

Primary Gastric Lymphoma: A Review of 45 Cases

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Abstract—Primary gastric lymphoma accounts for about 2% of gastric neoplasms. The prognosis of patients affected with non-Hodgkin's gastric lymphoma appears better than for other lymphatic sites.

In a retrospective study, the authors have analyzed 45 patients, by evaluating the histopathologic characteristics and relative prognostic factors.

The main factors significantly influencing 5-yr survival are: serosal penetration (31.17% vs. 71.2%, $P < 0.05$), regional lymph node involvement (53.07% vs. 68%), and clinical stage of disease (I_E: 85.6%, IV_E: 10%, $P < 0.001$). The histologic characteristics, the high or low grade of malignancy, and patient age can also be considered important prognostic factors, but not statistically significant in our series of cases.

Comparison between overall survival and disease-free survival of patients in stages I_E and II_E who underwent surgery alone, with those who had chemotherapy and/or radiotherapy after surgery shows a higher survival (85.6%) of the group who had combined treatments, even though this difference is not statistically significant.

INTRODUCTION

NON-HODGKIN'S lymphomas (NHL) tend to originate in extra-nodal sites (ca. 20% of the cases) more than Hodgkin's lymphomas do. The extra-nodal site most frequently involved is the gastrointestinal (GI) tract (9% of the cases) with preferential location in the stomach [1-5].

The overall survival (OS) of patients treated for primary NHL of the stomach appears slightly higher than that indicated for other sites, independent of the stage of disease, with a percentage of patients with 5-yr disease-free survival (DFS) from diagnosis ranging from 40 to 60% [6-8].

Numerous factors with different prognostic significance are reported in the various case studies. Patient age, along with regional location of the neoplasm, serosal penetration and various degrees of nodal involvement which determine the stage of the disease, seem to be the main factors that have a significant influence on survival [1-4].

As far as histology is concerned, the unfavorable prognostic significance of high grades of malignancy seems to be confirmed also for primary gastric NHLs [9-11].

Besides surgery, the therapeutic-linked prognostic factors that assume greater importance are radiation therapy (size and number of fields, and dose), and chemotherapy [8, 12].

The aim of this study was to verify the role of the major prognostic factors in determining OS and DFS in a homogeneous series of NHL patients.

MATERIALS AND METHODS

The hospital records and histo-pathologic data of all patients treated for primary gastric NHL from 1973 to 1984 at the Oncology Departments of the city hospitals of Forlì and Ravenna were examined.

Forty-eight consecutive cases of PGL were retrospectively considered: 34 cases from the Forlì Oncology Dept. and 14 from the Ravenna Oncology Dept.

All the histological slides at the two institutions were reviewed by a single pathologist (G.G.) and reclassified according to Kiel's system [10]. The correlation between the Kiel and the modified Rappaport classification has been described at length in previous papers [3, 13].

Three cases were excluded at histologic review: two pseudo-lymphomas of the stomach and one undifferentiated gastric carcinoma. These patients had been treated with surgery alone.

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Pathologic staging, following the Ann Arbor criteria, was determined by evaluating the data from the hospital records of each patient. Staging examinations included bone-marrow biopsy for most of the patients, and lymphangiography only for part of them (50%). All patients underwent exploratory laparotomy with multiple abdominal biopsies, and radical surgery when possible.

Statistical analysis of the data was carried out on an Olivetti P 6066 computer and the actuarial survival life tables were constructed following the recommendations of the American Joint Committee for Cancer Staging and End Results Reporting. The OS and DFS curves were compared using statistical significance tests [14].

No patient was lost to follow-up, so that 45 patients were eligible for the study.

RESULTS

The median age of patients in the series was 62 yr (range 26–80) and most of the patients were in the 60–70 age group. The M/F ratio was equal to one.

Twenty-two patients were classified at pathologic stage I_E, 13 at stage II_E and 10 at stages III_E and IV_E. The patient characteristics and the TNM classification according to U.I.C.C. are reported in Table 1. The histologic classification following Kiel's criteria is illustrated in Table 2.

The ratio between high and low grade malignancy was 1:1.5. The most frequently represented histologic types were the centroblastic/centrocytic (33%), immunoblastic (31%), followed by centrocytic (22%), centroblastic (9%) and lymphoplasmacytoid (5%).

The region most involved was the pyloric antrum (*ca.* 48%), followed by the body and the fundus.

The symptoms most frequently reported were pain (21 patients), weight loss (16 patients) and dyspepsia (12 patients). Preoperative instrumental and biopsy diagnosis of gastric lymphoma was possible only in 21% of cases. In 65% of patients, the histologic diagnosis of the biopsy was unspecified malignant tumor. GI X-ray led to the diagnosis of a gastric neoplasm in 60% of the cases, and a suspected lymphoma in only 2–3%.

