Acta Med. Okayama, 2017
Vol. 71, No. 5, pp. 391–398

Acta Medica Okayama
http://escholarship.lib.okayama-u.ac.jp/amo/

Original Article

The Usefulness of Colonoscopy for the Detection of Ileal Involvement in Intestinal Follicular Lymphoma Patients

Masaya Iwamuro[a,b*], Katsuyoshi Takata[c], Eiko Hayashi[c], Seiji Kawano[a], Sakiko Hiraoka[a], Yoshiro Kawahara[d], Tadashi Yoshino[c], and Hiroyuki Okada[a]

Departments of [a]Gastroenterology and Hepatology, [b]General Medicine, and [c]Pathology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, [d]Department of Endoscopy, Okayama University Hospital, Okayama 700-8558, Japan

To evaluate the usefulness of colonoscopy for the detection of ileal involvement in patients with intestinal follicular lymphoma, seventeen patients with intestinal follicular lymphoma who underwent colonoscopy and biopsy sampling from the terminal ileum were enrolled. The patients were divided into 2 groups: cases with ileal involvement (n = 6) and cases without ileal involvement (n = 11). Patients' clinical backgrounds were compared between the two groups. Subsequently, 10 board-certified endoscopists independently evaluated the endoscopic pictures and determined whether the ileum was involved with follicular lymphoma. Infiltration of follicular lymphoma cells were identified in 6 patients (35.3%). Cases with positive ileal involvement were diagnosed with follicular lymphoma at a younger age than were cases without ileal involvement (55.4 ± 7.4 vs. 68.1 ± 10.3 years, $p = 0.011$). Macroscopically, in patients with ileal involvement, there were multiple polypoid elevations smaller than 5 mm in 4 cases, single polypoid elevation smaller than 5 mm in 1 case, and single polypoid elevation larger than 5 mm in 1 case. In patients without ileal involvement, there were no lesions in the terminal ileum in 7 cases, and multiple polypoid elevations smaller than 5 mm were seen in 4 cases. The accuracy of the macroscopic evaluation by 10 board-certified endoscopists was 68.8%. Colonoscopy is particularly recommended during the initial workup of patients with follicular lymphoma diagnosed at age ≤ 60 years. The diagnosis of ileal involvement based on morphology alone is difficult; thus, biopsy and pathologic diagnosis are required for accurate diagnosis.

Key words: follicular lymphoma, colonoscopy, ileal neoplasms, terminal ileum, small intestine

Follicular lymphoma is one of the indolent forms of non-Hodgkin lymphoma, arising from B lymphocytes [1, 2]. Follicular lymphomas can primarily or secondarily affect the gastrointestinal tract, and among the gastrointestinal organs, the duodenum is known to be the most frequently involved site. Typical endoscopic features of duodenal follicular lymphoma lesions observed during esophagogastroduodenoscopy are multiple whitish granules, usually identified in the second part of the duodenum [3, 4]. In addition, newly developed enteroscopy devices such as balloon-assisted enteroscopy and video capsule enteroscopy revealed that among follicular lymphoma patients presenting with intestinal involvement, 66.7% to 100% had multiple lesions in the jejunum and/or ileum [4-10]. However, these enteroscopy devices are only available in a limited number of secondary and tertiary care cen-

Received December 13, 2016; accepted May 2, 2017.
*Corresponding author. Phone: +81-86-235-7218; Fax: +81-86-225-5991
E-mail: iwamuromasaya@yahoo.co.jp (M. Iwamuro)

Conflict of Interest Disclosures: No potential conflict of interest relevant to this article was reported.

ters [10].

Compared to enteroscopy, colonoscopy is more widely performed worldwide, and it enables the evaluation of the terminal ileum. Indeed, there have been several reports describing cases in which the ileal involvement of various types of lymphomas was identified via colonoscopy [11, 12].

To date, no studies have been conducted to evaluate the role of colonoscopy in the detection of ileal involvement in intestinal follicular lymphoma patients, despite its widespread availability. In this paper, we describe our retrospective review of follicular lymphoma cases and our investigation of the prevalence of ileal involvement detected by colonoscopy. Macroscopic features of the ileal lesions and patients' characteristics were also analyzed. Moreover, the accuracy in assessing ileal involvement based on endoscopic pictures by 10 endoscopists was investigated.

Methods

A database search performed at our hospital's Department of Pathology identified 47 patients with follicular lymphoma and gastrointestinal involvement treated at our hospital between November 1996 and December 2015. The diagnosis of follicular lymphoma was made based on the World Health Organization (WHO) classifications [1, 13]. Histologic diagnosis was established based on the morphologic and immunophenotypic analyses of endoscopically biopsied specimens or surgically resected specimens (Fig. 1). The histopathologic grading was also determined according to the WHO criteria [1]. A subset of the 47 patients examined were subjects of our previous studies [3, 10, 14-21].

Three patients with grade 3 follicular lymphoma were excluded from this review because these cases are typically managed as diffuse large B-cell lymphoma cases. Of the remaining 44 patients, observation and biopsy sampling from the terminal ileum during colonoscopy was performed in 18 patients. One patient was additionally excluded since colonoscopy was performed after chemotherapy in this patient. Therefore, the cases of a total of 17 patients were analyzed in this study.

