Clinical outcomes of surgical management for primary gastrointestinal diffuse large B-cell lymphoma: At a single institution experience

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Purpose: The study aimed to analyze peri/postoperative outcomes and long-term oncologic outcomes after surgical management for primary gastrointestinal diffuse large B-cell lymphoma (DLBL).

Methods: Between January 2001 and December 2013, 19 patients who underwent surgery for primary gastrointestinal DLBL were retrieved from a retrospective database.

Results: With a median follow up of 49.2 months, the most common tumor locations were the terminal ileum and cecum (n = 14, 73.7%) and stomach (n = 4, 21.1%). The most common clinical symptoms were abdominal pain (n = 15, 78.9%) and intussusceptions (n = 5, 26.3%). None of the patients had B symptoms. Emergency surgery was undertaken in 36.8% (n = 7) of the patients. Mean mass size was 8.4 cm; 4 patients (21.1%) had a bulky mass (> 10 cm). The International Prognostic Index (IPI) scores were low (n = 11, 57.9%), low-intermittent (n = 7, 36.8%), and high-intermittent (n = 1, 5.3%). Patients' staging was IE (n = 9, 47.4%), IIE (n = 8, 42.1%), and IVE (n = 2, 10.5%) based on the Ann Arbor staging system, and I (n = 2, 10.5%), II1 (n = 5, 26.4%), IIE (n = 10, 52.6%), and IV (n = 2, 10.5%) based on the Lugano staging system. B-lymphocyte antigen CD20 was positive in most patients (n = 17, 89.5%) and Ki-67 was high (> 70%) in 12 patients (63.2%). Two types of chemotherapy were administered: cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisolone (n = 5, 26.3%), rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisolone (n = 13, 68.4%). The 5-year disease-free survival rate was 94.4% and the 5-year overall survival rate was 89.5%.

Conclusion: Surgery for primary gastrointestinal DLBL is feasible and acceptable. Low staging of primary gastrointestinal DLBL has good prognosis.

Keywords: Lymphoma, Diffuse large B-cell lymphoma, Gastrointestinal tract, Surgery

INTRODUCTION

Primary gastrointestinal lymphoma is a very rare disease; it only accounts for 1%–4% of all gastrointestinal cancers [1]. Malignant lymphoid neoplasms are classified into Hodgkin's disease and non-Hodgkin's malignant lymphoma. Non-Hodgkin's malignant

lymphomas are classified as nodal and extranodal lymphomas [2]. The gastrointestinal tract is the most common site of extranodal malignant lymphoma, accounting for 5%–20% of all cases [3]. The gastrointestinal tract is also the most common site of extranodal lymphoma for diffuse large B-cell lymphoma (DLBL) [2]. Primary gastrointestinal lymphoma has been classified histologically as B-cell lymphoma and T-cell lymphoma. The B-cell lymphoma group is divided into the following subtypes: mucosa associated lymphoid tissue, DLBL, follicular lymphoma, mantle cell lymphoma, and Burkitt lymphoma. The T-cell lymphoma group is divided into the following subtypes: enteropathy associated T-cell lymphoma, natural killer (NK)/T-cell lymphoma, and peripheral T-cell lymphoma [4]. Almost 90% of all gastrointestinal lymphomas are B-cell lymphomas, and the main histological subtype is DLBL, which constitutes 45%–59% of all gastrointestinal lymphoma [5,6]. Treatment of primary gastrointestinal DLBL is still a controversial

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issue. Because primary gastrointestinal DLBL is a very rare disease, and there are few large scale prospective randomized studies, there is no consensus on the optimal treatment. The present study aimed to analyze peri/postoperative outcomes and long-term oncologic outcomes after surgical management for primary gastrointestinal DLBL at the single institution.

METHODS

Ethical approval was not necessary as this study was based on retrospective review.

