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Invited Lecture

Primary gastric lymphoma of B-cell phenotype with special reference to low-grade B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) in Japan

Taizan SUCHI[1],
Kayoko AKAZA[2], Tadashi MOTOORI [3], Shigeo NAKAMURA [1],
Takashi KOSHIKAWA[1], Kuniyoshi KITOH[1], and Masaru KOJIMA[4]

[1]Department of Pathology and Clinical Laboratories, Aichi Cancer Center Hospital, Nagoya, Japan
[2]Department of Pathology, Fujita Health University, School of Medicine, Aichi, Japan
[3]Department of Pathology, Kitasato Institute Medical Center Hospital, Saitama, Japan
[4]Department of Pathology and Clinical Laboratories, Ashikaga Red Cross Hospital, Ashikaga, Japan

Abstract

Resection specimens from 83 patients with primary gastric lymphoma (PGL) of B-cell phenotype at Stage I_E and stage II_E according to the Ann Arbor classification were investigated. Histologically, these lymphomas could be divided into four types; Type I lesions (n=24) were entirely made up of MALT lymphoma, Type II lesions (n=13) were predominantly MALT lymphoma containing one to a few foci of high-grade B-cell lymphoma, Type III lesions (n=22) consisted largely of high-grade lymphoma with small areas of low-grade MALT lymphoma, and Type IV lesions (n=24) were of pure high-grade B-cell lymphoma mostly in the form of large cell type. All patients underwent primary gastric resection, and 14 received additional chemotherapy (n=12) or both chemotherapy and radiotherapy (n=2). The survival rate was significantly higher for Type I and II lymphomas than for Type III and IV tumors ($P<0.05$ by the generalized Wilcoxon test). The stages of disease according to the general rules for the gastric cancer study by Japanese Research Society for Gastric Cancer showed clearer distinction between each of them ($P<0.01$ by the generalized Wilcoxon test). This staging method seemed to serve well as a prognostic indicator. The histological typing of the PGL of the present series also seemed to correlate with the gross appearance, pathologic stage and prognosis.

Furthermore, the expression of cyclin D1, bcl-2 and p53 protein was immunohistochemically investigated in 42 cases of the present series. In a study for cyclin D1 protein, no cases showed the nuclear staining pattern characteristic for mantle cell lymphoma, and cytoplasmic staining frequently observed in the node-based large B-cell lymphoma was seldom identified in the PGLs. This discrepancy might suggest the lineage difference among the morphologically similar, but site-different, lymphomas. On the other hand, the bcl-2 protein overexpression was almost equal in frequency between the gastric and node-based high-grade B-cell lymphomas. This is in contrast to the reports from the western countries, in which the majority of gastric high-grade tumor was bcl-2 negative.

Key words: Primary gastric lymphoma, MALT-lymphoma, prognosis, cyclin D1, bcl-2, p53.

Introduction

The stomach is the most common site of primary extranodal lymphomas in Japan except for the Waldeyer's ring which is also extranodal, but not extralymphatic.[1-14] With the progression of diagnostic methods in gastroenterology, the number of primary gastric non-Hodgkin's lymphomas resected in their early stage is increasing, as in the case of gastric adenocarcinoma.[15-17] These so-called early lymphomas, i.e., lymphomas confined to mucosa and submu-

Address for Correspondence: Taizan SUCHI, Department of Pathology and Clinical Laboratories, Aichi Cancer Center Hospital, Kanokoden, Chikusa-ku, Nagoya 464, Japan.

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cosa, are curable by radical resection in localized stages, and frequently have a distinct morphology. In 1984, Isaacson and Wright[18,19] introduced a new concept of extranodal malignant lymphoma arising from mucosa-associated lymphoid tissue (MALT) in the stomach, salivary gland, lung, thyroid gland etc. Ever since, morphological, immunohistochemical, and genetic studies on gastrointestinal lymphomas have given special consideration to the MALT concept,[13,14,20-38] indicating the essential difference between extranodal and nodal lymphomas.[39-41] This is especially represented in the diagnosis of the "low-grade B-cell lymhphoma of MALT type", which is the most frequent type in the early gastric lymphomas.[14] However, the relationship of low-grade B-cell lymphomas of MALT type with the more commonly occurring large B-cell lymphoma of the stomach has been discussed only in a few reports, and the information regarding their clinical and prognostic significance is limited.[11,13,28,42]

To elucidate their relationship, we studied in detail the clinicopathologic features and surval of 83 cases of primary gastric non-Hodgkin's lymphomas (PGLs) of B-cell type. Diagnoses were established on gastrectomy specimens of PGLs at stage I_E and II_E according to the Ann Arbor classification as modified by Musshoff.[43,44] Lymphomas at stage III and IV were excluded because of uncetainty in establishing the stomach as the primary site.

