

Primary Gastrointestinal Non-Hodgkin Lymphoma Diagnosed After Emergency Surgery

ABSTRACT

Aim:

The aim of this study is to retrospectively evaluate the data of 15 patients who required immediate surgical intervention because of obstruction and/or perforation due to primary gastrointestinal Non-Hodgkin lymphoma.

Methods:

Patients who underwent surgical intervention due to gastrointestinal system bleeding, radiological evidence of perforation or intestinal obstruction and who were subsequently diagnosed with gastrointestinal lymphoma at Kocatepe University Department of General Surgery between August 2007 and September 2016 were examined retrospectively. Their medical records, clinical histories, symptoms, pathological reports, and treatment modalities were analysed.

Results:

There were 15 patients with primary gastrointestinal system lymphomas (male:8, female:7) and their mean age was 69.7 (40-90) years old. Tumors were determined in stomach for 7 (46.7%) patients (Kardia:3, Antrum:3, Corpus:1), in jejunum for one (6.6%), in ileum for 4 (26.7%), in right colon for 2 (13.3%), and in multiple organ involvement for one (6.6%) patient. Clinical manifestations were nausea and/or vomiting in 7 (46.6%) patients; loss of appetite in 8 (53.3%) patients; abdominal pain in 11 (73.3%) patients; and weight loss in 10 (66.6%) patients. The most common pathological subtype was diffuse large B-cell lymphoma (86.6%). All of 15 patients underwent surgical treatment and received postoperative chemotherapy. The mean follow-up period of the patients was 68 months (24-108 months). Only 1 (6.6%) patient died in the postoperative period.

31 **Conclusion:**

32 Initial presentation of primary gastrointestinal tract Non-Hodgkin lymphoma may be
33 obstruction, bleeding, or perforation. Clinicians and surgeons should keep this in mind while
34 assessing the patients with mechanic bowel obstruction.

35 **Key Words:** *Lymphoma, B-cell, ileus, perforation, bleeding, emergency*

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37 **INTRODUCTION**

38 Non-Hodgkin lymphoma (NHL) is a well-known hematologic malignancy. The
39 gastrointestinal (GI) tract is the most commonly involved extra nodal site. NHL is a group of
40 diseases with different morphology, immunophenotype, genetics, and clinical features. The
41 incidence of extranodal lymphomas in NHL has a considerable rate as high as 30–50%.
42 Primary gastrointestinal Non-Hodgkin Lymphoma (PGI NHL) is the most common
43 extranodal NHL, accounting for 30–45% in all extranodal NHLs [1,2]. Lymphomas can
44 involve any part of the GI tract from oral cavity to rectum. Surgical resection can play an
45 important role in the diagnosis and treatment of NHL involving the GI tract. Clinical
46 features, pathological features, and treatment of gastrointestinal NHL are different from other
47 extranodal lymphomas[1]. Obstruction, haemorrhage and perforation are rare and the
48 complications of lymphoma require life-threatening emergency operations. Diffuse large B-
49 cell lymphoma is the most common pathological subtype of PGI NHL. Diagnosis of PGI
50 NHL may be missed due to its unspecific clinical manifestation. Differential diagnosis of PGI
51 NHL from other types of GI tumors may not be possible in urgent surgeries[3].

52 The present study retrospectively summarized outcome of the 15 patients who underwent
53 emergency surgical intervention for gastrointestinal perforation or obstruction due to
54 gastrointestinal NHL and who were diagnosed with gastrointestinal NHL after the surgery.

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56 **MATERIALS AND METHODS**

57 Patients who underwent surgical intervention due to gastrointestinal system bleeding,
58 radiological evidence of perforation or intestinal obstruction and who were subsequently
59 diagnosed with gastrointestinal lymphoma at Kocatepe University Department of General
60 Surgery between August 2007 and September 2016 were examined retrospectively. Their
61 medical records, clinical histories, symptoms, demographic data, pathological reports and

treatment modalities were analysed. Radical surgery is defined as completely primary mass resection and regional lymph nodes dissection. Resection materials in the archive were fixed in 10% formol. Hematoxylin Eosin (HE) stained preparations obtained by paraffin embedding and immunohistochemical examination preparations were evaluated. Immunohistochemical staining was performed on a Leica-Bond device. Immunohistochemical studies are LCA, CD3, CD4, CD8, CD20, CD79a, CD10, Bcl-2, Bcl-6, CD5, Cyclin D1, CD138, and Ki-67. According to immunoprofile and histomorphology lymphoma subtype was performed

