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The treatment of primary gastric lymphoma - Role of Surgery -

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Introduction

Primary lymphoma of the gastrointestinal tract seems to be a clinicopathologically distinct entity and can be divided from nodal lymphomas both by its clinical behavior and its morphology. The stomach is the most common site of primary extranodal lymphoma. Primary gastric lymphoma present between 5 and 11% of all gastric malignancies in Europe (1), but in Japan the incidence is 1-2%, and the incidence of the primary gastric lymphoma increased recently. The conception and classification of the malignant lymphoma of the gastrointestinal tract are changed. Because of these reasons, the strategy for the primary gastric lymphoma is controversial. Whereas treatment strategies in nodal non-Hodgkin lymphoma are well established, there is much debate and controversy regarding the optimal approach in gastric lymphoma. Without larger prospective studies, treatment philosophies are mostly bases on retrospective analyses with only small patient numbers or studies conducted over periods of two decades or more. Gastrectomy usually is considered an essential component of multimodal treatment. However, completely non surgical treatment strategies have now been proposed even for early stage disease and for low-grade mucosa associated lymphoid tissue (MALT)-derived lymphoma. A late occurring systemic metastization and relatively slow growth lead to the possibility of radical resection of most of these lymphomas. Additional chemotherapy or radiotherapy may improve survival and diminish recurrence rates in patients with a later stage of the disease.

In this study we present the clinicopathological data of patients with primary gastric lymphoma.

Methodology

From 1973 to 1997, we treated 57 patients with primary gastric lymphoma. We performed gastrectomy for 48 patients. The General Rules for Gastric Cancer Study (11th edition) and Ann-Arbor's classification were used for staging of primary gastric lymphoma. Chemotherapy regimen changed during the long period of time.

Survival curves were drawn by the Kaplan-Maeier method, and the difference between curves was evaluated by the generalized Wilcoxon's test.

Results

The mean age was 58 years(range 27-93), with a slight predominant of males(36 : 21). In 15 patients, the depth of infiltration limited to the mucosa and submucosa(T1) . T2 (muscularis propria and subserosal layer) was observed in 13 patients and serosal invasion was observed in 13 patients. The invasion to adjacent viscera was confirmed in 7 patients histopathologically.

The incidence of pathologically confirmed regional nodal metastasis was 26 of 48 patients with gastrectomy. The correlation between depth of infiltration and nodal metastasis was significance($p<0.01$)(Table1). The 5-year survival curves according to the Japanese rule and Ann-Arbor's classification were shown in Fig.1,2. The Ann Arbor stage I_E cases had a better survival than did stage II_E cases, and stage II_E had a better than III_E. The difference was statistically significant, respectively (Fig1). Stage classification according to the Japanese Classification of

Table 1. Correlation between the depth invasion and lymph node metastasis

Depth of invasion	Lymph node metastasis Negative	Positive	
T1	25% (n=12)	6% (n= 3)	15
T2	10 (5)	17 (8)	13
T3	4 (2)	23 (11)	13
T4	6 (3)	8 (4)	7
Total	22	26	48

$p < 0.01$

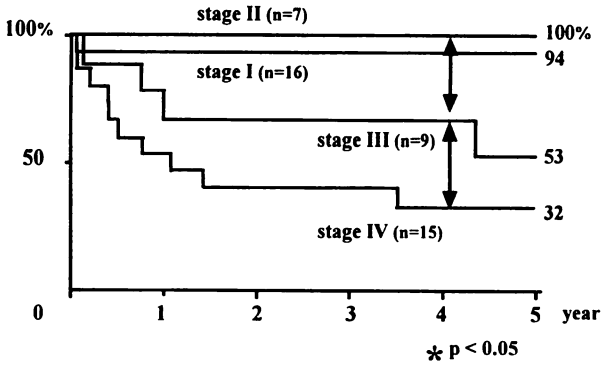

Figure 1. Survival curves according to the Japanes Rule for Gastric Cancer

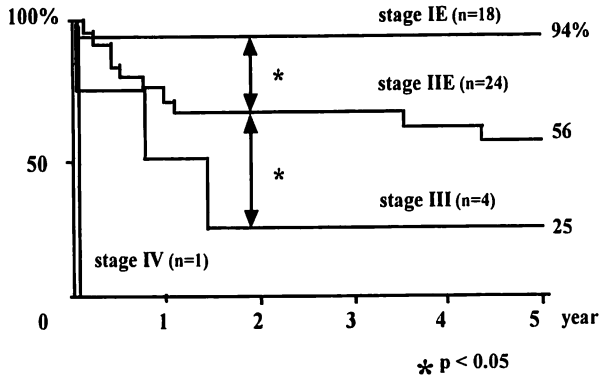

Figure 2. Survival curvs according to Ann-Arbor Classification

Gastric Carcinoma was also good indicator of prognosis.

