

Case Report

Colorectal Lymphoma, a Case Series from a Single Center

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Key Words

Colorectal lymphoma;
Surgery;
Diffuse large B-cell lymphoma

Purpose. This study aimed to characterize the initial clinical presentation, treatment and survival condition of patients with colorectal lymphoma.

Methods. This is a single-center, retrospective, non-randomized study. The study was from November 2008 to September 2019. The clinical manifestation, Ann Arbor stages and management were documented and analyzed.

Results. Sixteen patients who were diagnosed with colorectal lymphoma were included in the analysis. Seven underwent surgery, while nine underwent nonsurgical treatment. The most common symptom was lower gastrointestinal bleeding (31.25%). The most common site was ascending colon (43.75%), and the most common lymphoma subtype was diffuse large B-cell lymphoma (62.5%). Among the seven surgically treated patients, five underwent emergent surgery because of perforation (two patients, 28.6%), obstruction (2 patients, 28.6%), and anemia (hemoglobin < 10 g/dL) (one patient, 14.3%). In the surgical group, one patient died of lymphoma. In the non-surgical group, one patient also died of lymphoma. The five-year overall survival rate was 40% for surgery group, and 50% for non-surgery group.

Conclusion. Colorectal lymphoma is a rare disease, accounting for only 0.34% of colorectal malignancy in our study. It presented with various symptoms, and has a low lymphoma-related mortality rate. Further studies are required to elucidate the benefits of surgery for these patients.

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Primary colorectal lymphoma is a rare disease, accounting for less than 1% of all colorectal malignancies.¹⁻¹¹ Various clinical presentations have been reported, including weight loss, abdominal pain, low gastrointestinal bleeding, and obstruction. The incidence is higher in male, with a male-to-female ratio of 2:1 and is highest at ages 50 to 70 years.^{9,12-15}

The optimal treatment for colorectal lymphoma has been controversial. Some studies reported a marginal survival advantage with surgical resection, whereas other studies did not demonstrate a survival ad-

vantage via surgical resection.¹⁶⁻¹⁸ This study aimed to shed light on this topic by characterizing the initial clinical presentation, treatment, and survival condition of colorectal lymphoma in a single medical center.

Material and Method

Data of patients with colorectal lymphoma were retrospectively collected between December 2008 and September 2019, using the computer data base of

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Changhua Christian Hospital. The inclusion criteria were as follows: (1) patients diagnosed with colorectal lymphoma, who were identified using the International Classification of Diseases, 10th Revision, clinical modification 10 code (ICD-10-CM)-; (2) pathologic reports contained key words of lymphoma and the specimen collected via surgical resection or colonoscopic biopsy; and (3) data matched with the criteria of primary colorectal lymphoma defined by Lewin et al.,⁴ after comprehensive reviewing chart records. The definition of primary colorectal lymphoma by Lewin et al.⁴ includes patients who present with lymphoma which originated from an extranodal site, given that the extranodal component is clinically dominant. Among the selected patients, those who lost follow up at our hospital were excluded from this study. Information about gender, age, initial presentation of disease, Ann Arbor staging, primary tumor location, tumor cell type, comorbidity including diabetes mellitus, hypertension, viral hepatitis, survival months, cause of mortality were obtained. For patients who underwent surgery, details such as the type of surgery (elective or emergency), and the presence of perforation were also included.

Results

The study scheme is shown in Fig. 1. Between December 2008 and September 2019, 6508 patients had ICD-10 code between C18 and C20. After review of charts and pathologic reports, 22 patients with colorectal lymphoma were identified, and all of them met the criteria of primary colorectal lymphoma defined by Lewin et al.⁴ Among these identified patients, six were excluded due to loss to follow-up at our hospital. The characteristic data, including initial presentation, tumor location, Ann Arbor staging and cell subtype of tumor, are listed in Table 1. Of the 16 patients enrolled in study group, seven patients underwent surgery and nine were treated non-surgically. Among the surgically treated patients, five underwent emergent surgery, for the following indications: colonic perforation in two patients, colonic obstruction in two patients and severe anemia secondary to colonic bleed-