Ethical approval:

This study was approved by the institutional review board of Kocatepe University and supported by the research fund of Kocatepe University.(KU 29/2018)

RESULTS

At time of initial diagnosis of lymphoma, the patients' ages were between 40 and 90 years old with the mean age of 69.73 years. There were 15 patients that 7 were female and 8 were male. The patients presented with complaints of abdominal pain, distention nausea, vomiting, loss of appetite and weight. The clinical manifestations were nausea and/or vomiting in 7 (46.6%) patients; loss of appetite in 8 (53.3%) patients; abdominal pain in 11 (73.3%) patients; and weight loss in 10 (66.6%) patients. Tumor locations were in stomach for 7 (46.7%) patients (Kardia:3, Antrum:3, Corpus:1); in jejunum for 1(6.6%); in ileum for 4 (26.7%); in right colon for 2 (13.3%); and in multiple organ involvement for 1 (6.6%). Contrast-enhanced computed tomography (CT) of abdomen was performed on all patients for intestinal obstruction due to intraabdominal and/or intestinal mass. While 8 (53.3%) patients have only ileus, 8 (53.3%) patients had free fluid in their pelvis and pneumoperitoneum within the peritoneal cavity, which were compatible with perforation. We observed invagination in the CT scan of 1 (6.6%) patient (Table 1). All obstructions and perforations were the initial presentation of the intestinal lymphoma. There was no history of lymphoma in any of the patients Radical surgical treatment performed for the all patients. The lymphoma observed in the small bowel resection material obstructed, ulceration and infiltrated the entire wall of the intestine (Figure 1). Microscopic findings are shown in Figure 2a - 2b - 2c. Distributions of lymphomas were listed according to the HE analysis and immunophenotyping (Table 2).

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96 The mean follow-up period of the patients was 68 months (24-108 months). Only one (6.6%)
97 patient died in the postoperative period. The patient developed a pulmonary embolus on the
98 8th postoperative day. As a result, the patient was lost due to respiratory arrest. All patients
99 received chemotherapy or radiotherapy in the postoperative period.

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102 DISCUSSION

103 PGI NHL represents nearly 5-10% of all gastrointestinal malignancies [4,5]. NHL is the fifth
104 most common cancer in the UK (12,294 new cases in the UK in 2009), and the
105 gastrointestinal (GI) tract is the most common site of extranodal presentation (4–12% of all
106 NHL). However, this represents relatively small numbers (0.8– 1.2 cases per 100,000 persons
107 per year). NHL accounts for up to 10% of gastric malignancies, 18–24% of small bowel
108 cancers and just 0.2–0.4% of large bowel malignancies [6].

109 In this study, patients who referred to our emergency clinic during 9 years and operated after
110 their examinations were retrospectively investigated. Mean age at the onset of PGI NHL was
111 45-70 years old [1]. In our study, the mean age of the patients with PGI NHL was 69.7 years
112 old. The incidence of PGI NHL was approximately equal in women and men (male-female
113 ratio: 8/7), which was not consistent with previous studies [7,8,9]. This is likely due to the
114 small number of patients included in this study.

115 Stomach is the predominant site of PGI NHL followed by small intestine and colon [10]. The
116 results of our study are similar; stomach lymphoma is 46.6%, small intestinal bowel is 33.3%,
117 and colon is 13.3%. Furthermore, although the main clinical presentations of PGI NHL
118 include nonspecific gastrointestinal symptoms, others such as emergency patients, abdominal
119 pain, distention, nausea, vomiting and constipation are seen more common. Liang *et al.*
120 reported that the three most common symptoms at onset of 425 PGIL cases were abdominal
121 pain, gastrointestinal bleeding, nausea and vomiting [5]. In addition, Radic-Kristoet *et al.*
122 reported that the majority cases of PGI NHL were presented with epigastric pain (85%) and
123 dyspepsia (30%) [8]. Primary small bowel NHL has wide range of clinical presentations,
124 including nonspecific abdominal pain, ileus, weight loss, and perforation [11,12]. Clinical
125 manifestations in our patients were nausea and/or vomiting in 5 (33.3%) patients; loss of
126 appetite in 3 (20%) patients; abdominal pain in 14 (93.3%) patients; and weight loss in 2
127 (13.3%) patients. The ratios were similar to those seen in the previous studies [11,12].