The survival rate was almost same between stage I and II (Fig 2).

In 33 patients we performed total gastrectomy and 15 patients with localized lower body or antrum were treated by anterctomy and was considered the treatment of choice when total gastrectomy was considered when total gastrectomy was unnecessary by pre- and intraoperative criteria.

23 patients received postoperative chemotherapy

Discussion

Many authors recommend surgical resection as the first step of a multimodal treatment[1,2], other prefer chemotherapy and/or radiotherapy alone[3].

Surgical resection is generally considered to have a definitive role in the treatment of primary gastric lymphoma[1,4]. Arguments for surgery is the possibility of definite cure in early stages after radical resection, the exactness of intraoperative staging and the prevention of chemotherapy and radiotherapy related complications such as tumor perforation or bleeding[5].

The advantage of avoiding gastrectomy and sparing the stomach, however, must be balanced carefully against the toxicity of aggressive chemotherapy and the risk of emergency surgery for iatrogenic complications[6,7].

In spite of improved diagnostic tools including CT-scan and endoscopic ultrasound pretherapeutic staging of primary gastric lymphoma remains a problem without operative exploration. Preoperative misdiagnosis of gastric carcinoma is still common and often leads to operations in patients of any stage of lymphoma[3].

The incidence of treatment-related death secondary to the aggressiveness of the regimen; induction of secondary malignancies, such as acute non-lymphocytic leukemia and bladder cancer, also has been documented. The advantage of radiation therapy as an adjuvant to surgery has been refuted or remains unproven.

Arguments for primary conservative treatment is a low incidence of complications or side-effects after chemotherapy and the possibility of stomach conservation as the main argument[3].

The therapeutic benefits of radical gastrectomy have not been fully elucidated in the treatment of primary gastric lymphoma.

Though treatment strategies of gastric lymphoma are a subject of controversy, resection of lymph node might be beneficial for patients with gastric lymphoma in the most recent publication[8] for the following reasons. First, the incidence of nodal metastasis was high. Second, gastric lymphoma is not commonly associated with peritoneal dissemination. The 5-year survival rate for stage II_E gastric lymphoma actually exceeded 56%.

Nevertheless additional chemotherapy plays and important role in post operative treatment. Especially after palliative resections a prolonged survival could be demonstrated[9].

Chemotherapy is mandatory in stage III and IV disease, surgery should be confined to treatment of complications, residual tumor after initial chemotherapy or palliative treatment of non-responders to chemotherapy or radiotherapy.

Many of these patients will require total gastrectomy to achieve tumor-free resection margins, but patients with localized distal lymphoma of the stomach can be treated with subtotal gastric resection.

The TNM staging system and the Japanese Classification of Gastric carcinoma include data regarding both of invasion and nodal status, and the TNM system for primary gastric lymphoma. In our study, the Japanese classification discerned a significant difference in survival between stage I,II and III.

New aspects of tumor biology of intestinal Non-Hodgikin lymphoma have been demonstrated by Isaacson, who postulated the development of gastric lymphoma from mucosa associated lymphoid tissue (MALT- lymphoma) [10]. The next step was the proof of an infection of Helicobacter pylori in many of these cases, which is now thought to be a causal factor of MALT-lymphoma[11].

Several institutions have recently reported that grading according to the histopathologic concept of MALT has great prognostic relevance for primary gastric lymphoma.

The presence of minute elements of high-grade component could easily be missed by endoscopic biopsy, and the diagnosis of MALT lymphoma by serial endoscopic biopsies can be misleading. Final histopathologic diagnosis was obtained by careful scrutiny of surgically resected specimens. Surgery, therefore, is beneficial not only as a staging tool, but also for obtaining accurate pathologic diagnoses.

In conclusion we recommend surgical exploration and radical resection including lymphadenectomy for malignant lymphoma stages I_E and II_E.

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