Thirty-seven patients (82%) underwent radical surgery, 13 of which had total gastrectomy and 24 partial gastrectomy. Of the remaining patients, 4 underwent debulking of the neoplastic gastric mass, and 4 exploratory laparotomy with multiple abdominal biopsies. Over the course of the years, due to developments in the knowledge and treatment of NHL, the strategy used was not always uniform at equal stages. Radical surgery was always performed in all patients for whom it was possible.

Table 1. Primary gastric lymphomas: clinical data

Number of patients	45
Sex M : F	1 : 1
Age (yr)	
Average	58.5
Median	62
Range	26–80
Stage (no. of cases)	
I _E	22
II _E	13
III _E –IV _E	10
pT ₁ –pT ₂	18
pT ₃	16
pT ₄	11
pN ₀	23
pN ₊	22

Table 2. Histological classification

Morphology	LG	HG
Centroblastic/Centrocytic	15 (33%)	
Centrocytic	10 (22%)	
Lymphoplasmacytoid	2 (5%)	
Immunoblastic		14 (31%)
Centroblastic		4 (9%)
	27 (60%)	18 (40%)

LG = Low grade; HG = High grade.

In stage I_E and II_E patients chemo- or radiotherapy was combined with surgery in 50% of cases, while in stage III_E and IV_E patients chemotherapy and/or irradiation was the first-line therapy.

Abdominal irradiation was performed with a Cobalt Unit. The treatment volume extended from the domes of the diaphragm to the lower border of the pubis and laterally to include the abdominal walls, with opposite open portals both treated each day.

A total dose of 30 Gy was given with daily fraction of 1.25 Gy, shielding the kidneys posteriorly from the beginning and the liver up to 18–20 Gy. Thereafter a boost of 6–10 Gy was delivered to the tumor volume. The chemotherapy protocol most widely used was CVP or COP [15].

In stages I_E and II_E 10 patients received chemotherapy and two patients received radiotherapy after surgery, while three patients received both radiotherapy and chemotherapy.

All the data concerning survival were calculated to 31 December 1984. On that date 27 patients were alive with median survival of 36 months (range 4–56), and 22 of them showed complete clinical remission.

There were 18 deceased patients, with a median

survival of 12.5 months (range 1–120). It should be pointed out, however, that 4 out of these 18 patients died of causes not closely related to the lymphoma: 1 patient died due to postoperative complications, 1 of another histologically proven second neoplasm, and 2 cardiovascular disease.

Five-year OS calculated with the Kaplan–Meier actuarial method was 61.9% (S.E.: 8.3), and the 5-year DFS was 57.3% (S.E.: 8.1) (Fig. 1). By evaluating the influence of the stage of the tumor (Fig. 2), it can be observed that 5-year OS at stage I_E is equal to 85.6% (S.E.: 7.7), and DFS at the same interval is 81.8% (S.E.: 8.2). OS at stage II_E appears slightly lower, equal to 60.4% (S.E.: 16.7), with DFS at 54.78% (S.E.: 16.1). Stages III_E and IV_E present extremely low OS and DFS, equal to 12.2% (S.E.: 11.4) and 10% (S.E.: 9.5) respectively. Calculation of the statistical difference relative to survival between Stages I_E–II_E and

stages III_E–IV_E turned out to be highly significant ($P < 0.001$).

By subdividing the group of patients under study on the basis of serosal penetration (S+ = 11 cases, S- = 34 cases), we observed an OS of 71.2% in the S- cases and 31.17% in the S+ cases, with a statistically significant difference ($P < 0.05$).

Patients with positive nodes (22 cases) and negative nodes (23 cases) had an OS of 53.07% and 68% respectively.

This difference does not reach statistically significant values ($P = \text{N.S.}$).

By subdividing the patients according to grade of histologic malignancy, significant differences in the OS were not observed between high (18 cases) and low grade malignancy (27 cases). Low grade malignancy, however, presented higher OS percentages with respect to high grade (65.8% vs. 58.3%).

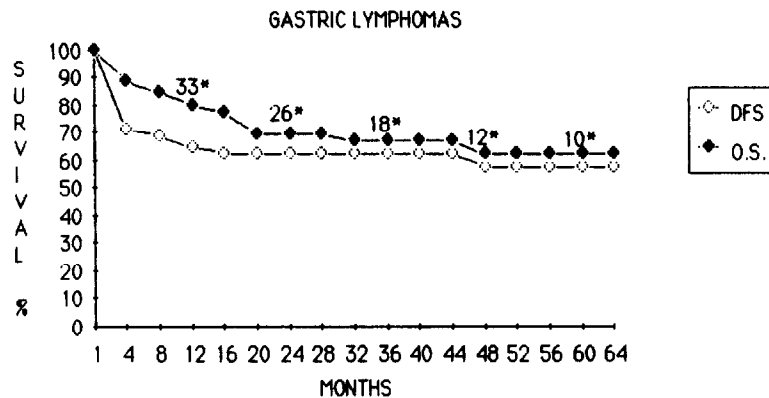


Fig. 1. Overall survival (O.S.) and disease-free survival (DFS) of all cases. *Number of patients at risk.