Materials and Methods

Incidence

In Aichi Cancer Center Hospital (ACCH), 4794 cases of gastric carcinoma were resected during the period from 1965 to 1992, while only 96 cases of gastric lymphomas were removed during the same period of time,accounting for about 2% of all gastric malignancies (Table 1). This low rate is likely a reflection of the high incidence of carcinoma in Japanese population. The number of the resected cases for gastric lymphoma in ACCH, however, has been increasing lately (Fig. 1),

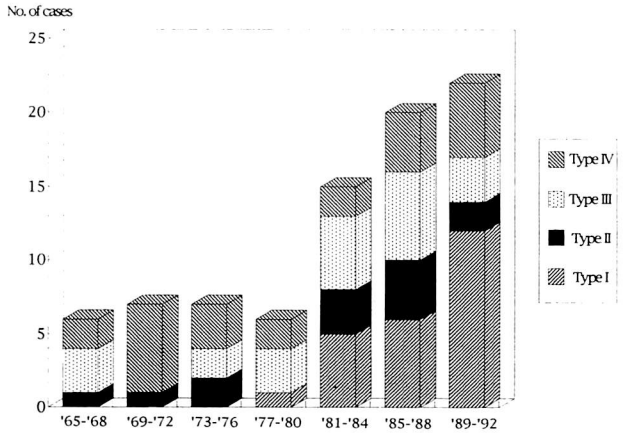

Fig. 1. Chronological change in No. of resected gastric lymphoma.

Table 1. Gastric cancers resected during the period from 1965 to 1992 in Aichi Cancer Center Hospital

Histology	No. of cases
Carcinoma	4647 (97.5%)
Malignant Lymphoma	96 (2.0%)
Others	22 (0.5%)
Total	4794

which might be due partly to the progress in diagnostioc methods, but also likely reflecting the true increase in incidence.

Diagnostic Criteria and Patients

Resected specimens of 83 PGLs of B-cell type, except for one follicular lymphoma and those with preceeding chemotherapy, were drawn from surgical pathology files from 1967 to 1991 at the Aichi Cancer Center Hospital. Histological sections were reexamined, and cases were reclassified according to the concept of MALT-derived lymphoma. All low-grade B-cell lymphomas of MALT type, including immunocytoma, and all high-grade B-cell lymphomas of the stomach with and without evidence of a low-grade component were included in this study. These cases were divided into four types, based on the extent of morphologically recognizable low- and high-grade component of the tumor (Table 2); Type I, pure low-grade B-cell lymphoma of MALT type (n=24): Type II, low-grade B-cell lymphoma of MALT type with small areas of high-grade lymphoma (n=13): Type III, high-grade lymphoma with small areas of low-grade component of MALT (n=22): and Type IV, pure high-grade lymphoma (n=24).

Low-grade gastric B-cell lymphomas of MALT type is defined by the following distinct morphology according to Isaacson and Wright.[18,19,24] The tumor is composed of centrocyte-like cells, clear cells and lymphoplasmacytoid cells. The infiltration of the tumor cells into the glandular epithelium produces a characteristic lymphoepithelial lesion. The tumor tissues usually contain various amount of plasma cells, immunoblasts and follicles with and without germinal centers.

Tissue Handling and Immunohistochemical Staining

Sections had been fixed in 10% formalin, embedded in paraffin, and routinely stained with H&E, Giemsa, periodic acid-Schiff PAS, and Gomori silver impregnation.