As reported in earlier studies, free intestinal perforation due to NHL may occur spontaneously or after chemotherapy [13,14]. The initial presentation in our study was the obstruction due to mass that caused ileus in 13 (86.6%) patients and perforation in 4 (26.7%) patients. PGI NHL was frequently encountered as a single lesion with the size of 8.6 cm (range: 3–20 cm). Approximately 60–80% of primary intestinal NHLs were B-cell derived [15,16]. In this study, B-cell NHL was accounted as 93.3%, of which 86.6% were diffuse large B-cell lymphoma, 6.6% were mantle cell lymphoma and 6.6% were T-cell NHL. Many current studies reported that the most common involvement in primary intestinal lymphoma was in the ileum [17]. In this study, ileum was the more common primary tumor site than jejunum with the proportion of 80% and 20%, respectively. Patients with primary intestinal NHL received surgery with postoperative chemotherapy and/or radiotherapy [18,19].

CONCLUSION

Primary gastrointestinal Non-Hodgkin lymphoma is often detected as a result of a number of general symptoms after examinations. Its first treatment is usually chemoradiotherapy. However the initial presentation of primary gastrointestinal Non-Hodgkin lymphoma can be obstruction, bleeding or perforation. These may require emergency surgery. Clinicians and surgeons should keep this in mind while assessing patient with mechanic bowel obstruction.

Consent Disclaimer:

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

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Table.1

Clinical characteristics of the patients

Variables Total (n=15)

Age (years)	69.7 (40-90)
Gender	
Male	8 (53,3%)
Female	7 (46,7%)
Symptoms	
Nausea and/or vomiting	7 (46,7%)
Loss of appetite	8 (53,3%)
Abdominal pain	11 (73,3%)
Weight loss	10 (66,6%)
Bleeding	2 (13,3%)

Computed tomography	
Ileus	8 (53,3%)
Intestinal mass	7 (46,7%)
Intraabdominal multiple lymph nodes	15 (100%)
Perforation	8 (53,3%)
Invagination	1 (6,7%)
Site of disease	
Stomach	
Cardiya	3 (20%)
Corpus	1 (6,7%)
Antrum	3 (20%)
Jejunum	1 (6,7%)
Ileum	4 (26,7%)
Colon	2 (13,3%)
Multi organ	1 (6,7%)

Figure 1. The lymphoma infiltrating the entire wall of the intestine and obstructive mass.



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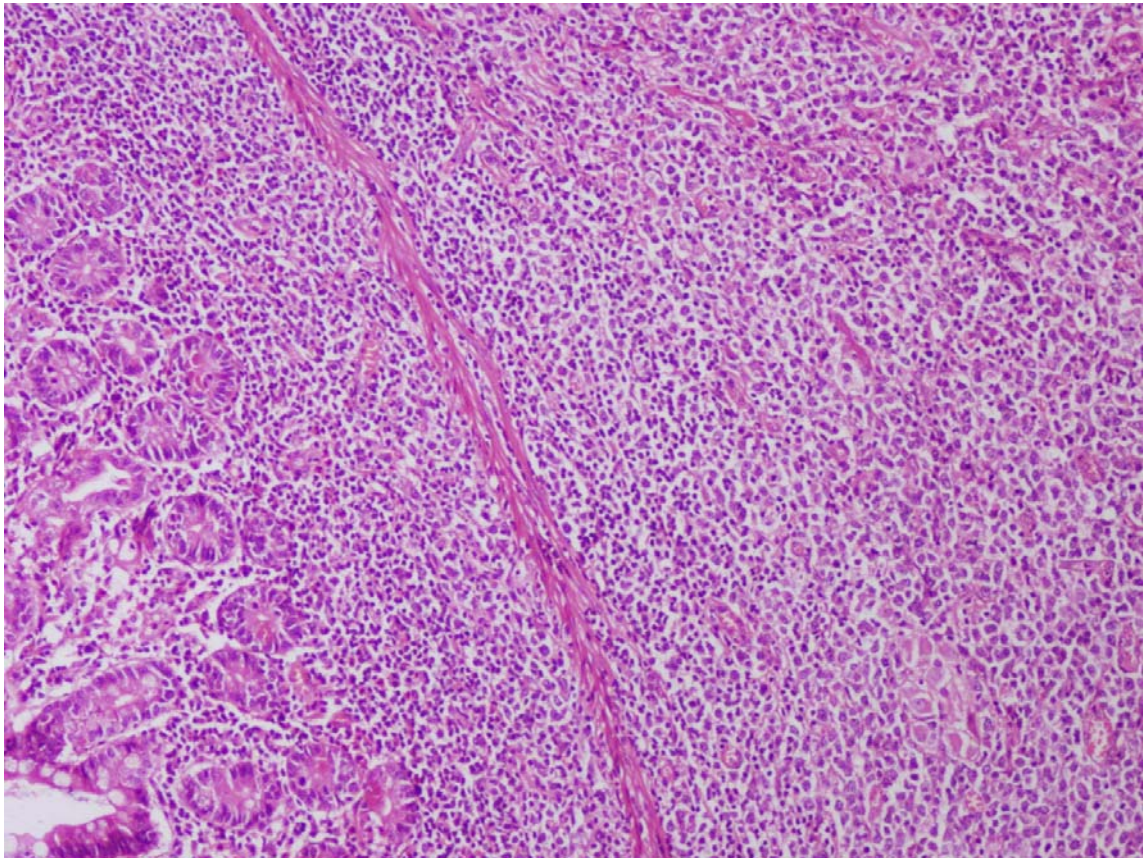
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229 **Figure 2a.** Atypical lymphocytes infiltrating the colon mucosa and submucosa. (x100 HE)