Between January 2001 and December 2013, all patients (n = 19) that underwent surgical management for primary DLBL were identified from a retrospective database. All data of the clinical and pathological features were reviewed retrospectively. Gastrointestinal DLBL satisfied the lymphoma definition of Lewin et

al. [7]. A total of 19 patients were included in this study, of which 69 were extranodal type of Non-Hodgkin lymphoma patients, 25 were gastrointestinal lymphoma and 21 were primary gastrointestinal DLBCL patients. Of these patients, a total of 19 patients were included in the study, excluding 2 patients who underwent palliative surgery during chemotherapy (Fig. 1). All patients underwent surgery and adjuvant chemotherapy using cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisolone (CHOP) or rituximab CHOP (R-CHOP) regimens except postoperative mortality. All patients underwent gastroduodenoscopy, colonoscopy, and a biopsy, staging scans (computed tomography scan of the chest, abdomen, and pelvis) and, occasionally, positron emission tomography-computed tomography scans. B symptoms were defined as fever ($> 38^{\circ}\text{C}$), weight loss without trying, exceeding 10% of body weight in 6 months, and drenching night sweats. The Eastern Cooperative Oncology Group (ECOG) performance status grade was used, as defined by Oken et al. [8]. Bulky mass was defined as a mass with a diameter greater than 10 cm. The International Prognostic Index (IPI) score was calculated using the following parameters: age ≥ 60 years, ECOG status ≥ 2 , elevated lactate dehydrogenase, Ann Arbor stage III or IV, ≥ 2 extranodal disease sites [9]. The IPI score was defined as follows: low (0 or 1), low-intermediate (2), high-intermediate (3), or high (4 or 5) [10]. The depth of the tumor invasion and the extent of nodal involvement were described as a parameter for stage classification in three staging systems: the Paris staging system, the Ann Arbor staging system, and the Lugano staging system (Table 1). The Paris staging system was based on the 6th edition of the American Joint Committee on Cancer's tumor-node-metastasis (TNM) [9]. In the Paris staging system the distribution of stage is: T1, tumor confined to the mucosa and/or submucosa; T2, tumor infiltrates the muscularis pro-

Fig. 1. Patients included in this study. MALT, mucosa-associated lymphoid tissue.

Table 1. Staging of gastrointestinal diffuse large B cell lymphoma

Stage	Lugano stage	Paris TNMB stage	Modified Ann Arbor stage	Tumor involvement
I	Confined to GI tract (single primary or multiple, noncontiguous)	T1N0M0B0	IE	Mucosa, submucosa
		T2N0M0B0	IE	Muscularis propria
		T3N0M0B0	IE	Serosa
II	Extending into abdomen	T1-3N1M0B0	IIE	Perigastric or peri-intestinal lymph nodes
	II1 = local nodal involvement II2 = distant nodal involvement	T1-3N2M0B0	IIE	More distant regional lymph nodes
IIE	Penetration of serosa to involve adjacent organs or tissues	T4N0M0B0	IE	Invasion of adjacent structures
IV	Disseminated extranodal involvement or concomitant supradiaphragmatic nodal involvement	T1-4N3M0B0	IIIE	Lymph nodes on both sides of the diaphragm
		T1-4N0-3M1B0	IVE	Distant metastases (e.g., bone marrow or additional extranodal sites)
		T1-4N0-3M0-1B0	IVE	