In all cases, the T-and B-cell nature of the infiltrates were tested with a panel of antibodies applicable to paraffin-embedded sections, including L26, UCHL-1 (Dako Japan, Kyoto, Japan), and MT1 (Bio-science Products, Emmenbruecke, Switzerland), using the

Table 2. Histological grouping of cases with surgically resected primary gastric lymphoma (PGL) of B-cell phenotype with special reference to low-grade B-cell lymphoma of mucosa-associated lymphoid tissue (MALT)

Types of PGL	Histology	No. of cases
Type I	Pure low-grade B-cell lymphoma of MALT	24
Type II	Low-grade B-cell lymphoma of MALT with small areas of high-grade lymphoma	13
Type III	High-grade lymphoma with small areas of low-grade component of MALT	22
Type IV	Pure high-grade lymphoma	24
	Total	83*

MALT, mucosa-associated lymphoid tissue.
*A case of follicular lymphoma and those with preceeding chemotherapy were excluded in the present study.

indirect immunoperoxidase technique.[45] Expression of cyclin D1 protein (5D4, kindly supplied by Dr. Seto),[46,47] bcl-2 protein (bcl-2, Dako), and p53 protein (DO-7, Dako) was also assessed in paraffin-embedded sections with the use of the same technique, because the corresponding monoclonal antibodies recognize epitopes resistant to formalin fixation. A case was regarded as positive for cyclin D1, bcl-2, or p53, if 15% or more of the malignant cells stained with the antobodies, although marking was evident in <5% of their cells in a few p53 or bcl-2- "negative" cases.

Survival Rates and the Staging System

For follow-up study, clinical information was obtained from the hospital records and the clinicians. We included only patients at stage I_E and II_E in this study, excluding those at stages III_E and IV. The stage of each case was reevaluated according to the general rules for the gastric cancer study by Japanese Research Society for Gastric Cancer. Actuarial survival was calculated by the Kaplan-Meier test. Significance of differences between the survival curves were determined according to the generalized Wilcoxon test.

Result

Clinical Presentation

The patients consisted of 49 men and 34 women. The ages ranged from 21 to 79 years (mean age, 55 years) with a peak in the sixth decades (Table 3). There were no significant differences among the types in clinical symptoms, laboratory data and patients' age, but the sex-ratio of Type IV showed considerable male predominance in our series. The most frequent chief complaint was an abdominal pain, which was recorded in 81% of all cases while weight loss was seen in 7%.

Treatment

All patients underwent primary resection of the stomach, documented as either subtotal (n=39) or

Table 3. Clinical presentation of patients with primary gastric lymphoma (PGL) of B-cell phenotype

Types of PGL		Age range in years (mean)	Male/female (ratio)	Symptoms		
				Abdominal pain	Weight loss	None
Type I	(n=24)	27-68 (53)	14/10 (1.4)	19 (79%)	0 (0%)	4 (17%)
Type II	(n=13)	34-69 (51)	7/6 (1.2)	11 (85%)	1 (8%)	0 (0%)
Type III	(n=22)	40-79 (61)	11/11 (1.0)	19 (86%)	2 (9%)	1 (5%)
Type IV	(n=24)	21-79 (54)	17/7 (2.4)	18 (75%)	2 (8%)	1 (4%)
Total	(n=83)	21-79 (55)	49/34 (1.4)	67 (81%)	5 (6%)	6 (7%)

total gastrectomy (n=34). Fourteen patients received additional chemotherapy (n=12) or both chemotherapy and radiation (n=2). Combination chemothrapeutic regimens containing doxorubicin (most frequently in regimens of cyclophosphamide, doxorubicin, vincristine, and prednisolone [CHOP],[48] doxorubicin, cyclophosphamide, prednisolone, and doxorubicin [VEPA], or VEPA plus methotrexate [VEPA-M])[49] were given to most patients of PGL with advanced stages (II-IV). Patients with Stage I lymphoma were treated only with surgery. In our series, only one patient, who underwent subtotal gastrectomy for a seemingly benign lesion 2 and 1/2 years earlier, developed a diffuse large cell lymphoma of B-cell phenotype in the residual stomach. Retrospectively, the initial lesion was that of PGL Type II.