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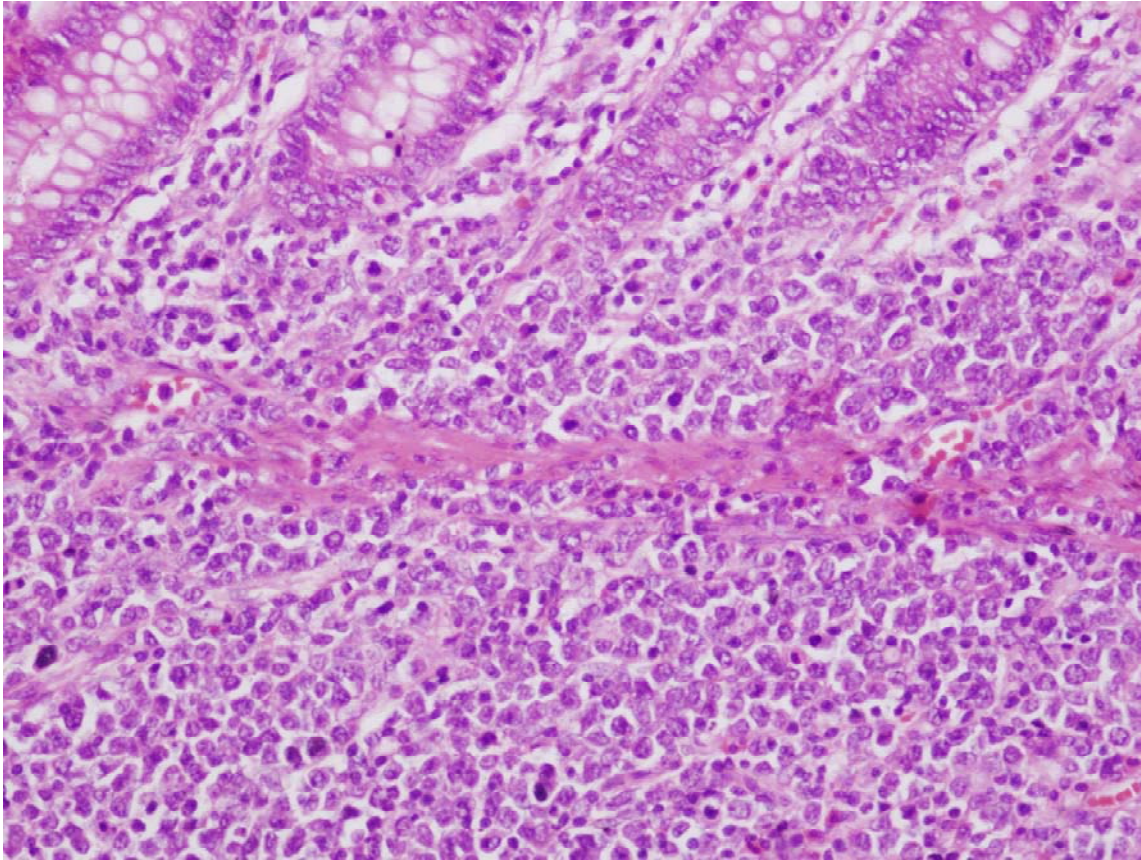