pria and/or submucosa; T3, tumor penetrates the serosa (visceral peritoneum) without invasion of adjacent structures; T4, tumor perforates the serosa or invades the adjacent structures organs; N1, involvement of regional lymph nodes; N2, involvement of intra-abdominal lymph nodes beyond the regional area; N3, the tumor spreads to the extra-abdominal lymph nodes; M1, non-continuous involvement of a separate site in the gastrointestinal tract (e.g., stomach and rectum); M2, non-continuous involvement of other tissues (e.g., peritoneum pleura) or organs (e.g., tonsils, parotid gland, ocular adnexa, lung, liver, spleen, kidney, breast, etc.); BX, involvement of bone marrow not assessed; B0, no evidence of bone marrow involvement; and B1, lymphomatous infiltration of bone marrow [10,11]. In the Ann Arbor staging system, the distribution of stage is: I, if a single lymph node region is involved; IE, if a single extralymphatic organ or site is involved; II, if two or more lymph node regions on the same side of the diaphragm are involved; IIE, if involvement is localized to an extralymphatic organ or site and one or more lymph node regions on the same side of the diaphragm; III, if lymph node regions on both sides of the diaphragm are involved; IIIE, if the extralymphatic site is involved; and IV, diffuse or disseminated involvement of one or more extralymphatic organs or tissues; with or without associated lymph node involvement [12]. In the Lugano staging system, the distribution of stage is: I, confined to GI tract (single primary or multiple, noncontiguous); II1, extending into the abdomen with local nodal involvement; II2, extending into the abdomen with distant nodal involvement; IIE, penetration of the serosa to involve adjacent organs or tissues; and IV, disseminated extranodal involvement or concomitant supradiaphragmatic nodal involvement [13]. In the present study, the patients received close follow-up and the findings were recorded in a database until death or August 2017. The patients received follow-up every 3–6 months for up to 5 years after surgery. Disease-free survival (DFS) was defined from the date of surgery to the date of the detection of recurrence or the last follow-up, or death.

Statistical analysis

All statistical analyses were performed using SAS ver. 9.1.3 (SAS Institute Inc., Cary, NC, USA) and IBM SPSS software, ver. 24.0 (IBM Corp., Armonk, NY, USA). The categorical variables were analyzed using the χ^2 or Fisher's exact test, and the continuous variables were analyzed using the Student t-test/Mann-Whitney U rank tests. Cumulative-incidence methods were used to estimate the rate of cancer recurrence. Overall survival (OS) and DFS were analyzed using the Kaplan-Meier method.

RESULTS

Patient characteristics

The mean age of the patients was 52.5 ± 15.8 years. Of the 19 patients, 14 (73.7%) were male and 5 (26.3%) were female. Mean weight was 63.7 ± 12.6 kg and mean height was 165.0 ± 8.3 cm. Mean body mass index (BMI) was 23.1 ± 3.2 kg/m². The American society of anesthesiologists scores were 1 (n = 11, 57.9%), 2 (n = 3, 42.1%), and 3 (n = 0, 0.0%). The ECOG performance status results were 0 (n = 14, 73.7%), 1 (n = 4, 21.1%), and 2 (n = 1, 5.3%). The tumor was located in the stomach in 4 patients (21.1%), the terminal ileum in 4 (21.1%) patients, the terminal ileum and cecum in 7 (36.8%) patients, the cecum in 3 (15.8%) patients, and the appendix in 1 (5.3%) patient. Adjuvant chemotherapy was administered using CHOP (n = 5, 26.3%) and R-CHOP (n = 13, 68.4%) (Table 2).

Clinical symptoms

The primary clinical symptom was abdominal pain (n = 15,

Table 2. Patients characteristics (n=19)

Characteristic	Patients (n = 19)
Age (yr)	52.5 ± 15.8 (15–82)
Sex	
Male	14 (73.7)
Female	5 (26.3)
Weight (kg)	63.7 ± 12.6 (40.0–83.0)
Height (cm)	165.0 ± 8.3 (150.0–179.3)
BMI (kg/m ²)	23.1 ± 3.2 (15.8–27.5)
ASA score	
1	11 (57.9)
2	8 (42.1)
3	0
ECOG performance status	
0	14 (73.7)
1	4 (21.1)
2	1 (5.3)
Tumor location	
Stomach	4 (21.1)
Terminal ileum	4 (21.1)
Terminal ileum & cecum	7 (36.8)
Cecum	3 (15.8)
Appendix	1 (5.3)
Adjuvant chemotherapy	
CHOP	5 (26.3)
R-CHOP	13 (68.4)

Values are presented as mean ± standard deviation (range) or number (%). BMI, body mass index; ASA, American society of anesthesiologists; ECOG, Eastern Cooperative Oncology Group; CHOP, cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone; R-CHOP, rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisolone.