The presence or absence of ileal involvement with follicular lymphoma was defined according to the results of the pathologic analysis of the endoscopically biopsied specimen. Based on the presence of ileal involvement, we divided the 17 patients into 2 groups: the Positive group was the patients with positive ileal involvement, and the Negative group was those without ileal involvement. We used the patients' clinical records

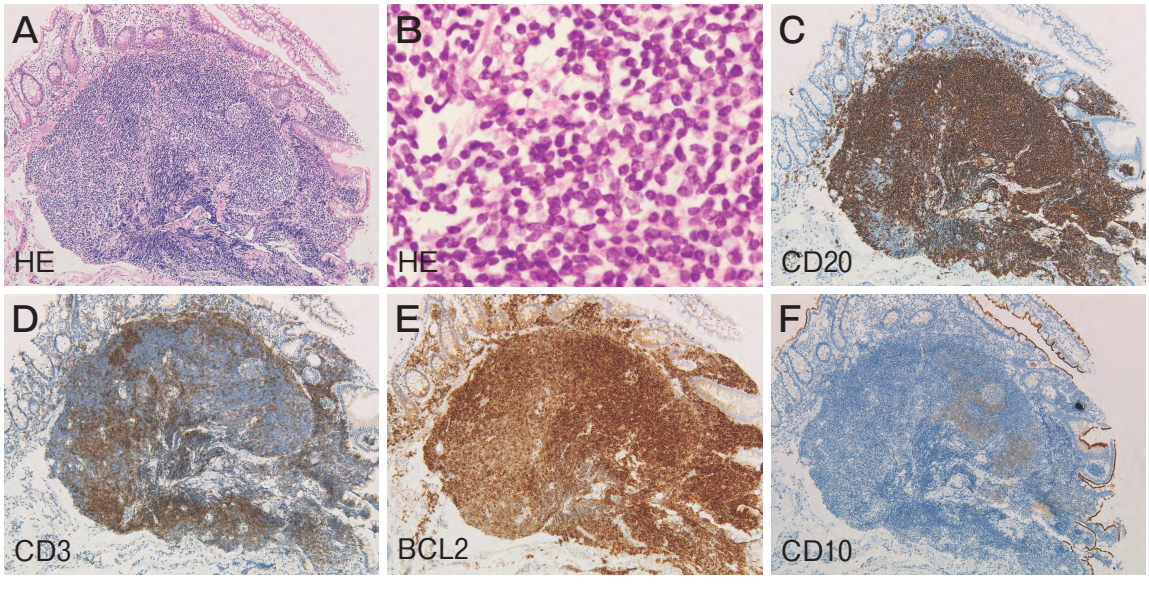

Fig. 1 Pathologic images of a typical ileal follicular lymphoma. In this 67-year-old male with stage I follicular lymphoma involving the duodenum and ileum, a lymphoid follicle was seen in the ileal mucosa (**A**). The lymphoid follicle was composed of small to medium-sized lymphoid cells (**B**). Lymphoid cells were predominantly positive for CD20 (**C**) compared to CD3 (**D**). These cells were strongly positive for BCL2 (**E**) and partly positive for CD10 (**F**).

to analyze the data from their endoscopic, radiological, biological, and pathological examinations. We used the Lugano staging system for the classification of gastrointestinal lymphoma to determine each patient's clinical stages [22, 23]. The morphology of the ileal lesions, the patient's sex, age at the initial diagnosis of follicular lymphoma, the involved gastrointestinal site, clinical stage, presence of bone marrow involvement, and tracer avidity in positron emission tomography (PET) scanning were compared between the Positive and Negative groups.

Subsequently, 10 board-certified endoscopists independently evaluated the endoscopic pictures of the ileum of the 17 patients. Patient information such as age, sex, chief complaint, and results of esophagogastroduodenoscopy, CT scanning, and bone marrow examination were disclosed to all evaluators. Discussions were not permitted individually or in groups. Pictures were distributed in a randomized order to each evaluator. Evaluators judged whether the ileum was involved with follicular lymphoma. For the comparisons of the 2 groups, statistical analyses including *t*-tests, chi-square tests, and F-tests were performed using JMP 12.0.1 software (SAS Institute, Cary, NC, USA). *P*-values < 0.05 were considered significant.

The study design was approved by the ethics committee of Okayama University Hospital (No. 1602-023) and adhered to the Declaration of Helsinki.

Table 1 Characteristics of the 17 patients with intestinal follicular lymphoma

	n	%
Male	9	52.9
Female	8	47.1
Mean age at FL diagnosis (range; years)	63.6	(43–83)
Involved gastrointestinal tract:		
Stomach	2	11.8
Duodenum	15	88.2
Jejunum	8	47.1
Ileum	6	35.3
Colon	1	5.9
Rectum	1	5.9
WHO grade:		
grade 1	10	90.9
grade 2	1	9.1
Lugano staging system:		
I	10	58.8
II_1	1	5.9
IV	6	35.3
Bone marrow involvement:		
Positive	3	17.6
Negative	11	64.7
Not examined	3	17.6
Tracer uptake in the ileum by PET scanning:		
Positive	0	0.0
Negative	16	94.1
Not examined	1	5.9

FL, follicular lymphoma; WHO, World Health Organization; PET, positron emission tomography.