ing in one patients. Two patients were treated with elective surgery, and they did not suffer colonic perforation, however, one of them manifested with ascending-to-transverse fistula. The most common tumor location was cecum (n = 3) and ascending colon (n = 3) in surgical group and the ascending colon (n = 4) in nonsurgical group. One of non-surgically treated patient presented with multifocal tumor at the cecum, transverse colon, and sigmoid colon. Most of the surgically treated patients were at Ann Arbor stage IV (n = 5), while nearly half of the non-surgical treated patients were at Ann Arbor stage II (n = 4). The most common cell type was diffuse large B-cell lymphoma (DLBCL) (n = 7) in the surgical group, and DLBCL (n = 3) and mucosa-associated lymphoid tissue (MALT) lymphoma (n = 3) in the non-surgical group (Table 1). The clinical events of surgically treated patients are listed at Table 2, and that of non-surgically treated patients are listed at Table 3.

Among the seven patients treated with surgery,

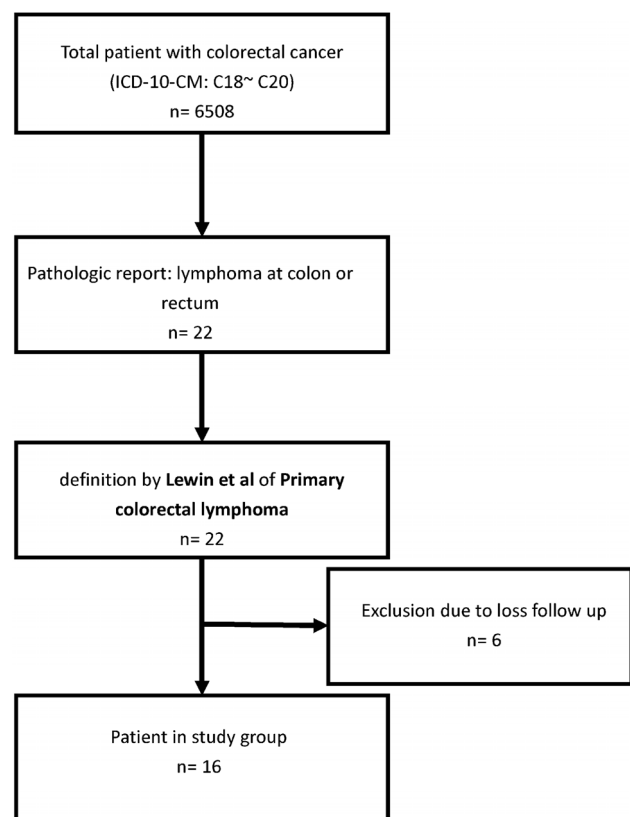


Fig. 1. Diagram outlining data for the patients involved in the study.

Table 1. Patient demographics

Characteristics	Surgical group (n = 7)	Non-surgical group (n = 9)
Presentation, n (%)		
LGIB	3 (42.86%)	2 (22.22%)
Abdominal pain	1 (14.28%)	1 (11.11%)
Incidental/screening	1 (14.28%)	3 (33.33%)
Obstruction	2 (28.57%)	2 (22.22%)
Body weight loss	0 (0%)	1 (11.11%)
Tumor location		
Cecum	3 (42.86%)	2 (22.22%)
Ascending	3 (42.86%)	4 (44.44%)
Transverse	1 (14.28%)	0 (0%)
Descending	0 (0%)	2 (22.22%)
Sigmoid	0 (0%)	0 (0%)
Rectum	0 (0%)	0 (0%)
Multifocal (colorectal)	0 (0%)	1 (11.11%)
Disease severity		
Ann Arbor stage I	0 (0%)	0 (0%)
Ann Arbor stage II	2 (28.57%)	4 (44.44%)
Ann Arbor stage III	0 (0%)	2 (22.22%)
Ann Arbor stage IV	5 (71.43%)	3 (33.33%)
Bone marrow biopsy+	0 (0%)	2 (22.22%)
Laboratory data		
Hemoglobin, mean (SD), g/dL	9.7 (3.63)	11.63 (3.48)
WBC, mean (SD), cells/ μ L	10.53 (4.39)	10.43 (7.63)
Subtype		
DLBCL	7 (100%)	3 (33.33%)
Mantle cell	0 (0%)	2 (22.22%)
MALT	0 (0%)	3 (33.33%)
Unclassified	0 (0%)	1 (11.11%)

LGIB: lower gastrointestinal bleeding; WBC: white blood count; DLBCL: diffuse large B-cell lymphoma; MALT: mucosal-associated lymphoid tissue.