78.9%). The second most common symptom was intussusception (n = 5, 26.3%). Other symptoms were nausea (n = 3, 15.8%), palpable mass (n = 3, 15.8%), vomiting (n = 2, 10.5%), hematochezia (n = 2, 10.5%), and bowel perforation (n = 2, 10.5%). None of the patients had any B symptoms. Three of the 19 patients had no any symptoms (15.8%). None of the patients had anemia. Mean hemoglobin level was 12.9 ± 1.5 g/dL (range, 15.4–10.6 g/dL). Mean albumin level was 4.0 ± 0.4 g/dL (range, 4.6–3.1 g/dL). Mean lactate dehydrogenase level was 419.8 ± 148.1 IU/L (717.0–244.0 IU/L). The number of elevated lactate dehydrogenase patients was 5 (26.3%). Mean carcinoembryonic antigen level was 1.1 ± 0.6 ng/mL (1.82–0.07 ng/mL) (Table 3).

Surgery for gastrointestinal DLBL

The indications for surgery were symptomatic and had a mass in gastrointestinal tract, which was to improve the symptoms. In addition, if the tumor is found without any symptoms and the malignancy is suspected, surgery is performed. A total of 14 patients (73.7%) were suspected of having malignancy, and 3 patients (21.4%) had no symptoms among these patients. Subtotal gastrectomy with lymph node dissection for rule out malignancy was performed in 4 patients (21.1%). Right hemicolectomy with lymph node dissection for rule out malignancy was performed in 10 patients (52.6%). Ileocectomy was performed in 2 patients (10.5%). Segmental resection small bowel was performed in 2 patients (10.5%). Appendectomy was performed in 1 patient (5.3%). Emergency surgery was performed in 7 patients (36.8%). Laparoscopic

Table 3. Clinical symptoms of gastrointestinal diffuse large B cell lymphoma

Clinical symptoms	Patients (n = 19)
Abdominal pain	15 (78.9)
Nausea	3 (15.8)
Vomiting	2 (10.5)
Hematochezia	2 (10.5)
Palpable mass	3 (15.8)
B symptom	0
No symptom	3 (15.8)
Intussusception	5 (26.3)
Perforation	2 (10.5)
Hemoglobin (g/dL)	12.9 ± 1.5 (15.4–10.6)
Albumin (g/dL)	4.0 ± 0.4 (4.6–3.1)
LDH (IU/L)	419.8 ± 148.1 (717.0–244.0)
Elevated LDH, no (%)	5 (26.3)
CEA (ng/mL)	1.1 ± 0.6 (1.82–0.07)

Values are presented as number (%) or mean $\pm$ standard deviation. LDH, lactate dehydrogenase level; CEA, carcinoembryonic antigen.

surgery was performed in 2 patients (10.5%). Open surgery was performed in 17 patients (89.5%). A total of 5 patients (26.3%) had postoperative complications. Two patients (10.5%) had ileus. Three patients (15.8%) had a wound infection. One patient (5.3%) had disseminated intravascular coagulation. Postoperative mortality occurred in 1 patient (5.3%). The reason of mortality was massive postoperative bleeding and disseminated intravascular coagulation. The patient was 70 years old female and was performed subtotal gastrectomy.

Mean mass size was 8.4 ± 5.3 cm (range, 3.0–26.0 cm). Four patients (21.1%) had a bulky mass (> 10 cm). Mean harvested lymph node was 23.2 ± 21.1 (range, 0–62.0). The number of positive lymph nodes was 2.2 ± 3.8 (range, 0.0–11.0) (Table 4).

Pathologic findings after gastrointestinal DLBL surgery

All patients were diagnosed with DLBL through pathologic results after surgery. Distribution of stage was classified using the Paris classification system, the Ann Arbor staging system, and the Lugano staging system. The Paris classification results were: T1 (n = 0, 0.0%), T2 (n = 3, 15.8%), T3 (n = 14, 73.7%), T4 (n = 2, 10.5%), N0 (n = 10, 52.6%), N1 (n = 4, 21.1%), N2 (n = 5, 26.3%), N3 (n = 0, 0.0%), M0 (n = 19, 0.0%), M1 (n = 0, 0.0%), M2 (n = 0, 0.0%), Bx (n = 17, 89.5%), B0 (n = 2, 10.5%), and B1 (n = 0, 0.0%). The Ann Arbor staging results were: IE (n = 9, 47.4%), IIE (n = 8, 42.1%), IIIE

