ORIGINAL ARTICLE

Primary small intestinal non-Hodgkin lymphoma diagnosed after emergency surgery

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ABSTRACT

BACKGROUND: The aim of this study was to investigate clinical manifestation, diagnosis, treatment, and prognosis of patients with primary gastrointestinal non-Hodgkin lymphoma (PGI NHL), whose initial presentation was bowel obstruction or perforation.

METHODS: Data of patients who underwent surgical intervention due to radiological evidence of perforation or intestinal obstruction and were subsequently diagnosed with intestinal lymphoma at Baskent University hospitals between January 2007 and November 2014 were examined retrospectively. Medical records, clinical history, symptoms, pathological reports, and treatment modalities were analyzed.

RESULTS: Study population comprised 17 patients (8 male, 9 female) with PGI NHL and mean age of 52±20.2 years. Symptoms reported by the patients were abdominal pain, nausea, vomiting, weight loss, and loss of appetite. All 17 patients underwent surgical treatment; 12 also received postoperative chemotherapy. Most common pathological subtype was diffuse large B-cell lymphoma (70.5%). Mean follow-up time was 26 months (range: 1–69 months) and 5-year survival rate was 64.3%.

CONCLUSION: Initial presentation of PGI NHL may be obstruction with or without perforation; clinicians and surgeons should keep this in mind while assessing patient with bowel obstruction, and particularly patient in fifth decade of life.

Keywords: Emergency treatment; general surgery; ileus, intestinal perforation; lymphoma; small intestine.

INTRODUCTION

Primary gastrointestinal non-Hodgkin lymphoma (PGI NHL) is most common type of extranodal lymphoma (30% to 50% of all extranodal lymphomas). PGI NHL is most often seen in the stomach, followed by the colon and small intestine.[1] Diffuse large B-cell lymphoma is most common pathological subtype of PGI NHL. Diagnosis of PGI NHL may be missed due to its unspecific clinical manifestation. Differential diagnosis of PGI NHL from other types of gastrointestinal (GI) tumors may not be possible. It has been reported that approximately 20% of all small bowel malignancies are newly diagnosed NHL.[2] Most frequently seen symptom of GI lymphoma is abdominal pain; however, signs and symptoms are generally nonspecific. "B symptoms," such as fever, weight loss, and night sweats, are not common in nonsystemic disease, and are seen in fewer than 12% of patients.[3] Some 30% to 50% of patients are admitted to hospital with acute abdominal pain, and 25% of these have GI perforation.[4] Obstruction and perforation are uncommon and life-threatening complications of lymphoma that can occur either at diagnosis or during the treatment course. Occurrence of obstruction or perforation increases mortality rate as result of circumstances such as sepsis, multi-organ failure, prolonged hospitalization, impaired wound healing, and delay of chemotherapy.

The present study retrospectively summarized outcome of 17 patients who underwent emergency surgical intervention for intestinal perforation or obstruction due to intestinal NHL and were diagnosed with intestinal NHL after surgery.

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MATERIALS AND METHODS

Records of patients who underwent surgical intervention following radiological evidence of perforation or intestinal obstruction and were diagnosed with intestinal lymphoma after the surgery at Baskent University Faculty of Medicine, Ankara; Baskent University Adana Training and Research Hospital; and Baskent University İzmir Zübeyde Hanım Training and Research Hospital between January 2007 and November 2014 were examined retrospectively. Data of medical records, clinical history, symptoms, preoperative investigations, pathology reports, and details of management were analyzed. This study was approved by Baskent University institutional review board and supported by Baskent University research fund (KA14/143).

Statistical Analyses

Statistical analyses of the data were performed using SPSS software, version 11.5 (IBM Corp., Armonk, NY, USA) Descriptive statistics for continuous and discrete numeric variables were expressed as mean±standard deviation or median (minimum-maximum) values and categorical variables as number of cases (%). Annual cumulative survival rate, median survival time, and 95% confidence interval were calculated using Kaplan-Meier survival analysis.

RESULTS

At time of initial diagnosis of lymphoma, the patients were between 25 and 82 years of age, with median age for the group of 52 years. Of 17 patients, 9 were female and 8 were male. The patients presented with complaints of abdominal pain, nausea and/or vomiting, loss of appetite, and weight loss; most common symptom was abdominal pain. Physical examinations revealed abdominal tenderness and muscular rigidity. Contrast-enhanced computed tomography (CT) of the abdomen was performed on all patients for intestinal obstruction due to intraabdominal and/or intestinal mass. In 11 patients, only ileus was seen, whereas in 4 patients, free fluid in the pelvis and pneumoperitoneum within the peritoneal cavity, which were compatible with perforation, were detected. In 1 patient, invagination was observed in CT scans. Tumor localization was jejunum in 8 patients and ileum in 9 patients (Figure 1a–c). All obstruction and perforation events were initial presentation of intestinal lymphoma. There was no history of lymphoma in any of the patients; Patient 5 had history of acute lymphocytic leukemia, Patient 6 had history of renal-cell carcinoma, and Patient 17 had history of coeliac disease (Table 3).

