



Diagnostic accuracy of endoscopic biopsies for the diagnosis of gastrointestinal follicular lymphoma: a clinicopathologic study of 48 patients

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ABSTRACT

The purpose of this study was to reveal the diagnostic accuracy of initial pathologic assessment of biopsied samples in patients with gastrointestinal follicular lymphoma lesions. A total of 48 patients with follicular lymphoma (Lugano system stage I: n = 30; II₁: n = 4; II₂: n = 4; IV: n = 10) with gastrointestinal involvement who underwent endoscopic biopsy were enrolled and retrospectively reviewed. Nine (18.8%) of the 48 patients were not appropriately diagnosed as having follicular lymphoma at the initial biopsy. The initial pathological diagnosis included extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (n = 4), necrotic tissue (n = 2), duodenitis (n = 1), or suspected lymphoma of unspecified subtype (n = 2). The reasons for these inappropriate diagnoses were insufficient histopathologic analysis lacking CD10 and BCL2 staining (n = 7) and unsuitable biopsy samples taken from erosions or ulcers that contained scanty lymphoma cells or no lymphoid follicles (n = 2). In conclusion, incomplete histopathologic analysis and unsuitable biopsy samples are pitfalls in the diagnosis of gastrointestinal follicular lymphoma.

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1. Introduction

Follicular lymphoma is a neoplasm that originates in germinal center B cells and primarily or secondarily involves the gastrointestinal tract. Most of the gastrointestinal involvement of follicular lymphoma arises in the small intestine, including the duodenum [1–3]. Its representative endoscopic feature is well known as small whitish polypoid nodules up to 2 mm in diameter [4,5]. In contrast, various macroscopic forms such as ulcerative, superficial, or submucosal tumor-like lesions are seen in the rare cases with gastric, colonic, or rectal involvement [6]. Generally, diagnosis of these lesions is made by pathological analysis of endoscopically biopsied samples or surgically resected specimens.

During the review process of our cases with gastrointestinal follicular lymphoma, we noticed that some patients were initially misdiagnosed as having other types of lymphomas or even benign diseases such as inflammation or necrotic tissue. Such cases required repeat biopsies or surgical resection before reaching the correct diagnosis of follicular lymphoma. The purpose of this study was to reveal the diagnostic accuracy of the initial pathologic assessment of

biopsied samples taken from the intestinal follicular lymphoma lesions. Pitfalls of the pathological diagnosis for this disease entity are also discussed.

2. Materials and methods

A database search performed at the Department of Pathology of our institute identified 58 patients with follicular lymphoma and gastrointestinal involvement treated at our institute and 4 collaborating institutions between November 1996 and October 2011. The diagnosis of follicular lymphoma was made according to World Health Organization classifications [2,7]. A histologic diagnosis was done based on the morphologic and immunophenotypic analyses of endoscopically biopsied specimens or surgically resected specimens. Histopathologic grading was also determined according to World Health Organization criteria [2]. Patients with grade 3 follicular lymphoma were excluded from this study because these cases are typically managed as cases of diffuse large B cell lymphoma [2]. A subset of the 58 patients examined were also subjects of our previous studies [1,3,6,8–12].

Of the 58 patients identified, 7 were excluded since they were diagnosed by lymph node biopsy prior to the biopsy examination of the gastrointestinal mucosa. Three patients were further excluded from this study because their diagnoses were made by pathological

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Table
Characteristics of the 48 patients

	n	%
Female sex	28	58.3
Mean age (range; y)	64.5	38–85
Lugano staging system		
Stage I	30	62.5
Stage II ₁	4	8.3
Stage II ₂	4	8.3
Stage IV	10	20.8
Sites where the initial biopsy was done		
Stomach	3	6.3
Duodenum	41	85.4
Ileum	1	2.1
Colon	1	2.1
Rectum	2	4.2
Initial pathological diagnosis		
Follicular lymphoma	39	81.3
MALT lymphoma	4 ^a	8.3
Necrotic tissue	2 ^b	4.2
Suspected lymphoma ^c	2	4.2
Duodenitis	1	2.1

^a Two cases from the duodenum and 2 cases from the stomach.

^b One case from the stomach and 1 case from the duodenum.

^c Lymphoma was suspected, but the distinct subtype was undetermined.

assessment of surgically resected gastrointestinal lesions, without endoscopic biopsy examinations before the surgery. Therefore, a total of 48 patients were enrolled in this study. Data regarding the endoscopic, radiological, biological, and pathological examinations performed were retrospectively reviewed from their clinical records.

The Lugano staging system for the classification of gastrointestinal lymphoma was used to determine the patients' clinical stages [13,14].