Figure 2b. Large, nucleus specific, mitotic rich nucleus, narrow eosinophilic cytoplasmic infiltrating lymphocytes located in the mucosa and submucosa. (x200 HE)

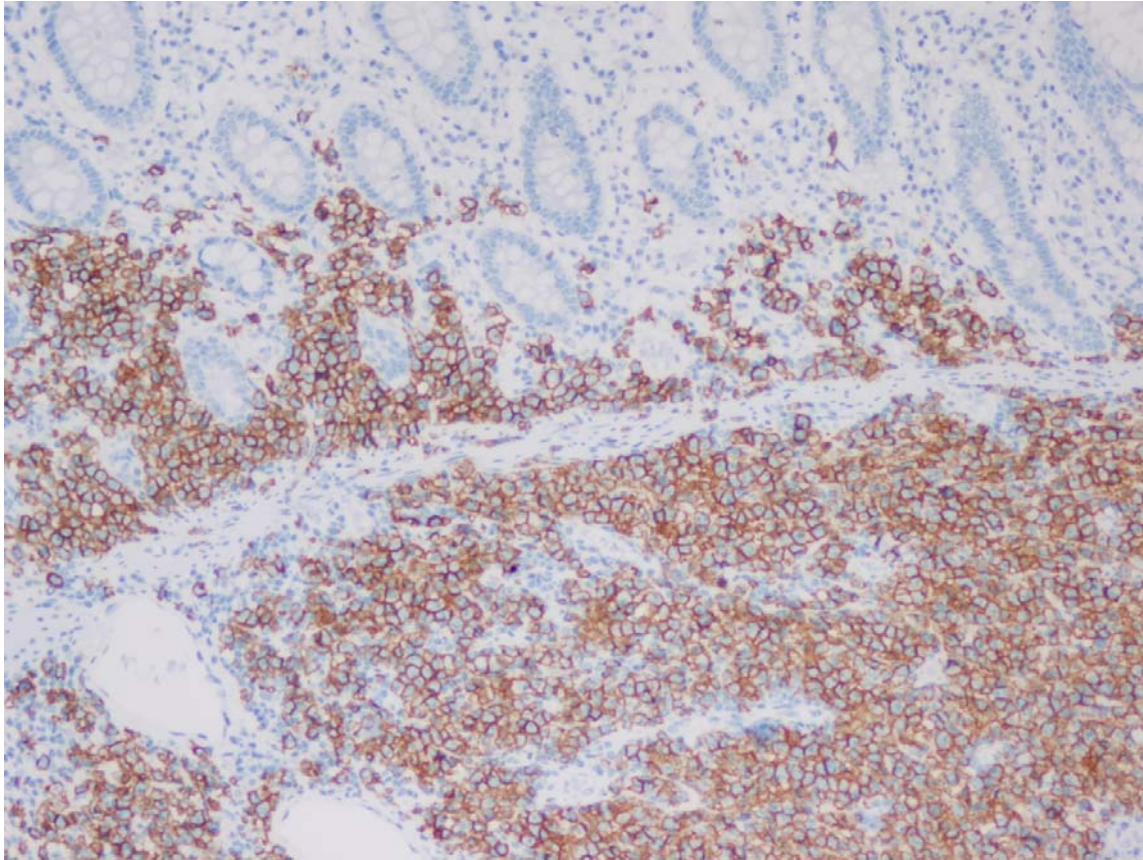


Figure 2c. Strong cytoplasmic reaction with atypical lymphocytic infiltration obtained by CD20 immunohistochemical study. (x100)

Table 2. Operation types and pathologic results

Tumor Size (cm)	8.6
Histological Subtype	
Diffuse large B cell lymphoma	13(86,6%)
Mucosa-associated lymphoid tissue lymphoma	1 (6,6%)
T cell lymphoma	1 (6,6%)
Clinical Stage	
I	2 (13,3%)
II	5 (33,4%)
III	6 (40%)
IV	2 (13,3%)

Chemotherapy after surgery	15 (100%)
Death	1 (6,6%)

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