Results

The patients' backgrounds are summarized in Table 1. There were nine men and eight women. The mean age at the initial diagnosis of follicular lymphoma was 63.6 years. Ten patients were at clinical stage I, and one patient was at clinical stage II1. These patients were considered to have primary gastrointestinal follicular lymphoma. Six patients were at stage IV. These patients were considered to have systemic follicular lymphoma with secondary involvement of the gastrointestinal tract.

The pathologic analyses of the specimens biopsied from the terminal ileum during colonoscopy identified infiltration of follicular lymphoma cells in 6 patients (35.3%). Our comparison of the patients' background in the Positive and Negative groups revealed that the patients with positive ileal involvement (n = 6) were diagnosed with follicular lymphoma at significantly younger ages (mean ± SD, 55.4 ± 7.4 years) compared to the patients without ileal involvement (n = 11; 68.1 ± 10.3 years) ($p = 0.011$, Table 2). Five patients with ileal involvement (83.3%) were diagnosed at ≤ 60 years of age, whereas only one patient without ileal involvement (9.1%) was diagnosed at ≤ 60 years of age.

Macroscopically, all patients with follicular lymphoma involvement in the ileum showed polypoid elevation in the terminal ileum during colonoscopy (Figs. 2, 3). Multiple polypoid elevations < 5 mm in size were seen in four patients with ileal involvement (Fig. 2) and four patients without ileal involvement (Fig. 4). These elevated lesions were covered with normal villi, resembling physiological or hyperplastic lymphoid follicles. A single polypoid elevation < 5 mm was seen in one patient with ileal involvement (Fig. 3A, B). A single polypoid elevation ≥ 5 mm was observed in another patient with ileal involvement (Fig. 3C, D). However, seven patients demonstrated no polypoid elevation. Random biopsy examinations from the ileal mucosa without polypoid elevation revealed that all seven

patients had no follicular lymphoma cell infiltration in the ileum. The ileum was significantly more frequently affected in patients with elevated lesions compared to the patients without elevated lesions in the ileum. There were no significant differences between the 2 groups with regard to other patient parameters such as sex,

Table 2 Comparison of the positive and negative ileal involvement groups

	Positive ileal involvement	Negative ileal involvement	*p*-value
No. of patients (n)	6	11	
Male/female	5/1	4/7	0.131
Age at FL diagnosis			
years, mean ± SD	55.4 ± 7.4	68.1 ± 10.3	0.011
≤60/>60	5/1	1/10	0.005
Gastrointestinal involvement (pos./neg.):			
Stomach	1/5	1/10	1.000
Duodenum	4/2	11/0	0.110
Jejunum	1/3	7/2	0.217
Ileum	6/0	0/11	–
Colon	1/5	0/11	0.353
Rectum	1/5	0/11	0.353
Lugano staging system (I&II$_1$/IV):	3/3	8/3	0.600
WHO grade (grade 1/grade 2)	6/0	10/1	1.000
Bone marrow involvement (pos./neg.)	1/3	2/8	1.000
Tracer uptake in the ileum by PET (pos./neg.)	0/5	0/11	1.000
Morphology of the ileal mucosa			
No granules	0	7	0.035*
Solitary polypoid elevation, <5 mm	1	0	
Solitary polypoid elevation, ≥5 mm	1	0	
Multiple polypoid elevations, <5 mm	4	4	

*Polypoid elevations are present vs. absent.