Table 4. Surgery for gastrointestinal diffuse large B cell lymphoma

Surgery	Patients (n = 19)
Subtotal gastrectomy	4 (21.1)
Right hemicolectomy	10 (52.6)
Ileocectomy	2 (10.5)
Segmental resection	2 (10.5)
Appendectomy	1 (5.3)
Emergency surgery	
Yes	7 (36.8)
No	12 (63.2)
Laparoscopic surgery	2 (10.5)
Open surgery	17 (89.5)
Total number of postoperative complication	5 (26.3)
Ileus	2 (10.5)
Wound infection	3 (15.8)
Bleeding	0
Disseminated intravascular coagulation	1 (5.3)
Mortality	1 (5.3)
Mass size (cm)	8.4 ± 5.3 (3.0–26.0)
Bulky mass (> 10 cm)	4 (21.1)
Harvested no. of lymph nodes	23.2 ± 21.1 (0.0–62.0)
No. of positive lymph node	2.2 ± 3.8 (0.0–11.0)

Values are presented as number (%) or mean $\pm$ standard deviation (range).

(n=0, 0.0%), and IVE (n=2, 10.5%). The Lugano staging results were: I (n=2, 10.5%), II1 (n=5, 26.4%), II2 (n=0, 0.0%), IIE (n=10, 52.6%), and IV (n=2, 10.5%). The depths of the tumor invasion were: mucosa/submucosa (n=0, 0.0%), muscularis propria (n=3, 15.8%), subserosa (n=4, 21.1%), serosa/adjacent organ involve-

ment, or perforation (n=10, 52.6%). The IPI scores were: low (n=11, 57.9%), low-intermittent (n=7, 36.8%), high-intermittent (n=1, 5.3%), and high (n=0, 0.0%) (Table 5).

Table 5. Pathologic finding after surgery of gastrointestinal diffuse large B cell lymphoma

Pathologic results	Patients (n = 19)
Paris classification	
T stage	
1	0
2	3 (15.8)
3	14 (73.7)
4	2 (10.5)
N stage	
0	10 (52.6)
1	4 (21.1)
2	5 (26.3)
3	0
M stage	
0	19 (100.0)
Bone marrow biopsy	
1	0
2	0
Bx	17 (89.5)
BO	2 (10.5)
B1	0
Depth of invasion, no. (%)	
Mucosa/submucosa	0
Muscularis propria	3 (15.8)
Subserosa	4 (21.1)
Serosa/adjacent organ involvement, or perforation	10 (52.6)
Ann Arbor stage	
IE	9 (47.4)
IIE	8 (42.1)
IIIE	0
IVE	2 (10.5)
Lugano stage	
I	2 (10.5)
II1	5 (26.4)
II2	0
IIE	10 (52.6)
IV	2 (10.5)
IPI score	
Low (0 or 1)	11 (57.9)
Low-intermittent (2)	7 (36.8)
High-intermittent (3)	1 (5.3)
High (4 or 5)	0

IPI, international prognostic index.

Immunohistochemistry results for gastrointestinal DLBL

In the present study, B-lymphocyte antigen (CD20) was positive (n=17, 89.5%) in most of the patients. B-cell lymphoma 2 (BCL-2) was positive in 5 patients (26.3%). B-cell lymphoma 6 (BCL-6) was positive in 4 patients (21.1%). CD3 was positive in only 1 patient (5.3%). CD10 was positive in 4 patients (21.1%). CD79a was positive in 5 patients (26.4%). Multiple myeloma oncogene-1 (MUM-1) was positive in 4 patients (21.1%). A high level of Ki-67 (>70%) was found in 12 patients (63.2%) (Table 6).