3. Results

The patients' backgrounds are summarized in Table. Thirty patients were in clinical stage I, and 4 patients were in clinical stage II₁. These patients were considered to have primary gastrointestinal follicular lymphoma. On the other hand, 4 patients were in stage II₂ and 10 patients in stage IV. These patients were considered to have

systemic follicular lymphoma with secondary involvement of the gastrointestinal tract. Initial biopsy examinations were performed in the duodenum in most (41/48) of the patients. This result is consistent with the fact that gastrointestinal follicular lymphoma predominantly arises in the duodenum [1,5]. Other sites where the initial biopsy was performed include the stomach (n = 3), ileum (n = 1), colon (n = 1), and rectum (n = 2).

Pathologically, 39 (81.3%) of the 48 patients were appropriately diagnosed as having follicular lymphoma based on the initial biopsy examinations. The remaining 9 patients (18.8%) were judged as having extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma; n = 4), necrotic tissue (n = 2), duodenitis (n = 1), or suspected lymphoma in which the distinct subtype was not determined (n = 2).

We further analyzed the methods used to make the appropriate diagnosis of follicular lymphoma in these 9 patients. In the 2 patients who were diagnosed as having necrotic tissue, the follicular lymphoma lesions presented macroscopically as erosions or an ulcerative tumor. The details of the former case with erosions in the duodenum were separately reported in our previous case report [10]. In that case, 3 specimens were taken from the erosions at the initial biopsy, but the specimens lacked an adequate number of lymphoma cells or lymphoid follicles to assist in the diagnosis of follicular lymphoma. Subsequent biopsy specimens taken from the peripheral mucosa showed infiltration of the lymphoma cells forming lymphoid follicles, which led to the appropriate diagnosis. The latter case with an ulcerative lesion in the stomach is illustrated in Fig. 1. In this case, the gastric lesion resembled a submucosal tumor measuring 5 cm with an ulcer (Fig. 1A, B). Esophagogastroduodenoscopy was performed twice, and 9 specimens were taken from the ulcerative tumor in total. However, these specimens contained only necrotic tissue (Fig. 1C). A surgical resection was subsequently performed for pathological evaluation, and the correct diagnosis of gastric follicular lymphoma was made based on the infiltrated lymphoma cells forming lymphoid follicles (Fig. 1D, E).

In 7 cases, the diagnosis of follicular lymphoma was made by immunohistochemical staining for CD10 and BCL-2 after repeat biopsy examination or surgical resection. The initial diagnoses of these patients were MALT lymphoma (n = 4; Fig. 2), duodenitis (n = 1; Fig. 3), or suspected lymphoma of unspecified subtype (n = 2). All 7 of these

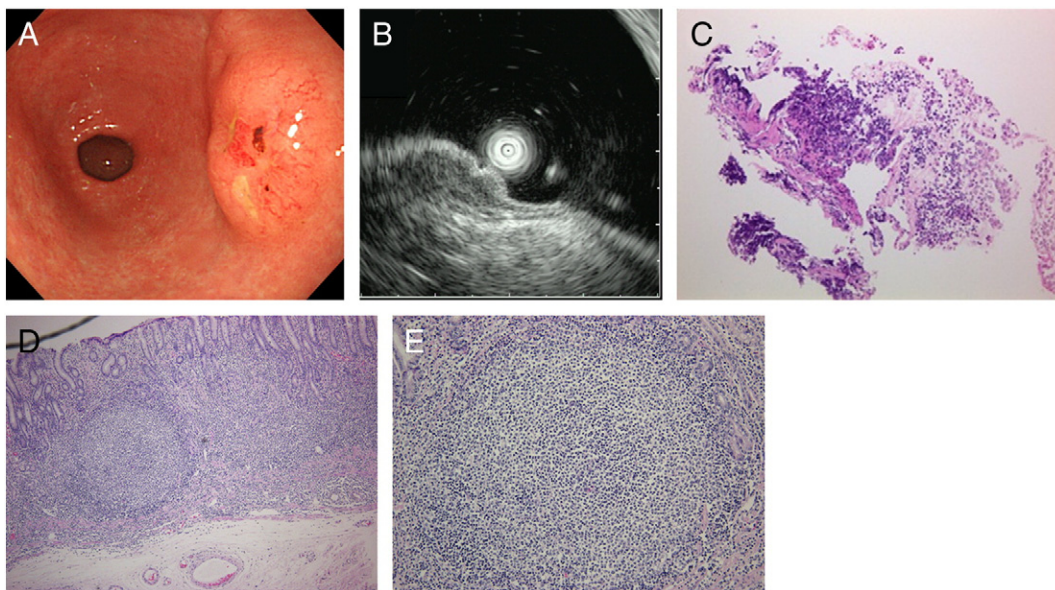


Fig. 1. A case of gastric follicular lymphoma. (A) Esophagogastroduodenoscopy revealed an elevated lesion resembling a submucosal tumor measuring 5 cm with an ulcer. In endosonography, the tumor was located in the mucosal and submucosal layers. (C) Biopsy samples taken from the tumor contained only necrotic tissue. (D, E) Pathological evaluation of the surgically resected specimen revealed infiltration of lymphoma cells forming lymphoid follicles, which led to the final diagnosis of follicular lymphoma.

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