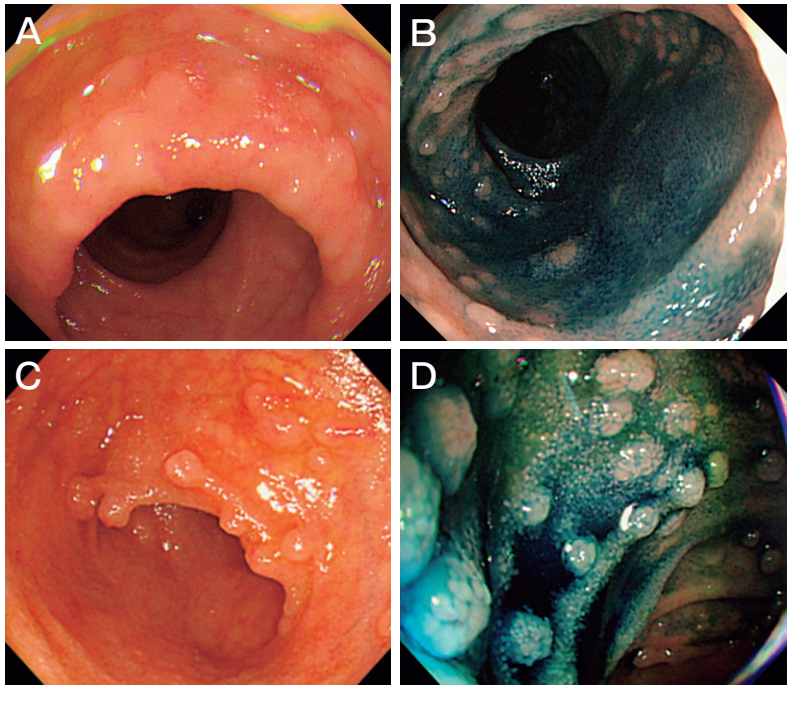

Fig. 2 Endoscopic pictures of cases with follicular lymphoma involvement in the terminal ileum. Multiple polypoid elevations <5 mm in size were seen in Case 1 (**A**, **B**) and Case 2 (**C**, **D**). Indigo carmine spraying outlined the polypoid elevations more clearly.

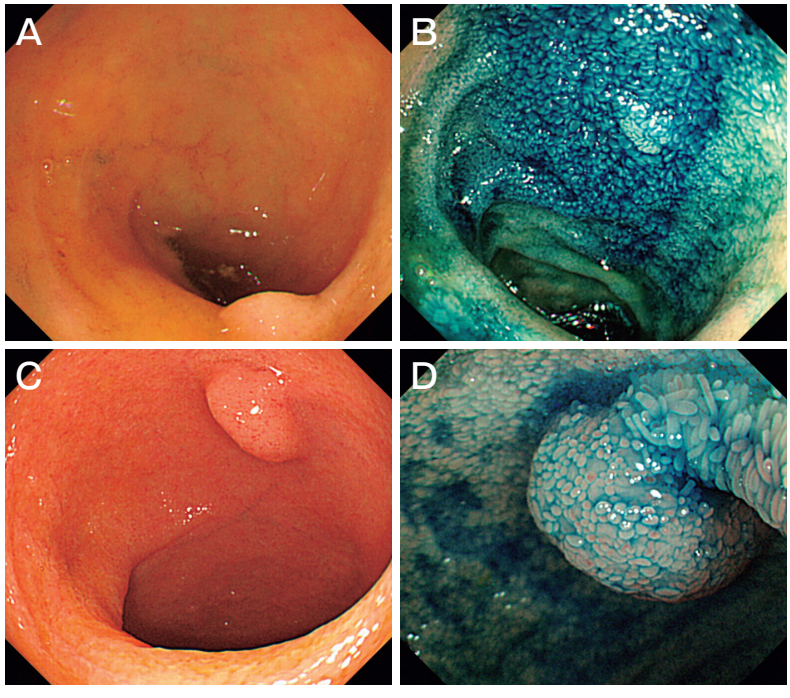

Fig. 3 Endoscopic pictures of cases with follicular lymphoma involvement in the terminal ileum. Case 3 showed a single polypoid elevation <5 mm in the ileum (**A**, **B**). In Case 4, a single polypoid elevation >5 mm was observed (**C**, **D**).

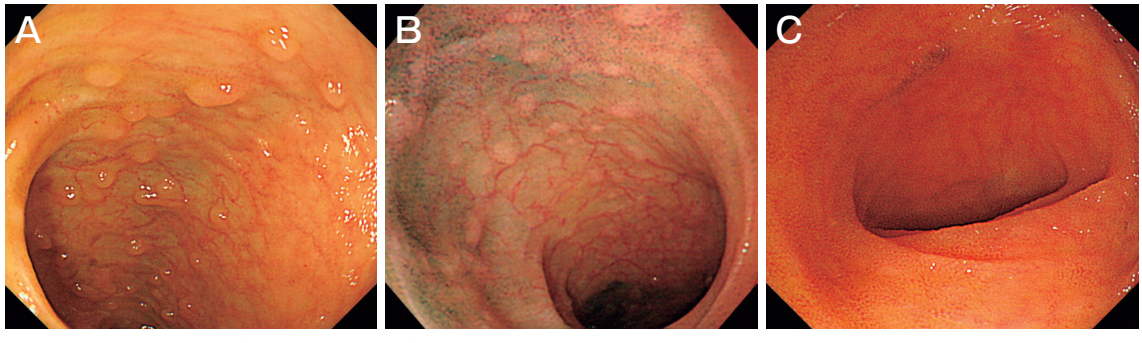

Fig. 4 Endoscopic pictures of cases without follicular lymphoma involvement in the terminal ileum. Multiple polypoid elevations <5 mm in size were seen in Case 5 (**A**) and Case 6 (**B**). Although no lymphoma cells were identified in the biopsied specimen, these cases showed macroscopic features similar to those in the cases with lymphoma involvement. In Case 7, there were no elevations, erosions, or ulcers (**C**).

clinical stage, WHO grade, bone marrow involvement, and gastric, duodenal, jejunal, colonic, and rectal involvement. PET scanning was performed in all cases except for a patient with positive ileal involvement. No patient had tracer uptake in the ileum.