Histological Classification

Thirty-seven cases of low-rade B-cell lymphoma of MALT type, including 13 cases with small areas of high grade lymphoma (Type II), were distinguished from 22 cases of high-rade B-cell lymphoma with a few foci of low-grade component usually at the tumor margins (Type III) and 24 cases of high-grade B-cell lymphoma without evidence of a low-grade component (pure high-grade lymphoma; Type IV) (Table 1). Diffuse infiltrates of centrocyte-like cells, scattered immunoblasts, and plasma cells were chracteristic features of low-grade B-cell lymphomas of MALT type (Fig.2). In the so-called early lymphomas, plasma cells were accumulated preferentially in the superficial part of the mucosa, and reactive-appearing lymphoid follicles were often found in the lower part of the mucosa and in the submucasa. These follicles were often infiltrated by the centrocyte-like or monocytoid cells, which sometimes appeared to be larger than those distributed around the follicles, and this phenomenon was called as follicular colonization by Isaacson et al.[33] Submucosal infiltration of the tumor cells was sometimes accompanied with hyaline sclerosis of amyloid diposit-like pattern (Fig. 3). The high-grade lymphomas of Type III and IV are basically of the same histological characteristics. Lymphoepithelial lesions, appearing as circumscribed centrocyte-like cell infiltrates in some gastric glands, were a hallmark of all cases of the low-grade MALT type (Fig. 4-a), whereas reactive lymphoid follicles and/or follicular colonization were found in 100%, 100%, 77% and 36% of these cases, respectively. On the other hand, lymphoepithelial lesions formed by the

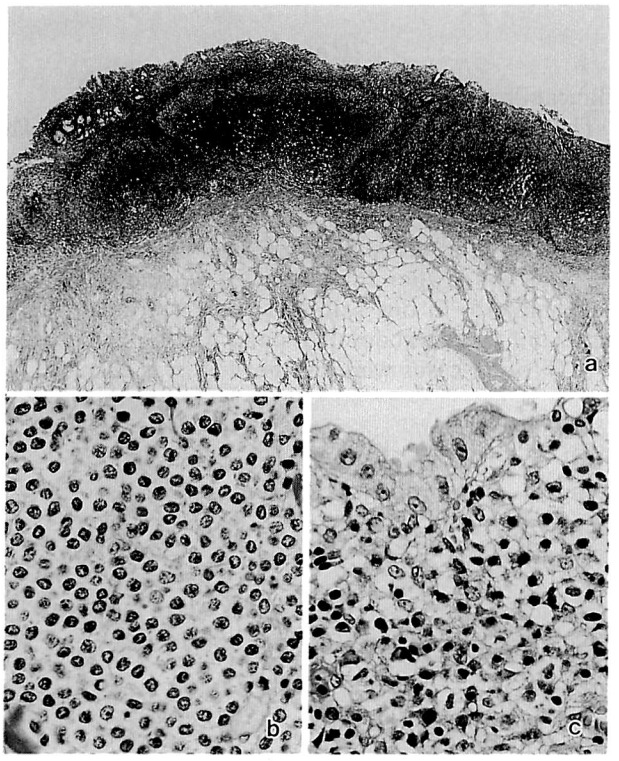

Fig. 2. Low-grade B-cell lymphoma of mucosa-associated lymphoid tissue (MALT). a) Neoplastic lymphoid cells infiltrate in the perifollicular area of the gastric mucosa. Note the lymphoepithelial lesions at the upper field and the lymph follicles at the lower field. b) The lesion is consisted of centrocyte-like cells. c) Lymphoplasmacytoid and plasma cells are predominantly disributed beneath she luminal surface.

