscopically by a subtotal gastrectomy, then a subtotal resection should be performed. If not, a total gastrectomy is necessary.

Of much more importance than involvement or noninvolvement of the resection margin to overall survival is the stage of the disease at the time of surgery[12-14](Table III). Jones et al in their series showed the survival to be longest in those with lymphoma confined to the gastric wall alone (Stage IA & IB)[15]. These patients have a median survival of 32 months. Those where the tumour has penetrated through to the serosa (Stage IC) have a median survival of 18 months. Stage II patients are those with perigastric lymph node involvement. These have a median survival of 22 months. Patients with Stage III disease with distant lymph node involvement survived 8 months.

Table III - Staging of gastric lymphomas[2]

Stage I	Disease confined to the stomach A - disease limited to the mucosa B - disease with submucosal penetration C - disease with serosal penetration
Stage II	Tumours with any degree of tumour penetration and with perigastric lymph nodes in the immediate vicinity of the primary tumour.
Stage III	Tumours with any degree of tumour penetration and nodes at a distance from the primary tumour or both curvatures of the stomach without distant metastasis.
Stage IV	Distant metastasis including spleen and liver.

In our series, the two deaths due to disease have been in the two patients with the most extensive disease. Both would be classified under Stage III. One died 7 months after diagnosis and the other 17 months after surgery. Postoperative DXT and chemotherapy did not make any difference. We suspect that the extent of surgery would not make any difference either.

Current treatment recommendations for primary gastric lymphoma depend on adequate preoperative diagnosis and staging. This would include an upper gastrointestinal endoscopy with biopsy, abdominal CT-scanning, and bone marrow biopsy[16].

The following guidelines to management may be offered in the light of current literature[17]:

1. Tumours confined to the gastric mucosa and submucosa seldom relapse and may be managed by gastric resection alone.
2. Tumours with deeper penetration but not involving the serosa have a tendency to relapse and adjuvant therapy deserves consideration.
3. Where the tumour has invaded the serosa, is large ie more than 7 cm or is associated with nodal disease, the risk of relapse is high after resection and adjuvant therapy is definitely indicated.
4. Stage III and Stage IV disease should have as the principal modality of treatment, systemic chemotherapy with radiation therapy as an adjunct for local control of bulky disease.

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