Enteroscopy was performed in 13 patients. Among the 6 patients with ileal involvement (the Positive group), 3 underwent video capsule enteroscopy and 1 underwent per-anal double balloon enteroscopy. The video capsule enteroscopy revealed both jejunal and ileal lesions in one patient and ileal lesions in another patient. In the remaining patient, although a biopsy during colonoscopy showed the involvement of the terminal ileum, the jejunum and ileum were macroscopically determined to be intact with the use of video capsule enteroscopy. The per-anal double balloon enteroscopy performed in one patient revealed ileal lesions, which had already been diagnosed during a colonoscopy.

Among the 11 patients without ileal involvement (the Negative group), 9 patients underwent video capsule enteroscopy. Among them, 7 patients had jejunal

Table 3 Accuracy of ileal involvement based on the endoscopic pictures, as judged by 10 board-certified endoscopists

	Accuracy (%)
Total (n=17)	68.8
Positive involvement (n=6)	73.3
Negative involvement (n=11)	66.4

lesions. There were no patients in whom ileal lesions were identified during enteroscopic examinations despite the negative involvement of the terminal ileum as diagnosed via colonoscopy.

The results of the assessment of ileal involvement by 10 board-certified endoscopists are shown in Table 3. In total, 68.8% of the patients were accurately judged as having positive or negative involvement based on the endoscopic pictures of the terminal ileum. The accuracy for patients with ileal involvement and without ileal involvement was 73.3% and 66.4%, respectively.

Discussion

To the best of our knowledge, this is the first study evaluating the role of colonoscopy in assessing ileal involvement with follicular lymphoma. Infiltration of follicular lymphoma cells was identified in 6 patients (35.3%) based on the pathologic analysis of the biopsied specimen taken during colonoscopy. It is noteworthy that, although enteroscopic examinations were performed in 13 patients and ileal lesions were revealed in 3 patients, all 3 of these patients had been already diagnosed with ileal involvement with the use of colonoscopy. Moreover, in another patient, the ileum was judged to be intact despite the positive infiltration of lymphoma cells as revealed by colonoscopy.

The difficulty of differentiating ileal follicular lymphoma lesions from physiological lymphoid follicles by video capsule enteroscopy alone has been described [7]. In this context, colonoscopy is more advantageous than video capsule enteroscopy for evaluations of ileal involvement, since biopsy sampling is unavailable via video capsule enteroscopy. Consequently, although there is no doubt that enteroscopic examinations such as video capsule enteroscopy and balloon-assisted enteroscopy are essential for evaluating the entire small intestine, we consider that colonoscopy also plays a significant role in evaluating the disease extent of follicular lymphoma patients, because it enables the observation of the terminal ileum and biopsy sampling from the ileal mucosa.

Harada *et al.* recently reported that among 21 patients with duodenal follicular lymphoma were treated with radiation therapy, there were four relapses outside the involved field [24]. These patients had relapses in the jejunum, terminal ileum, mesenteric lymph nodes, and bone marrow. Therefore, precisely evaluating the extent of the intestinal lesions in follicular lymphoma patients is particularly vital when planning radiotherapy, because treatment failures occur outside the involved field of irradiation [25]. However, our previous retrospective multicenter survey of 110 follicular lymphoma patients with gastrointestinal involvement collected from 17 institutions revealed that a total of only 34 patients (30.9%) underwent enteroscopy [10], emphasizing the inaccessibility of enteroscopic examinations in a majority of institutions. In this context, patients under consideration for radiotherapy should first undergo colonoscopy and biopsy sampling from the terminal ileum before enteroscopy, because radiotherapy should not be applied to patients with positive terminal ileal involvement.

In the present study, the overall accuracy in determining terminal ileum involvement based on endoscopic pictures by 10 board-certified endoscopists was 68.8%. This result underscores the difficulty in determining terminal ileum involvement by morphology alone. In this analysis, patients with ileal involvement showed solitary polypoid elevation of <5 mm in dia. ($n=1$), solitary polypoid elevation of ≥ 5 mm ($n=1$), and multiple polypoid elevations of <5 mm ($n=4$). However, multiple polypoid elevations of <5 mm were also seen in patients without ileal involvement ($n=4$). Such morphological similarities between the 2 groups seemed to be the main cause of the misjudging of ileal involvement.

Generally, physiological lymphoid follicles exist in the mucosa of the terminal ileum, and are called Peyer's patches. The numbers and sizes of lymphoid follicles are occasionally increased in association with physiological conditions or diseases such as infections and food allergies [26-33]. This feature is known as lymphoid hyperplasia. As described in previous reports, in the present study it was challenging to distinguish follicular lymphoma lesions from lymphoid hyperplasia and physiological lymph follicles based on macroscopic features. Moreover, in this study, PET scanning was not useful

for detecting ileal involvement, because none of our patients, even those with pathological involvement in the ileum, showed tracer accumulation in the ileum. It is known that small follicular lymphoma lesions in the gastrointestinal tract often show false-negative results in PET scanning [3,20]. An accurate diagnosis of ileal involvement is thus difficult to achieve, both morphologically and radiologically, and it requires biopsy sampling and pathological assessment.