Table 2. Clinical events of surgically treated patients

No	Age	Gender	Initial presentation	LDH (u/L)	Cell type/location	Ki-67	Ann Arbor	Elective or emergent	Perforation	Current condition or survival length
1	87	M	LGIB	Nil	DLBCL/cecum	70-80	II	Emergent	+	Mortality after 4 months, sepsis
2	76	F	FOBT positive (screen)	138	DLBCL/cecum	> 90	IV	Emergent	+	Mortality after 25 months, sepsis
3	66	M	Abdominal pain	158	DLBCL/A-colon	80	IV	Elective	-	Survival
4	63	M	Obstruction	146	DLBCL/A-colon	High	IV	Emergent	-	Mortality after 5 months, OHCA
5	47	M	LGIB	Nil	DLBCL/A-colon	70	II	Emergent	-	Survival
6	72	F	LGIB	140	DLBCL/T-colon	70	IV	Elective	T-A fistula	Survival
7	64	M	Obstruction	Nil	DLBCL/cecum	Nil	IV	Emergent	-	Mortality after 1 month, sepsis and pneumonia

LDH: lactate dehydrogenase; LGIB: lower gastrointestinal bleeding; FOBT: fecal occult blood test; M: male; F: female; DLBCL: diffuse large B-cell lymphoma; A-colon: ascending colon; T-colon: transverse colon; T-A fistula: transverse colon to ascending colon fistula; OHCA: out-of-hospital cardiac arrest.

five patients received chemotherapy, while two did not. One of the two patients who did not receive chemotherapy was an 87-year-old male patient, who underwent emergent surgery due to perforation; his family required hospice care. The other patient of the two received emergent surgery due to colonic obstruction, and he died of pneumonia within one month after surgery. Six of the nine non-surgically treated patients received chemotherapy, and three of them did not. Of the three patients treated non-surgically, one was admitted due to anemia, and was diagnosed with DLBCL during the survey of anemia; she died of pneumonia within one month after admission. The other two patients had MALT lymphoma and survived until the last follow up. There was one patient in our study who received radiotherapy for brain metastasis and underwent emergent surgery for colonic obstruction followed by chemotherapy. However, this patient suffered from a cardiac arrest outside the hospital.

Of the seven surgically treated patients, four patients (57.14%) developed mortality, and one of them (14.28%) had cancer related mortality. Of the nine non-surgically treated patients, three patients (33.33%) developed mortality, and one of them (11.11%) had cancer related mortality. None of the patients who opted for nonsurgical treatment experienced any indication for emergent surgery, such as perforation or obstruction. Three complete remissions occurred among the surgically treated patients, all of whom received

Table 3. Clinical events of non-surgically treated patients

No.	Age	Gender	Initial presentation	LDH (u/L)	Cell type/location	Ki-67	Ann Arbor	Current condition or survival length
1	73	F	Body weight loss	159	DLBCL/D-colon	> 95	III	Survival
2	60	M	Obstruction	183	MALT/A-colon	Nil	II	Survival
3	77	M	LGIB	159	Mantle cell lymphoma/A-colon	10	III	Mortality after 5 months, OHCA
4	75	F	LGIB	Nil	DLBCL/A-colon	Nil	IV	Mortality after 1 month, pneumonia
5	74	F	FOBT positive (screen)	339	High-grade B-cell lymphoma/cecum	Nil	IV	Survival
6	64	M	FOBT positive (screen)	130	MALT/A-colon	Mild increased	II	Survival
7	46	M	Colonoscopy (screen)	165	Mantle cell lymphoma/cecum, T, S colon	Nil	II	Survival
8	68	F	Abdominal pain	Nil	MALT/D colon	Low	II	Survival
9	86	M	Obstruction	330	DLBCL/cecum	Nil	II	Mortality after 3 months, sepsis

LDH: lactate dehydrogenase; M: male; F: female; LGIB: lower gastrointestinal bleeding; FOBT: fecal occult blood test; DLBCL: diffuse large B-cell lymphoma; MALT: mucosal-associated lymphoid tissue; A-colon: ascending colon; D-colon: descending colon; D, S-colon: descending and sigmoid colon; OHCA: out-of-hospital cardiac arrest.

chemotherapy. None of patients with complete remission suffered colonic perforation.