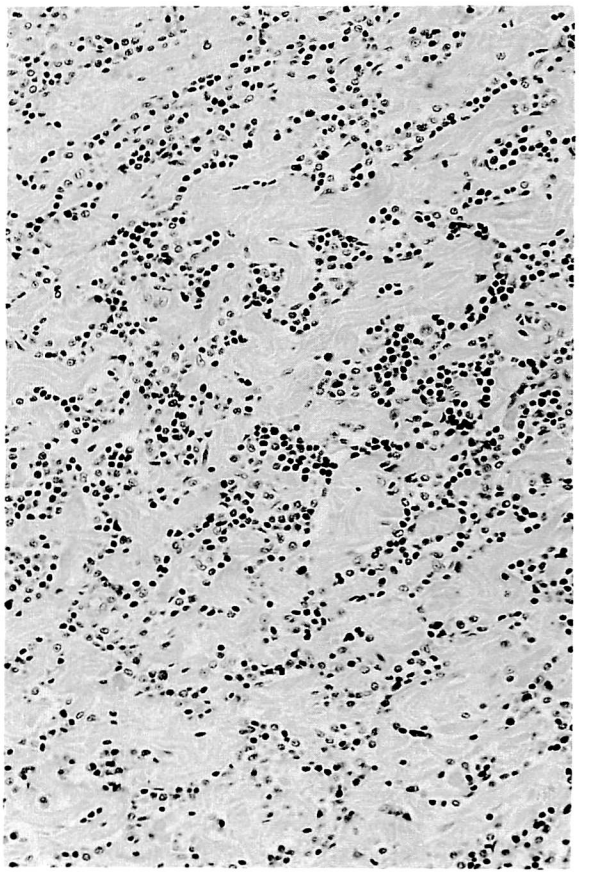

Fig. 3. Submucosal sclerosis of so-called amyloid-like pattern.

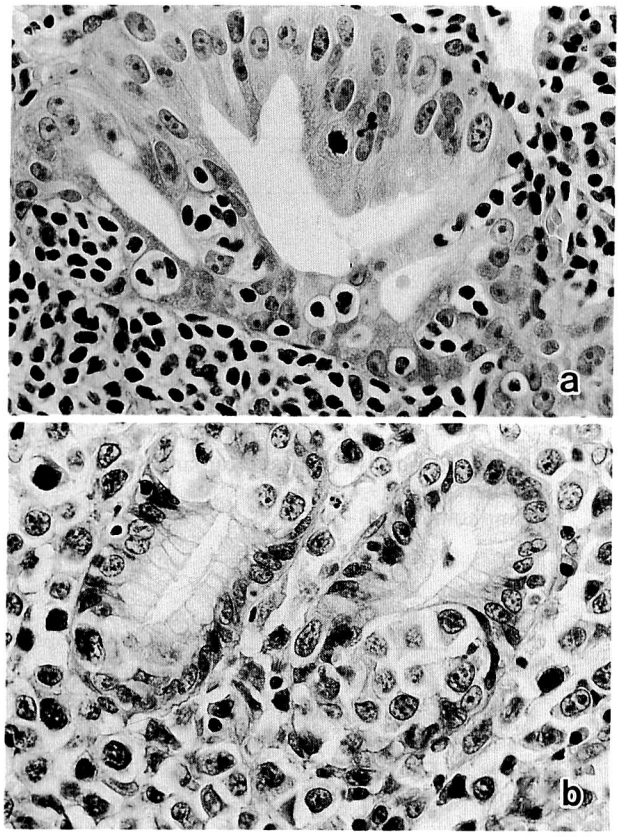

Fig. 4. Lymphoepithelioid lesions (LELs) by low-grade and high-grade lymphomas. a) Lel by centrocyte-like cells in low-gade MALT lymphoma. b) LEL by high-grade large B-cell lymphoma cells.

blastic cells were observed in 42% of Type IV tumors by careful scrutinization of sll slides (Fig. 4-b).

Gross Appearance

The macroscopic appearances of the resected stomach varied form irregular surface with multiple erosions, shallow ulcers with similarly rough surface, to elevated or protruded, and excavated centrally with elevated margins. These macroscopic appearances were roughly correlated with the histological types (Table 4); Type I and II were usually superficial, without and with ulcerations, while Type III and IV predominantly showed tumor masses often with central excavation.

Extent of Involvement and Staging

Lymph node involvement was incerased in rate as the advancement of types up to Type III (Table 5). The lymphoma was resteicted to the mucosa in 5, invaded into submucosa in 35, involved the muscularis prapria in 11, and involved all layers of the gastric wall in 32 cases. Their stages, which were determined according to the rules of the Japanese Society for Gastric Cancer Research, progressed as the histological types were advanced up to the Type III, while the Thpe IV somewhat differs from the others in that their stages were fairly evenly distributed from I to IV. Lymph node metastasis at times histologically resembled very much a nodal monocytoid B-cell lymphoma. Seven cases of Type IV tumor infiltrated directly into the adjacent organs such as liver, pancreas and colon.