In this study, no lymphoma cell infiltration was detected in the cases with ileal mucosa without polypoid elevation. This suggests that biopsy examination during colonoscopy can be omitted in patients with morphologically intact ileal mucosa. However, further research is required before reaching any conclusions about this proposition, since our findings are based on a small number of patients. At this time, we consider that biopsy sampling from the ileal mucosa is required for all patients with follicular lymphoma during the initial workup.

Colonoscopy is useful in follicular lymphoma patients not only for evaluating the terminal ileum but also for the screening of the cecum, colon, and rectum, although the prevalence of colorectal involvement is lower than that of terminal ileum involvement. In our previous work, we reviewed 12 patients with colorectal follicular lymphoma and reported that they presented with papular (n=4), polypoid (n=4), and flat elevated lesions (n=4) [18]. No erosions or ulcers were seen in any of the lesions. We also demonstrated that most of the previously reported cases of colorectal follicular lymphoma lacked erosions or ulcers, and that they were morphologically categorized as papular, polypoid, or flat elevated lesions as well [34-40]. A biopsy and a consultation with pathologists to ensure appropriate immunostaining are required once an endoscopist observes such lesions in the colorectum [16, 18].

Our present comparative analysis of the patients' clinical backgrounds revealed that patients with ileal involvement were diagnosed at significantly younger ages compared to the patients without ileal involvement. It was noteworthy that, among the 6 patients aged ≤60 years, all but one had ileal involvement. However, we have no clear explanation for this difference, because other aspects of the patients' clinical backgrounds such as clinical staging, WHO grade, and the presence or absence of bone marrow involvement were not significantly different between the 2 groups. Regardless, patients with intestinal follicular lymphoma diagnosed at 60 years of age or younger should be screened for ileal lesions, since the ileum seems to be frequently involved in these patients.

Our study has several limitations. First, the sample sizes were small in both groups, due mainly to the rarity of this disease. Second, sampling error may have occurred during the biopsies of the ileal mucosa. Consequently, an underestimation of the prevalence of ileal involvement may have existed. Third, not all of the patients with intestinal follicular lymphoma underwent biopsy sampling from the ileal mucosa during colonoscopy. These examinations might be waived in patients with morphologically intact ileal mucosae. Therefore, biases may have existed in patient selection. Although a prospective observational study in a single institution is unlikely to be conducted due to the infrequency of the disease, we believe that future multicenter observational studies with routine biopsy sampling from the ileal mucosa will reveal the precise prevalence and patient characteristics.

In conclusion, colonoscopy and biopsy from the terminal ileum revealed a 35.3% prevalence of follicular lymphoma involvement in the ileum. Morphologically, the ileal lesions of follicular lymphoma were indistinguishable from the physiological lymphoid follicles and lymphoid hyperplasia. Therefore, biopsy and pathologic diagnosis are mandatory for the diagnosis of ileal involvement. Although the evaluation of the entire intestines by esophagogastroduodenoscopy, colonoscopy, and enteroscopy is essential, colonoscopy and biopsy sampling from the ilea mucosa is particularly recommended for patients with intestinal follicular lymphoma who are diagnosed at the age of ≤60 years, in light of the high prevalence of ileal involvement in this age group.

References

1. Harris NL, Swerdlow SH, Jaffe ES, Ott G, Nathwani BN, de Jong D, Yoshino T and Spagnolo D: Follicular lymphoma: in WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Swerdlow SH, Campo E, Harris NL, Jaffe E, Pileri SA, Stein H, Thiele V and Vardiman JW eds. IARC, Lyon (2008) pp220–226.
2. Dreyling M, Ghielmini M, Marcus R, Salles G, Vitolo U and Ladetto M: Newly diagnosed and relapsed follicular lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and followup. Ann Oncol (2014) 25 Suppl 3: iii76–iii82.
3. Yoshino T, Miyake K, Ichimura K, Mannami T, Ohara N, Hamazaki S and Akagi T: Increased incidence of follicular lymphoma in the duodenum. Am J Surg Pathol (2000) 24: 688–693.
4. Schmatz AI, Streubel B, Kretschmer-Chott E, Puspok A, Jager U,