Clinical characteristics, clinical symptoms (or signs), clinical features, and outcome of the 17 patients with intestinal obstruction or perforation are summarized in Table 1, Table 2, and Table 3.

Resection of affected segment and end-to-end anastomosis

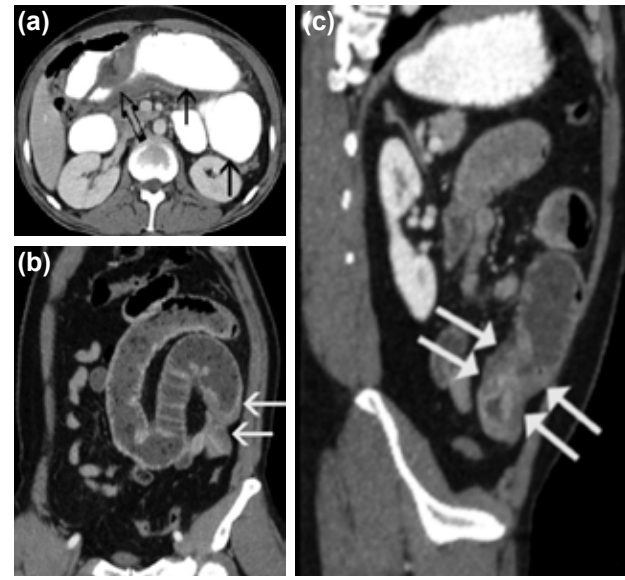

Figure 1. (a) A 25-year-old man presented with weight loss and loss of appetite. Oral and intravenous contrast-enhanced axial computed tomography image obtained from upper abdominal level demonstrates obstruction of the jejunum (open arrow) and extreme dilatation of proximal jejunal loops (arrows). Histopathology diagnosis was diffuse large B-cell lymphoma; **(b)** A 40-year-old man presented with nausea and vomiting. Coronal **(b)** and sagittal oblique **(c)** images reveal thickening of the small bowel wall at jejunal level (arrows in B and double arrows in **(c)** and mild dilatation of proximal loops. Histopathology diagnosis was T-cell lymphoma.

Table 1. Clinical characteristics of patients

Variables	Total (n=17)
Age (years; median)	52 (25–82)
Gender, n (%)	
Male	8 (47)
Female	9 (53)
Symptoms, n (%)	
Nausea and/or vomiting	5 (29.4)
Loss of appetite	3 (17.6)
Abdominal pain	14 (82.3)
Weight loss	2 (11.7)
Computed tomography, n (%)	
Ileus	13 (76.4)
Intestinal mass	5 (29.4)
Intraabdominal mass	6 (35.2)
Intraabdominal multiple lymph nodes	3 (17.6)
Perforation	4 (23.5)
Invagination	1 (5.8)
Site of disease, n (%)	
Ileum	9 (53)
Jejunum	8 (47)

Table 2. Clinical symptoms or signs of patients

Variables	Total (n=17)
Size (cm; median)	5 (1–13)
Histological subtype, n (%)	
Diffuse large B cell lymphoma	12 (70.5)
Mucosa-associated lymphoid tissue lymphoma	2 (11.7)
Anaplastic T-cell lymphoma	1 (5.8)
Peripheral T-cell lymphoma	1 (5.8)
Enteropathy type T-cell lymphoma	1 (5.8)
Clinical stage, n (%)	
I	5 (29.4)
II	5 (29.4)
III	7 (41.1)
IV	–
Chemotherapy after surgery, n (%)	12 (70.5)
Metastasis	4 (23.5)
Lung	1 (5.8)
Liver	1 (5.8)
Intraabdominal	4 (23.5)
Death, n (%)	5 (29.4)