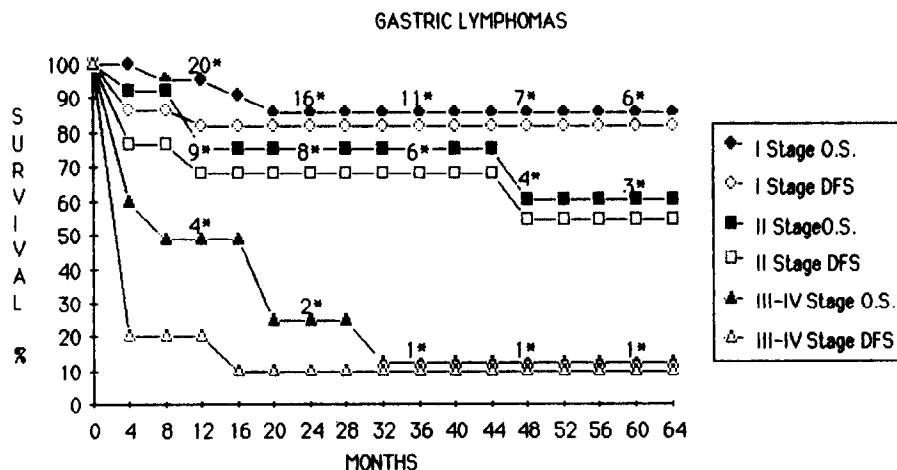


Fig. 2. Overall survival (O.S.) and disease-free survival (DFS) in stage I, II, and III–IV. *Number of patients at risk.

According to our data, the age of the patients seems to influence the prognosis. Patients over the age of 65 showed a 5-yr OS equal to 49.2% vs. 72.22% of the patients under age 65, but the difference does not reach statistical significance.

Thirty-seven patients underwent radical surgery, but the extent of the resection did not influence survival. The status of the resection margins (M₊) was positive in only a limited number of cases (6 patients in stages I_E and II_E) and it was not possible to draw significant conclusions.

By comparing OS and DFS of the patients in stage I_E and II_E who had surgery alone with those who underwent combined therapy (surgery + chemotherapy and/or radiotherapy), it was found that the patients who had combination treatment (18 cases) showed an 80.7% OS, while those patients treated with surgery alone (16 cases) showed a 60.7% OS ($P = \text{N.S.}$).

These results were also obtained in the patients in stages I_E and II_E with the unfavorable S₊ and N₊ prognostic factors.

The examination of relapse-patterns (local and/or distant) shows that the failures observed were mostly distant ones, both in patients who underwent surgery alone and in those who had combination treatment.

DISCUSSION

Other authors, who examined the various prognostic factors in primary gastric NHL, concurred in evaluating how serosal penetration of the lymphoma, involvement of the regional lymph nodes, a high or low grade of histologic malignancy, the location of the neoplasm within the gastric regions (pyloric antrum, fundus, body) and the age of the patient (under or over 65 yr) can have a negative influence on the prognosis [4, 8].

Examination of our series (45 cases) has made it possible to point out that serosal penetration of

the lymphoma is a statistically significant negative prognostic factor in our group of patients too.

The age of the patients (> 65 yr), the regional lymph node involvement and the high grade of histologic malignancy are negative prognostic factors in stages I_E and II_E. The difference between the various groups compared for OS and DFS, however, does not reach statistically significant values. The stage of the disease at diagnosis (I_E+II_E and III_E+IV_E) does, on the other hand, represent a highly significant prognostic factor ($P < 0.001$).

Patients in stage I_E had the highest 5-yr survival rate (85.6%) and a high survival rate (72%) was obtained with surgery alone. The role of radiotherapy and/or chemotherapy, also with regard to negative prognostic factors (S₊, M₊), is still to be determined.

Patients in stage II_E should preferably be treated with combination treatment, even though the best treatment for this group needs further study.

In the literature [13] the group with involvement of surgical margins, serosal penetration, and involvement of a high number of regional lymph nodes has been codified as a more unfavorable prognostic subgroup (5-yr OS = 25–38%). In this subgroup irradiation and chemotherapy seem to enhance the probability of survival.

In short, neither the doses and techniques of radiotherapy nor the chemotherapy regimens have been definitively standardized.

The natural history of PGL in stages III_E and IV_E is well known. Consequently, the treatment strategies we followed were the generally accepted ones. In pathologic stages I_E and II_E PGL, however, prospective controlled studies are necessary to define the role of radiotherapy and chemotherapy. The prognostic parameters discussed above must be the basis for stratification in designing these studies.

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