Table 4. Gross appearance of primary gastric lymphoma of B cell phenotype according to Sano's classification*

Types of PGL		Superficial	Ulcerated	Protruded	Excavated	Giant fold
Type I	(n=24)	5 (21%)	18 (75%)	0 (0%)	1 (4%)	0 (0%)
Type II	(n=13)	0 (0%)	9 (69%)	0 (0%)	4 (31%)	0 (0%)
Type III	(n=22)	0 (0%)	4 (18%)	1 (5%)	14 (64%)	3 (14%)
Type IV	(n=24)	0 (0%)	4 (17%)	3 (13%)	16 (67%)	1 (4%)
Total	(n=83)	5 (6%)	35 (42%)	4 (5%)	35 (42%)	4 (5%)

*Refer to Sano.[50]

Table 5. Lymph node involvement and stage of primary gastric lymphoma (PGL) of B-cell phenotype

Types of PGL		Lymph node involvement	Stage*			
			I	II	III	IV
Type I	(n=24)	2 (8%)	22 (92%)	1 (4%)	1 (4%)	0 (0%)
Type II	(n=13)	4 (31%)	9 (69%)	2 (15%)	2 (15%)	0 (0%)
Type III	(n=22)	16 (73%)	3 (14%)	8 (36%)	10 (45%)	1 (5%)
Type IV	(n=24)	16 (67%)	5 (21%)	8 (33%)	5 (21%)	6 (25%)
Total	(n=83)	38 (46%)	39 (47%)	19 (23%)	18 (22%)	7 (8%)

*Stage was determined after surgical resection according to the general rules for the gastric cancer study by Japanese Research Society for Gastric Cancer.

Follow-up Data

Detailed information on the clinical courses was available in all 83 patients. Follow-up periods ranged from 0 to 325 months (mean follow-up period, 87 months). 61 patients remained free of disease for from 12 to 324 months (mean, 105 months), and 22 patients had recurrence within from 1 to 187 months. Local relapse, including recurrent disease in regional lymph nodes or in perigastric tissue, occurred in 11 patients, and three patients had local relapse together with infiltration of the liver. Distant relapse was reported in 14 cases: i.e., bone marrow (n=1), liver (n=2), liver and distant lymph node (n=2), distant lymph nodes (n =4), retropertoneal space (n=1), lung (n=1), pleura (n=1), tonsil (n=1), and brain (n=1). The survival curves of each Type of PGL is shown in Figure 5. The 10-year survival rates were 100% for Type I, 68% in Type II, 72% in Type III and 65% in Type IV. The survival rate was significantly higher for Type I and II lymphomas than for Type III and IV tumors ($P<0.05$ by the generalized Wilcoxon test). The survival curves according to the stage of the disease are shown in Figure 6. The 10-year survival rates of each stage were 90%, 85%, 68% and 40% respectively.

Expression of Cyclin D1 Protein, bcl-2 Protein, and p53 Protein.

The tissue samples from 42 patients with PGL (Type I, n=15; Type II, n=8; Type III, n=9; and Type IV, n =10) were examined for immunohistochemical staining of cyclin D1 protein, bcl-2 protein and p53 protein, and the results are summarized in Table 6. With the staining for cyclin D1 protein, none showed nuclear staining pattern which is characteristic for mantle cell lymphoma, and only two cases with certain plasma cell differentiation showed cytoplamic positivity. The bcl-

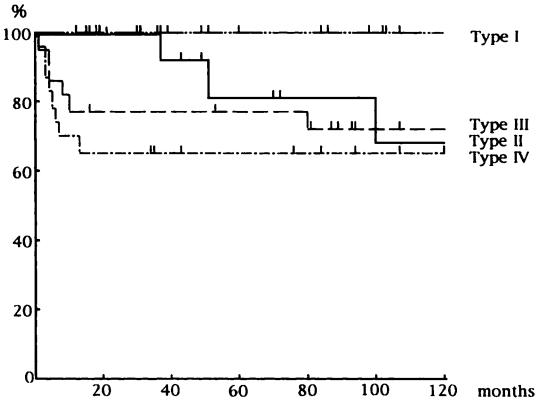

Fig. 5. Actuarial survival (after Kaplan and Meier) of patients with each Type of primary gastric lymphoma of B-cell type.