Oncologic outcomes of surgical management for gastrointestinal DLBL

The response to adjuvant chemotherapy after surgery was good in most of the patients. Complete remission occurred in 16 patients (84.2%), partial remission with stable disease occurred in 1 patient (Ann Arbor Stage IVa) (5.3%). Two patients (10.5%) died. One patient (Ann Arbor Stage IVa) had neutropenic sepsis during adjuvant chemotherapy, and one other patient (Ann Arbor Stage IE) had disseminated intravascular coagulation after surgery. There

Table 6. The result of immunohistochemistry for gastrointestinal diffuse large B cell lymphoma

	BCL-2	BCL-6	CD3	CD10	CD20	CD79a	MUM-1	Ki-67 (%)
1	ND	+	-	-	+	ND	+	50-60
2	+	ND	-	-	+	ND	ND	80
3	ND	-	-	-	+	ND	+	80-90
4	ND	ND	-	ND	+	+	ND	30
5	ND	ND	-	ND	+	ND	ND	High
6	ND	-	-	-	+	ND	-	90
7	+	+	-	+	+	ND	ND	90
8	ND	+	-	+	+	ND	+	60-70
9	+	-	ND	-	+	ND	ND	90
10	+	ND	-	-	+	ND	ND	80
11	-	+	ND	ND	ND	+	ND	High
12	ND	ND	-	-	+	ND	+	70-80
13	+	ND	-	+	+	+	ND	90
14	ND	ND	-	ND	+	ND	ND	10
15	-	-	ND	ND	+	+	ND	80
16	ND	ND	-	+	+	ND	ND	80
17	ND	ND	+	ND	-	ND	ND	Low
18	ND	ND	-	ND	+	ND	ND	60
19	ND	ND	ND	ND	+	+	ND	ND

BCL, B-cell lymphoma; CD, cluster of differentiation; MUM-1, multiple myeloma oncogene-1; ND, not done.

Fig. 2. Oncologic outcomes of surgical management for gastrointestinal diffuse large B cell lymphoma.

was no disease progression in the present study. With a median follow up of 49.2 months, the 5-year DFS rate was 94.4% and the 5-year OS rate was 89.5% (Fig. 2).

DISCUSSION

Extranodal DLBL occurs in the gastrointestinal tract, and DLBL is the most common subtype in the small intestine and large intestine and the second most common subtype in the stomach and duodenum, after mucosa-associated lymphoid tissue lymphoma and follicular lymphoma, respectively [14]. In the present study, small intestine and large intestine DLBL ($n = 15$, 78.9%) were the most common subtypes. The second most common subtype was stomach DLBL ($n = 4$, 21.1%). In the small and large intestine, the sites that were most involved were the terminal ileum ($n = 4$, 21.1%), the terminal ileum and the cecum ($n = 7$, 36.8%), the cecum ($n = 3$, 15.8%), and the appendix ($n = 1$, 5.3%). In the present study, no other sites were involved.

The most common symptoms of gastrointestinal DLBL are abdominal pain, nausea, and abdominal discomfort; B symptoms are very rare [15]. Hematochezia or hematemesis account for 20%–30% of advanced stage DLBL [16]. In the present study, the most common symptoms were abdominal pain ($n = 15$, 78.9%) and hematochezia, which occurred in 2 patients (10.5%). Moreover, none of the patients had B symptoms. Intussusception is usually associated with benign lesions, and in 14% of all cases it is associated with malignant lesions [17]. Primary lymphomas in the small intestine account for less than 2% of all gastrointestinal malignancies and 10%–20% of small intestine malignancies [18]. In the present

study, 5 patients (26.3%) had intussusceptions, all of which occurred in the ileocecal area. Perforation is an unusual symptom of gastrointestinal DLBL; however, the occurrence of perforations is potentially life threatening and related to morbidity from sepsis, multiple organ failure, prolonged hospital stay, and postoperative complications, including wound infection and delayed adjuvant therapy. Vaidya et al. [19] reported that, among patients with primary gastrointestinal lymphoma, 49 of 1,062 patients (4.61%) had perforation as an initial symptom. In the present study, 2 of the 19 patients (10.5%) had bowel perforation as an initial presenting symptom, and the perforation sites were the terminal ileum and the cecum.