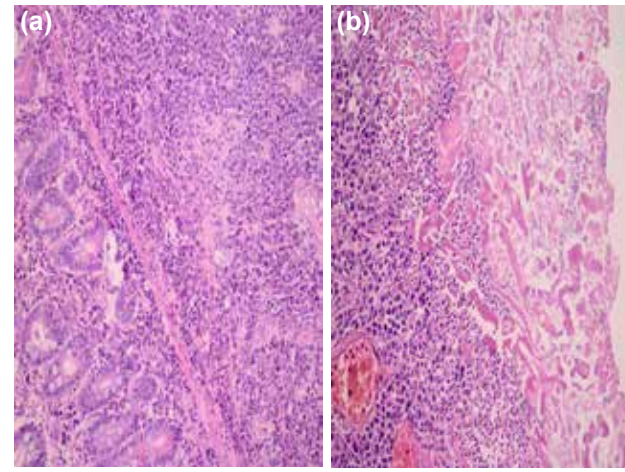

Figure 2. (a) Infiltration of medium to large neoplastic lymphocytes beneath the colonic glands, **(b)** Ulceration and Candida hyphae and spots on the surface (A: HE x100; B: HE x100).

tistically significant correlation between tumor stage and survival rate, which was 75% in patients with stage I-II, and 83.3% in patients with stage III (p=0.784). Despite achieving remission, 4 of these patients relapsed within median disease-free period of 31.5 months (range: 19-46 months). In all 4, relapse occurred in distant lymph node location with or without extranodal involvement. Two of the 7 patients who

Table 3. Clinical features and outcomes of patients

Patients	Medical history	Site of disease	Radiological findings	Histological subtype	Stage	Results	Follow-up (months)
1	–	Jejunum	Perforation	MALToma	IIIE	Death	–
2	–	Jejunum	Ileus	Diffuse large Bcell lymphoma	IIIE	Remission	8
3	–	Jejunum	Ileus, Intraabdominal mass	Peripheral T-cell lymphoma	IE	Metastasis	21
4	–	Jejunum	Ileus, Intraabdominal mass	Diffuse large B-cell lymphoma	IE	Metastasis	19
5	Acute lymphocytic leukemia	Ileum	Ileus, Intraabdominal mass	Diffuse large B-cell lymphoma	IIE	Death	–
6	Renal-cell carcinoma	Jejunum	Ileus, Intraabdominal mass	Diffuse large B-cell lymphoma	IIIE	Remission	9
7	–	Jejunum	Ileus, Intraabdominal mass	Diffuse large B-cell lymphoma	IIIE	Death	–
8	–	Ileum	Perforation	Diffuse large B-cell lymphoma	IIE	Remission	69
9	–	Ileum	Perforation	Anaplastic T-cell lymphoma	IIE	Death	–
10	–	Jejunum	Ileus, Intraabdominal mass	Diffuse large B-cell lymphoma	IIIE	Metastasis	46
11	–	Ileum	Ileus, Intraabdominal mass	MALToma	IIE	Remission	46
12	–	Ileum	Ileus, Intraabdominal mass	Diffuse large B-cell lymphoma	IIIE	Metastasis	42
13	–	Ileum	Ileus, Intraabdominal mass	Diffuse large B-cell lymphoma	IE	Remission	25
14	–	Jejunum	Perforation	Diffuse large B-cell lymphoma	IIIE	Remission	3
15	–	Ileum	Invagination	Diffuse large B-cell lymphoma	IE	Remission	13
16	–	Ileum	Ileus, Intraabdominal mass	Diffuse large B-cell lymphoma	IIE	Death	4
17	Coeliac disease	Ileum	Ileus, Intraabdominal mass	Peripheral T-cell lymphoma	IIIE	Remission	3

MALToma: Mucosa –associated lymphoid tissue lymphoma.

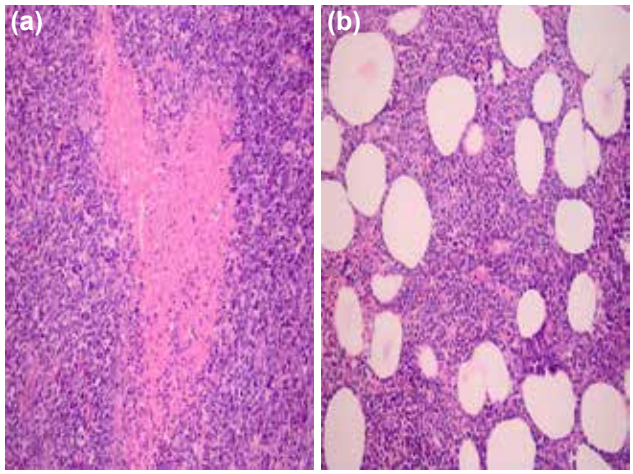

Figure 3. (a) Necrosis and **(b)** periserosal adipose tissue infiltration (A: HE x100; B: HE x100).