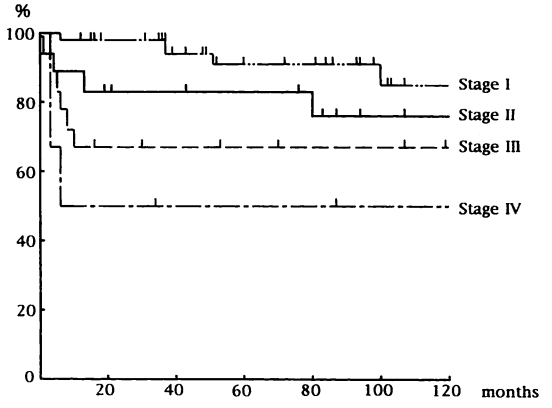

Fig. 6. Actuarial survival (after Kaplan and Meier) according to the rules for staging of the disease by Japanese Research Society for Gastric Cancer in the patients with primary gastric lymphoma of B-cell type.

Table 6. Details of immunoproliferative disorders studied and patterns of immunostaining for PCNA, cyclin D1 protein, bel-2 protein and p53 protein

	cyclin D1		bcl-2		p53	
PGL type I	2/15*	(13%)	12/15	(80%)	1/15	(7%)
PGL type II						
low-grade area	2/8*	(25%)	8/8	(100%)	0/8	(0%)
high-grade focus	0/8	(0%)	4/8	(50%)	2/8	(25%)
PGL type III						
low-grade focus	0/9	(0%)	8/9	(89%)	1/9	(11%)
high-grade area	0/9	(0%)	4/9	(44%)	4/9	(44%)
PGL type IV	0/10	(0%)	5/10	(50%)	5/10	(50%)
Node-based B-cell lymphoma						
centroblastic	7/15*	(47%)	9/15	(60%)	7/15	(47%)
centroblastic/centroblastic	2/10*	(20%)	4/6	(67%)	0/6	(0%)

*Immunohistochemistry showed cytoplasmic positivity without nuclear staining.

2 protein was expressed in 80 to 100% of the low-grade lesions of PGL Type I, II, and III, and in 44 to 50% of the high-grade lesions of PGL Type II, III, and IV, while p53 was inversely found in 0 to 11% of the former and in 25 to 50% of the latter. In the study of bcl-2 and p53 protein expression, the significant difference was not found between the node-based diffuse large B-cell lymphoma and the gastric high-grade lesions.

Discussion

In Japan, the term "reactive lymphoreticular hyperplasia (RLH)" was coined for the lymphoproliferative lesion of the stomach with borderline histological appearnces by Nakamura in 1966,[51] and has been widely used as a synonym for the pseudolymphoma.[11] Its histological picture is that of a low-grade B-cell lymphoma of mucosa-associated lymphoid tissue (MALT), introduced by Isaacson and Wright.[18,19] In the present study, we made a clinicopathologic investigation on the premary gastric lymphomas in the light of the MALT concept. The histological appearances of the PGL were markedly variable from part to part in the specimen and among the cases. Besides the reactive components such as non-neoplastic follicles and plasma cells, variable amount of larger transformed cells are seen both in outside follicles and in the colonied follicles in the low-grade MALT lymphoma. More obvious foci of high-grade transformation was also observed in the low-grade MALT lymphomas and many high-grade lymphomas showed coexistence of low-grade disease. Because this mixture of grades is so common, it is sometimes difficult to decide whether a PGL is low grade with a high-grade component or of high grade. In this study, we divided PGLs into four types; according to the relative extent of MALT and high-grade lesions (Type I, II, III and IV). Their numbers were 24, 13, 22, and 24 cases respectively, totaling 83 cases. The presence of readily identifiable confluent clusters or sheets of transformed cells outside the colonized follicles is defined as a high-grade component that has supervened on low-grade MALT lymphoma, as counting of large cells is impractical because of the variability of their percentage from area to area.[14,42]

The survival curves by histological types revealed that the majority of the gastric lymphmas are of a curable disease if adequately resected. No case of Type I showed recurrence after surgery. Interestingly, the curve of Type II overlapped with that of Type III after 5 years of surgery, which is probably a reflection of tumor progression. Furthermore, there was no significant difference in the 10 year survival rate among Type II, III, and IV, which appears to indicte that the presence or absence of synchronous low grade element make little difference on survivals.