Primary gastrointestinal DLBL generally expresses pan B-cell markers, such as CD19, CD20, CD22, CD79a, occasionally MUM-1+, and bcl-2+, and 50%–75% of cases express surface or cytoplasmic immunoglobulins [20,21]. In a study of 49 primary gastrointestinal DLBL cases, the histology and immunophenotyping showed that CD20+ and CD3- were the markers in all the cases [22]. On average, the Ki-67 labeling index was 68.3% (range, 35%–90%) and CD10 was positive in 44.9% of the cases, CD5 was positive in 4.1% of the cases, and c-MYC was positive in 23.4% of the cases [22]. In the present study, CD20 was positive in most of the cases (89.5%) and BCL-2 was positive in 26.3% of the cases, BCL-6 was positive in 21.1% of the cases, CD 10 was positive in 21.1% of the cases, CD 79a was positive in 26.4% of the cases, and MUM-1 was positive in 21.1% of the cases. A high level of Ki-67 (> 70%) was found in 12 patients (63.2%).

In the present study, 18 of the 19 patients underwent surgery with radical resection; one patient underwent an appendectomy.

Emergency surgery was performed for 36.8% (n = 7) of the patients in the present study. One published study from Turkey reported that the 5-year survival rate was 64.3% in 17 primary small intestinal non-Hodgkin's lymphoma patients (12 patients DLBL) after emergency surgery [23]. In the present study, the prognosis of all cases with emergency surgery was good. The treatment of primary intestinal DLBL is a controversial issue. Because primary intestinal DLBL is a very rare disease, and there are few large scale prospective randomized studies, there is no consensus on the optimal treatment. Various treatment models, such as systemic chemotherapy, have been used to treat nodal DLBL; primary surgical resection of gastrointestinal lesions and postoperative chemotherapy has also been used. One multicenter study (Korean Lymphoma Group) reported on the oncologic outcomes of 345 patients diagnosed with primary intestinal DLBL [24]. That study reported that patients with localized disease (Lugano stage I/II) that underwent surgery plus chemotherapy had a lower relapse rate (15.3%) than patients that only received chemotherapy (36.8%, $P < 0.001$) [24]. The 3-year OS rate was 91.0% in the surgery plus chemotherapy group and 62.0% in the group that only received chemotherapy ($P < 0.001$) [24]. In another prospective non-randomized study of 40 patients, all patients received primary resection with lymph node dissection and postoperative CHOP chemotherapy; the 5-year OS rate was 88.9% and the 5-year DFS rate was 83.1% [25]. In a retrospective study of 56 patients with surgery plus chemotherapy, a 5-year OS rate of 86.4% was reported [26].

There are several prognosis factors for primary gastrointestinal DLBL. Surgical resection plus chemotherapy is an independent prognostic factor for OS. In a retrospective study of 224 patients, the bulk of the tumor (> 5 cm) proved to be a significant prognostic factor for DLBL treatment outcome [27]. The OS rate was affected by the tumor bulk, which was 91.23% vs. 86.8% if the tumor bulk was less than versus more than or equal to the median, respectively ($P = 0.05$) [27]. In another retrospective multicenter study of 345 patients, multivariate analysis demonstrated that surgical resection plus chemotherapy was an independent prognostic factor for OS [24]. In that study, because most of the patients with Lugano stage I/II and low IPI risk underwent surgery, the prognostic value was diluted in the multivariate analysis [24]. In another retrospective multicenter study of 114 patients, multivariate analysis identified treatment response, elevated serum lactic acid dehydrogenase (LDH) levels, and ECOG performance status as independent predictors of survival [28]. In a retrospective study of 85 patients, the IPI score was found to be an independent prognosis risk factor of OS (risk ratio = 3.609, 95% confidence interval, 2.2034–6.404; $P < 0.01$) [29]. In the present study, most patients had a low IPI score and Lugano stage I/II, and their prognosis was

good with median follow up of 49.2 months. In conclusion, surgery for primary gastrointestinal DLBL is feasible and acceptable. Low staging of primary gastrointestinal DLBL has good prognosis.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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