Mannhalter C, Tiemann M, Ott G, Fischbach W, Herzog P, Seitz G, Stolte M, Raderer M and Chott A: Primary follicular lymphoma of the duodenum is a distinct mucosal/submucosal variant of follicular lymphoma: a retrospective study of 63 cases. J Clin Oncol (2011) 29: 1445–1451.
5. Akamatsu T, Kaneko Y, Ota H, Miyabayashi H, Arakura N and Tanaka E: Usefulness of double balloon enteroscopy and video capsule endoscopy for the diagnosis and management of primary follicular lymphoma of the gastrointestinal tract in its early stages. Dig Endosc (2010) 22: 33–38.
6. Kodama M, Kitadai Y, Shishido T, Shimamoto M, Fukumoto A, Masuda H, Tanaka S, Yoshihara M, Sakai A, Nakayama H and Chayama K: Primary follicular lymphoma of the gastrointestinal tract: a retrospective case series. Endoscopy (2008) 40: 343–346.
7. Nakamura M, Ohmiya N, Hirooka Y, Miyahara R, Ando T, Watanabe O, Itoh A, Kawashima H, Ohno E, Kinoshita T and Goto H: Endoscopic diagnosis of follicular lymphoma with small-bowel involvement using video capsule endoscopy and double-balloon endoscopy: a case series. Endoscopy (2013) 45: 67–70.
8. Higuchi N, Sumida Y, Nakamura K, Itaba S, Yoshinaga S, Mizutani T, Honda K, Taki K, Murao H, Ogino H, Kanayama K, Akiho H, Goto A, Segawa Y, Yao T and Takayanagi R: Impact of double-balloon endoscopy on the diagnosis of jejunoileal involvement in primary intestinal follicular lymphomas: a case series. Endoscopy (2009) 41: 175–178.
9. Nakamura S, Matsumoto T, Umeno J, Yanai S, Shono Y, Suekane H, Hirahashi M, Yao T and Iida M: Endoscopic features of intestinal follicular lymphoma: the value of double-balloon enteroscopy. Endoscopy (2007) 39 Suppl 1: E26–E27.
10. Iwamuro M, Okada H, Kawano S, Shiode J, Takenaka R, Imagawa A, Inaba T, Suzuki S, Nishimura M, Mizuno M, Araki M, Mannami T, Ueki T, Kobashi H, Fukatsu H, Tanaka S, Omoto A, Kawai Y, Kitagawa T, Toyokawa T, Takata K, Yoshino T, Takaki A and Yamamoto K: A multicenter survey of enteroscopy for the diagnosis of intestinal follicular lymphoma. Oncol Lett (2015) 10: 131–136.
11. Mansoor MS and Wolfsohn DM: Resolution of Small Bowel Follicular Lymphoma With Treatment of Concomitant Hepatitis B. J Clin Gastroenterol (2015) 49: 885–887.
12. Iturrino J, Sweetser S and Baron TH: Localized primary ileal lymphoma found on colonoscopic examination. Am J Gastroenterol (2012) 107: 955–956.
13. Harris NL, Jaffe ES, Diebold J, Flandrin G, Muller-Hermelink HK, Vardiman J, Lister TA and Bloomfield CD: World Health Organization classification of neoplastic diseases of the hematopoietic and lymphoid tissues: report of the Clinical Advisory Committee meeting-Airlie House, Virginia, November 1997. J Clin Oncol (1999) 17: 3835–3849.
14. Takata K, Miyata-Takata T, Sato Y and Yoshino T: Pathology of follicular lymphoma. J Clin Exp Hematop (2014) 54: 3–9.
15. Takata K, Okada H, Ohmiya N, Nakamura S, Kitadai Y, Tari A, Akamatsu T, Kawai H, Tanaka S, Araki H, Yoshida T, Okumura H, Nishisaki H, Sagawa T, Watanabe N, Arima N, Takatsu N, Nakamura M, Yanai S, Kaya H, Morito T, Sato Y, Moriwaki H, Sakamoto C, Niwa Y, Goto H, Chiba T, Matsumoto T, Ennishi D, Kinoshita T and Yoshino T: Primary gastrointestinal follicular lymphoma involving the duodenal second portion is a distinct entity: a multicenter, retrospective analysis in Japan. Cancer Sci (2011) 102: 1532–1536.
16. Iwamuro M, Okada H, Takata K, Nose S, Miyatani K, Yoshino T and Yamamoto K: Diagnostic accuracy of endoscopic biopsies for the diagnosis of gastrointestinal follicular lymphoma: a clinicopathologic study of 48 patients. Ann Diagn Pathol (2014) 18: 99–103.
17. Iwamuro M, Imagawa A, Kobayashi N, Kubota Y, Miyatani K, Takata K and Okada H: Synchronous adenocarcinoma and follicular lymphoma of the stomach. Intern Med (2013) 52: 907–912.
18. Iwamuro M, Okada H, Takata K, Takenaka R, Inaba T, Mizuno M, Kobashi H, Tanaka S, Yoshioka M, Kondo E, Yoshino T and Yamamoto K: Colorectal Manifestation of Follicular Lymphoma. Intern Med (2016) 55: 1–8.
19. Iwamuro M, Okada H, Takata K, Kawai Y, Kawano S, Nasu J, Kawahara Y, Tanaka T, Yoshino T and Yamamoto K: Magnified endoscopic features of duodenal follicular lymphoma and other whitish lesions. Acta Med Okayama (2015) 69: 37–44.