The survival curves according to the stage of disease by Japanese Research Society for Gastric Cancer showed clearer distinction between each of them than those by the histological typing. This staging method employs the depth of invasion into the gastric wall as a factor for staging, which is reported to be prognostically significant in previous studies.[2,9,13,42,52,53] The Ann Arbor staging system lacks this factor.[43,44]

The histological division of the PGL into the 4 types as in the present study thus seemed to be correlated with the gross appearances, stage and prognosis. From what have been shown so far, it can be said that the tumors of Type I, II and III constitute a continuous clinicopathologic spectrum, and most likely all originated from the mucosa-associated lymphoid tissue. They comprised 72% of the primary gastric lymphomas. A similar study has been made by Cogliatti et al.[13] Although there were many common findigs in both studies, there seemed to be a question left, with regard to the true nature of the tumors of Type IV, namely pure high-grade lymphomas; i.e., whether they are essentially also of high-grade MALT lymphomas or represent the neopoastic counterpart of other subsets such as follicular center cells. In this regard, the type of histology often taken by the high-grade gastric lymphoma, which is composed of blastic large cells having a greater amount of basophilic cytoplasm and various cells including those with some plasmacytoid features, differs subtlely from the typical nodal large B-cell lymphomas. Moreover, lymphoepithelial lesions formed by blastic cells were found in 10 cases out of 24 of Type IV tumors by careful search. In addition, the survial rate of the high-grade MALT lymphoma was more favorable than the equivalent nodal disease. Our assumuption taken from these findings is that st least a portion, if not all, of pure high-grade gastric lymphomas may well be also of high-grade MALT lymphomas.

Recent studies favor the hypothesis that there is a certain difference in molecular genetic characteristics and pathogenesis between the lymphomas originating in the MALT and node-based lymphomas in spite of their morphological similarity.[39-41] However, the role of proliferation, apoptosis and its inter-relationship is yet to be established in the gastrointestinal lymphoma.[40,54-56] The immunohistochemical staining for cyclin D1 protein (marker for the overexpression of its mRNA),[46,47] bcl-2 protein (marker for impaired apoptosis) and p53 protein (marker for p53 mutation) [55-59] was made to elucidate the biologic apecificity of the PGL.

Firstly, overexpression of cyclin D1 protein with nuclear staining pattern which is specific to pathogenesis of mantle cell lymphoma[46,47] was completely lacking in both low-grade MALT and high-grade lymphomas of stomach examined. The cytoplasmic positivity for cyclin D1 protein was seen in a portion of the low-grade MALT lymphoma, whereas completely absent in the high-grade gastric lesions. The cytoplasmic staining was however fairly frequent in the node-based large B-cell lymphoma. This difference is likely

to suggest the lineage difference between these morphologically resembling high-grade B-cell lymphomas.

The bcl-2 protein was expressed with high frequency (80-100%) in the low-grade MALT lymphoma, while it was about 40% in the high-grade gastric lymphoma. The bcl-2 expression in the low-grade MALT lymphomas in our series was about equal to the data from the western literatures.[40,56-59] On the other hand, its expression in the gastric high-grade lymphomas was higher in frequency in ours than in the cases reported from the Western countries,[40,57] and not much different from the nodal high-grade lesions. Some of the Western literatures show much higher incidences of bcl-2 protein expression in the nodal large B-cell lymphoma which, they assert, is a significant difference from gastric high-grade lesions.[40] This aspect needs to be further investigated. Inhibition of apoptosis via bcl-2 protein expression appears to be significant for oncogenesis in case of low-grade MALT lymphoma, whereas in the high-grade lymphomas, bcl-2 expression may not be as significant as in the former for oncogenesis.

Detectable p53 protein overexpression was high in the high-grade gastric tumors, which may possibly be related with transformation from the low-grade MALT lymphoma, as previously reported on the high-grade transformation of the follicular lymphomas.[60,61]

The normal gastric mucosa contains no organized lymphoid tissue.[62,63] Helicobacter pylori infection is hypothesised with the acquisition of MALT[62,63] and the subsequent development of malignant lymphoma.[14,64] Recent studies have shown dependence of low-grade gastric MALT lymphoma on growth stimulation by intratumoral H. pylori-specific T-cells,[37] and that eradication of H. pylori with antibiotics resulted in regression of the early tumors in a small number of patients.[38,65] Further study is needed on this aspect of the gastric lymphomas.

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