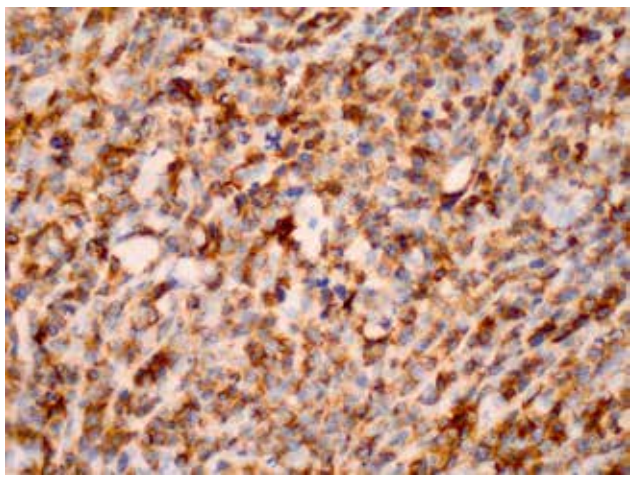

Figure 4. Immunohistochemical stain indicating strong, diffuse CD3 positivity in the neoplastic lymphocytes (CD3 x200).

had stage III tumor died, as well as 3 of the 10 patients who had stage I-II tumor.

DISCUSSION

The gastrointestinal tract is the most common site of extranodal NHL. However, primary small bowel lymphoma, which is second most common small bowel neoplasm after adenocarcinoma, is relatively rare.[3,4] It has been reported that approximately 20% of all small bowel malignancies are newly diagnosed NHL.[2] Some 30% to 50% of patients are admitted to hospital with acute abdomen and 25% of them have GI perforation.[4]

Research of 7-year period at 3 different centers yielded only 17 patients who underwent surgical intervention with radiological evidence of perforation or intestinal obstruction and were diagnosed with intestinal lymphoma after surgery. Although there are many publications about small intestine lymphoma, PubMed search with keywords "lymphoma, small intestine, ileus" returned only 28 articles, most of which were case reports. None was related to Turkey or the immediate area. PubMed search using "lymphoma, small intestine, emergency treatment, general surgery, ileus, intestinal perforation" also yielded no results.

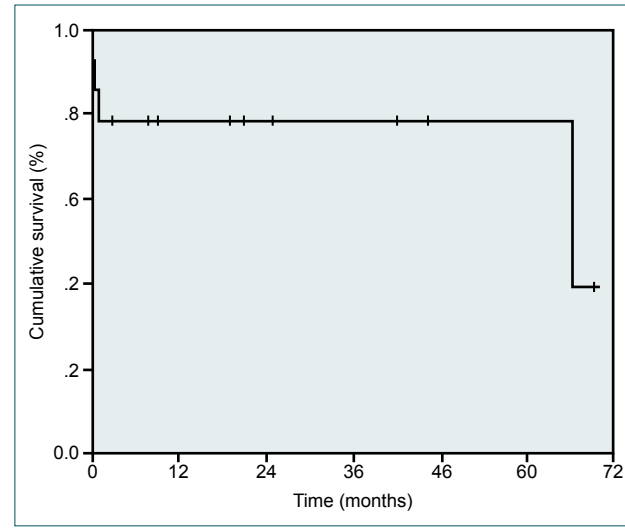

Figure 5. Kaplan-Meier survival curves for 14 cases of primary gastrointestinal non-Hodgkin lymphoma.

Particularly in patients over 50 years of age, primary small bowel NHL should be considered in differential diagnosis of patients with small bowel obstruction in addition to causes of intestinal obstruction such as hernia, adhesions, and bezoars. In our study, median age of the patients with PGI NHL was 52 years (range: 25–82 years). Incidence of PGI NHL was higher in women than in men (male:female ratio: 8:9), which was not consistent with previous studies.[5,6] This is likely due to small number of patients included in present study.

In recent research, associations between intestinal lymphoma and immunosuppression after transplantation, inflammatory bowel disease, or human immunodeficiency virus infection have been found.[7–9] Medical history of our patients was insignificant, except for coeliac disease in Patient 17. Patient 5 had history of acute lymphoblastic leukemia (ALL) and Patient 6 had history of renal cell carcinoma (RCC). To our knowledge, there are no data available regarding correlation between these 2 diseases and intestinal lymphoma. Further studies could be conducted to investigate potential associations between intestinal lymphoma and ALL or intestinal lymphoma and RCC.

Primary small bowel NHL has wide range of clinical presentations, including nonspecific abdominal pain, ileus, weight loss, and perforation.[10,11] Clinical manifestations in our patients were: nausea and/or vomiting in 5 (29.4%) patients; loss of appetite in 3 (17.6%) patients; abdominal pain in 14 (82.3%) patients; and weight loss in 2 (11.7%) patients. These ratios were similar to those seen in previous studies.