Discussion

Chemotherapy for lymphoma varies with different cell type. Management of diffuse large B cell lymphoma involves treatment with an R-CHOP – (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) like regimen as first line therapy. For MALT lymphoma, there is a paucity of data on ideal management. Antibiotics for *H. pylori* eradication is thought effective in gastric MALT lymphoma, but does not have the clear efficacy in non-gastric MALT lymphoma. For localized lesion, management depends on size and depth. Endoscopic submucosal resection is suitable for small, shallow lesion. For deeper or larger lesion, surgical resection and radiotherapy were reported beneficial. Adjuvant systemic chemoimmunotherapy can be considered if positive margins or the setting not amenable to RT. Disseminated MALT lymphoma is treated primarily with chemotherapy. A variety of regimens has been demonstrated, including alkylators, purine analogs, and anthracyclines.

All patients with complete remission in the studies were treated surgically and were followed by chemo-

therapy. Additionally all of them had a cell type of DLBCL. DLBCL has been reported to be the most common cell type affecting the gastrointestinal tract and colon.^{9,11} DLBCL is composed of rapidly proliferating cells and are more aggressive than other B cell lymphomas. Lymphomas with rapid proliferation such DLBCL or Burkitt's lymphoma, are usually sensitive to multiagent immunochemotherapy.¹ Some survival benefit of surgical resection for patients with DLBCL has been reported. A retrospective analysis that included 345 patients with stage I/II intestinal DLBCL demonstrated that surgery plus chemotherapy lead to a lower recurrence rate (15.3%), when compared with chemotherapy alone (36.8%) and an improved overall survival rate (91%) compared with chemotherapy alone (62%).¹⁹ However, in our study, there were three patients with DLBCL, and two of them died of a non-cancer cause within three months after diagnosis. Therefore, long term comparison was not obtained. Advantage provided by surgery could not be concluded in our study.

MALT lymphoma is known to have good prognosis, despite its lower response to chemotherapy.²⁰ There were three patients with MALT lymphoma in our study, all of whom were treated non-surgically, and survived until the last follow up. Two of them did not receive chemotherapy and survived for three years

and ten years until the last follow-up. The remaining patient received Rituximab x1 +RCOPx5 and survived for two years until the last follow-up. All surgically treated patients were diagnosed with DLBCL. Thus, whether surgical resection had any benefit on MALT lymphoma could not be identified.

There were some limitations in our study. One limitation is the small sample size. Tumor cell subtype, tumor location and staging were not well analyzed due to the small number of patients. Another limitation is that long-term follow-up could not be performed in some patients due to the limited surveillance. Studies enrolling larger patient number and longer surveillance are needed to identify whether survival benefit is provided by surgical resection.

Conclusion

In conclusion, colorectal lymphoma is a rare disease, accounting for 0.34% of colorectal malignancies in our study. The benefit of surgery requires further study with larger patient number and longer surveillance.

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病例報告

大腸直腸淋巴癌的單一中心病例研究

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目的 針對大腸直腸淋巴癌的臨床表徵，Ann Arbor 分期與給予的治療被記錄與分析。

結果 總共 16 個大腸直腸淋巴癌病患納入研究。7 名患者接受手術，9 名患者未接受手術。最常見的症狀是下消化道出血 (31.25%)，最常見的部位是升結腸 (43.75%)，最常見的細胞分類是瀰漫性大型 B 細胞淋巴瘤 (62.5%)。手術治療的 5 年存活率是 40%，非手術治療的 5 年存活率是 50%。

結論 大腸直腸淋巴癌是罕見的 (佔本院所有大腸直腸惡性腫瘤 0.34%)，有多樣化的症狀，淋巴瘤相關的死亡率是低的。手術治療是否改善存活有待更進一步研究。

關鍵詞 大腸直腸淋巴癌、手術、瀰漫性大型 B 細胞淋巴瘤。