20. Iwamuro M, Okada H, Takata K, Shinagawa K, Fujiki S, Shiode J, Imagawa A, Araki M, Morito T, Nishimura M, Mizuno M, Inaba T, Suzuki S, Kawai Y, Yoshino T, Kawahara Y, Takaki A and Yamamoto K: Diagnostic role of 18F-fluorodeoxyglucose positron emission tomography for follicular lymphoma with gastrointestinal involvement. World J Gastroenterol (2012) 18: 6427–6436.
21. Iwamuro M, Shinagawa K, Okada H, Takata K, Yoshino T and Yamamoto K: Elevated soluble IL-2 receptor levels correlate with tumor bulk of follicular lymphomas with intestinal involvement. Clin Biochem (2014) 47: 191–195.
22. Zucca E, Roggero E, Bertoni F and Cavalli F: Primary extranodal non-Hodgkin's lymphomas. Part 1: Gastrointestinal, cutaneous and genitourinary lymphomas. Ann Oncol (1997) 8: 727–737.
23. Rohatiner A, d'Amore F, Coiffier B, Crowther D, Gospodarowicz M, Isaacson P, Lister TA, Norton A, Salem P and Shipp M: Report on a workshop convened to discuss the pathological and staging classifications of gastrointestinal tract lymphoma. Ann Oncol (1994) 5: 397–400.
24. Harada A, Oguchi M, Terui Y, Takeuchi K, Igarashi M, Kozuka T, Harada K, Uno T and Hatake K: Radiation therapy for localized duodenal low-grade follicular lymphoma. J Radiat Res (2016) 57: 412–417.
25. Gustavsson A, Osterman B and Cavallin-Stahl E: A systematic overview of radiation therapy effects in non-Hodgkin's lymphoma. Acta Oncol (2003) 42: 605–619.
26. Capitanio MA and Kirkpatrick JA: Lymphoid hyperplasia of the colon in children. Roentgen observations. Radiology (1970) 94: 323–327 [PMID: 5308630].
27. Krauss E, Konturek P, Maiss J, Kressel J, Schulz U, Hahn EG, Neurath MF and Raithel M: Clinical significance of lymphoid hyperplasia of the lower gastrointestinal tract. Endoscopy (2010) 42: 334–337.
28. Raithel M, Albrecht H, Rieker R, Hagel A and Neurath MF: Potential utility of double-balloon enteroscopy for the diagnosis and evaluation of gastrointestinally mediated allergy. Endoscopy (2014) 46 Suppl 1 UCTN: E266–2667.
29. Kokkonen J and Karttunen TJ: Lymphonodular hyperplasia on the mucosa of the lower gastrointestinal tract in children: an indication of enhanced immune response? J Pediatr Gastroenterol Nutr (2002) 34: 42–46.
30. Hagel AF, de Rossi TM, Zopf Y, Lindner AS, Dauth W, Neurath MF and Raithel M: Small-bowel capsule endoscopy in patients with gastrointestinal food allergy. Allergy (2012) 67: 286–292.
31. Iacono G, Ravelli A, Di Prima L, Scalici C, Bolognini S, Chiappa S, Pirrone G, Licastri G and Carroccio A: Colonic lymphoid nodular hyperplasia in children: relationship to food hypersensitivity. Clin Gastroenterol Hepatol (2007) 5: 361–366.
32. Turunen S, Karttunen TJ and Kokkonen J: Lymphoid nodular hyperplasia and cow's milk hypersensitivity in children with chronic constipation. J Pediatr (2004) 145: 606–611.
33. Iwamuro M, Hiraoka S, Okada H, Kawai Y, Miyabe Y, Takata K, Kawano S and Yamamoto K: Lymphoid hyperplasia of the colon and its association with underlying allergic airway diseases. Int J Colorectal Dis (2016) 31: 313–317.
34. Ferreira A, Goncalves R and Rolanda C: A different kind of colon polyp. Gastroenterology (2012) 143: 1440, 1693–1694.
35. Yoshida N, Nomura K, Matsumoto Y, Nishida K, Wakabayashi N, Konishi H, Mitsufuji S, Kataoka K, Okanoue T and Taniwaki M: Detection of BCL2-IGH rearrangement on paraffin-embedded tissue sections obtained from a small submucosal tumor of the rectum in a patient with recurrent follicular lymphoma. World J Gastroenterol (2004) 10: 2602–2604.
36. Esaki M, Matsumoto T, Nakamura S, Suekane H, Ohji Y, Yao T and Iida M: Capsule endoscopy findings in intestinal follicular lymphoma. Endoscopy (2007) 39 Suppl 1: E86–87.
37. Dalal L: Primary multifocal non-Hodgkin lymphoma of the colon successfully treated with chemotherapy. Gastrointest Endosc (2008) 68: 1005–1006.
38. Kuroha M, Endo K, Sato Y, Shiga H, Kakuta Y, Takahashi S, Kinouchi Y and Shimosegawa T: Magnifying endoscopy findings in follicular lymphoma of the rectum using narrow band imaging. Endoscopy (2011) 43 Suppl 2 UCTN: E346–347.
39. Hiraide T, Shoji T, Higashi Y, Matsuda I and Terada T: Extranodal multiple polypoid follicular lymphoma of the sigmoid colon. Gastrointest Endosc (2011) 73: 182–184.
40. Kakati BR, Krishna K, Krishna SG, Sharma SG, Sanathkumar N and Rego RF: Extensive extramedullary disease involving the colon in multiple myeloma: a case report and review of literature. J Gastrointest Cancer (2012) 43: 379–381.