As reported in earlier studies, free intestinal perforation due

to NHL may occur spontaneously or after chemotherapy.[12,13] In our study, initial presentation was obstruction due to mass, which caused ileus in 13 patients and perforation in 4 patients. PGI NHL was frequently encountered as single lesion with size of 5.5±3.3 cm (range: 1–13 cm). Most primary intestinal lymphomas are of B-cell origin,[14,15] and our data confirmed this: 14 (82.3%) of masses were of B-cell origin, while 3 (17.6%) were of T-cell origin. In the present study, ileum was more common primary tumor site than jejunum, with proportion of 53% and 47%, respectively. Although difference between tumor locations was not statistically significant, it is consistent with results of previous studies indicating ileum was most common site.[16]

There is a lack of evidence to guide postoperative management of emergency presentations of intestinal NHL with respect to effect on overall prognosis and optimal timing of postoperative chemotherapy. Chemotherapy with CHOP regimen has been shown to be as effective as other chemotherapy regimes. For stage I–II intestinal NHL, surgical resection and postoperative chemotherapy seems to be preferred treatment choice and has 5-year survival rate of 50% to 67%. In stages III–IV, ideal treatment is less clear.[17–19] Three of our patients died in the first month due to postoperative complications, 1 patient died after 4 months, and 1 patient died after 5.5 years. Total of 12 patients received CHOP regimen after initial surgery. Our cumulative survival rate results were also different from those reported in the literature. It has been reported that patients at early stage (stage I-II) and patients with B-cell lymphoma have higher cumulative survival rate.[17,18] However, our data demonstrated no statistical difference in survival rate between B-cell and T-cell lymphoma, or between early stages and stage III. We propose that this contradiction may also be explained by small number of patients used here, and that if the patient number increases, results may be similar to previous studies.

In conclusion, our data demonstrated that primary small bowel B-cell lymphoma is more common than T-cell lymphoma. Initial presentation of the disease may be obstruction with or without perforation. Therefore, clinicians and surgeons should keep this in mind when assessing patient with bowel obstruction, and particularly patient in fifth decade of life.

Acknowledgments

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Conflict of interest: None declared.

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ORİJİNAL ÇALIŞMA - *ÖZET*

Acil cerrahi sonrası tanı alan primer ince bağırsak non-Hodgkin lenfomaları

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AMAÇ: Bizim bu çalışmamızda amacımız, hastaneye obstrüksiyon veya perforasyon bulgularıyla başvuran ve ameliyat sonrası primer intestinal non-Hodgkin lenfoma tanısı alan hastaların klinik bulgularını, tanı, tedavi ve prognozlarını incelemektir.

GEREÇ VE YÖNTEM: Başkent Üniversitesi Tıp Fakültesi Hastanesi Genel Cerrahi Anabilim Dalı'nda, Ocak 2007–Kasım 2014 yılları arasında, radyolojik olarak obstrüksiyon veya perforasyon varlığı kanıtlanmış ve ameliyata alındıktan sonra non-Hodgkin lenfoma tanısı alan hastaların özgeçmişleri, başvuru anındaki semptomları, patoloji raporları ve cerrahi tedavi sonrası takipleri geriye dönük olarak incelendi.

BULGULAR: Çalışmamıza dahil edilen primer intestinal non-Hodgkin lenfoma tanısı alan 17 hastanın ortalama yaşı 52±20.2, erkek: kadın oranı 8.9 idi. Hastaların başvuru anındaki semptomları; karın ağrısı, bulantı-kusma, kilo kaybı ve iştahsızlıktı. Tüm hastalar cerrahi olarak tedavi edildi ve 12 hastaya ameliyat sonrası dönemde kemoterapi uygulandı. En sık rastlanan patolojik alt tip diffüz B-hücreli lenfoma idi (%70.5). Hastaların takip süresi 26 (dağılım, 1–69) ay, sağkalım oranı %64.3 idi.

TARTIŞMA: Primer intestinal non-Hodgkin lenfoma hastalığının ilk prezentasyonu, hastalarda gelişen intestinal obstrüksiyon ve/veya perforasyon olabileceği için, özellikle 50. dekatta bağırsak obstrüksiyonu ile gelen hasta değerlendirilirken non-Hodgkin lenfoma akılda bulundurulmalıdır.

Anahtar sözcükler: Acil cerrahi; genel cerrahi; ileus; ince bağırsak; intestinal perforasyon; lenfoma.

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