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# Incidental Finding of a Primary Polypoid Low-Grade B-Cell Gastric Lymphoma Managed with Chemotherapy

Authors' Contribution: Study Design A Data Collection B Statistical Analysis C Data Interpretation D Manuscript Preparation E Literature Search F Funds Collection G BCEF MengHan Wang D BCEF NingNing Dong D DE YiJun Chen D

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Patient:	Male, 57-year-old
Final Diagnosis:	Primary polypoid low-grade B-cell gastric lymphoma
Symptoms:	Raised lesion in the gastric body, accompanied by chronic atrophic gastritis and a negative result for
	Hp infection
<b>Clinical Procedure:</b>	
Specialty:	Gastroenterology and Hepatology
Objective:	Unusual clinical course
Background:	This report describes the case of a 57-year-old man with an incidental finding of a primary polypoid low-grade
	B-cell gastric lymphoma managed with chemotherapy. The case has unique clinical features and represents
	an uncommon manifestation of gastric follicular lymphoma. This report seeks to raise awareness among clini-
	cians regarding early detection and diagnosis of this condition.
Case Report:	A middle-aged man was referred for further evaluation following the incidental detection of a gastric mass dur-
	ing a routine health check-up. Gastroscopy revealed an irregular lesion on the gastric wall. Contrast-enhanced
	CT showed a well-defined polypoid mass. Endoscopic biopsy was performed, and histopathological examina-
	tion showed neoplastic lymphoid follicles. Immunohistochemical staining was positive for CD20, CD10, and
	BCL-2, confirming a diagnosis of grade 2 follicular lymphoma. The patient underwent standard chemothera-
	py, consisting of rituximab, cyclophosphamide, doxorubicin (hydroxydaunorubicin), vincristine (Oncovin), and
	prednisone(R-CHOP), and the condition remained stable with no signs of recurrence during follow-up.
Conclusions:	Primary follicular lymphoma of the stomach is a rare type of gastric tumor, often overlooked in early diagnosis.
	Standard treatment regimens, such as R-CHOP, are effective in controlling the disease. This case highlights the
	importance of considering lymphoma in the diagnosis of gastric subepithelial lesions, even in asymptomatic
	patients. It underscores the value of early endoscopic evaluation and histopathological confirmation in guid-
	ing timely and effective treatment.
Keywords:	Diagnosis • Endoscopy • Lymphoma, Follicular Gastric Mucosa
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## Introduction

Follicular lymphoma (FL) is a common subtype of non-Hodgkin B-cell lymphoma. In the gastrointestinal tract, large B-cell lymphoma and mucosa-associated lymphoid tissue (MALT) lymphoma are more common, while FL is relatively rare [1]. Gastric lymphoma accounts for approximately 5% of gastric neoplasms but is the most common location for extranodal lymphomas, representing about 30% to 40% of these cases and 55% to 65% of lymphomas affecting the gastrointestinal tract [2]. Most FL cases occur in lymph nodes, whereas extranodal FL is less prevalent [1]. The gastrointestinal tract is the most common site for extranodal FL, accounting for approximately 40% of cases. Most gastrointestinal FLs are secondary to systemic lymphoma [3]. FL affecting the duodenum is more common, whereas primary gastric FL is extremely rare. A study by Takata et al revealed that out of 125 cases of primary gastrointestinal FL, 111 cases (89%) involved the duodenum, 50 cases (40%) involved the jejunum, 28 cases (22%) involved the ileum, 5 cases (4%) involved the colon, and only 2 cases (1.6%) involved the stomach [4]. In most reported cases, the disease remains confined to the gastrointestinal tract and regional lymph nodes, and even when the disease progresses, the prognosis is generally favorable [5].

Endoscopically, primary gastric FL typically presents as a submucosal tumor or slightly elevated lesion, while MALT lymphoma and diffuse large B-cell lymphoma often present as ulcerative or depressed lesions [6]. Endoscopic observation alone cannot reliably differentiate FL from other submucosal tumors, including gastric cancer, ectopic pancreas, neuroendocrine tumors, and leiomyomas [5]. Early diagnosis of primary gastric FL is a significant challenge for gastroenterologists. To overcome these diagnostic challenges, it is essential to integrate use of other diagnostic tools. Firstly, endoscopic ultrasound (EUS) has shown significant advantages in evaluating submucosal lesions [7]. A previous study has demonstrated that EUS can assist in identification of hypoechoic submucosal lesions and determination the layer of origin, which is crucial for distinguishing FL from other submucosal tumors such as gastrointestinal stromal tumors (GIST) or neuroendocrine tumors [3]. Additionally, fine-needle aspiration (FNA) under EUS guidance allows for precise tissue sampling, thus greatly improving diagnostic accuracy.

After performing the fine-needle aspiration, immunohistochemical analysis is essential to confirm the diagnosis of FL. It has been demonstrated in the literature that markers such as CD10, BCL-2, and BCL-6 are crucial in differentiating FL from other gastrointestinal lymphomas [8]. Furthermore, genetic testing, such as the detection of the t(14;18) translocation, can further confirm molecular characteristics of FL [2]. According to a previous report, over 85% of FL patients display BCL-2 gene translocations, a molecular feature that not only aids in diagnosis but also provides valuable insights for prognosis and treatment planning [9].

Although EUS and fine-needle aspiration biopsy have been shown to significantly improve the accuracy of FL diagnosis, advanced endoscopic imaging techniques such as narrow-band imaging (NBI) also demonstrate potential for early screening [10]. A study indicated that NBI can clearly display the vascular structure of submucosal lesions, thereby facilitating identification of the "tree-like appearance" of lymphoma cell infiltration, which is indicative of significant neovascularization [11]. Although NBI alone is not sufficient for diagnosis, its integration with conventional endoscopic techniques and pathology can significantly enhance the sensitivity of early detection.

Recently, we treated a 57-year-old man with an incidental finding of a primary polypoid low-grade B-cell gastric lymphoma managed with chemotherapy. The diagnosis was confirmed following multiple imaging and pathological examinations, including endoscopic biopsy. This article discusses the imaging findings, endoscopic features, and pathological results of this case, providing a reference for the future diagnosis and treatment of this rare disease. The requirement of written informed consent was waived by the Ethics Committee of our hospital.

#### **Case Report**

A 57-year-old man underwent an upper-gastrointestinal endoscopy during a routine health check-up, which revealed a raised lesion in the gastric body, accompanied by chronic atrophic gastritis and a negative result for *Helicobacter pylori* (Hp) infection. Due to the limited resources at the local hospital, he was referred to our hospital for further evaluation and treatment. An enhanced abdominal computed tomography(CT) scan revealed a soft-tissue density nodule on the greater curvature of the gastric body, measuring approximately 2.5×1.4 cm, with clear borders (**Figure 1**). A stalk-like structure was observed, connecting the nodule to the gastric wall. Enhanced scanning showed moderate enhancement during the arterial phase and significant enhancement during the venous phase. The imaging report diagnosed the nodule as a possible polypoid lesion.

To further investigate the nature of the lesion, upper-gastrointestinal endoscopy was performed. The white-light endoscopy revealed punctate erythema in the gastric fundus and body, with thickened mucosal folds exhibiting a serpentine appearance. A raised lesion with a central depression, measuring approximately 1.5×1.2 cm, was observed on the greater curvature of the middle gastric body. Endoscopic ultrasound revealed a homogeneous hypoechoic lesion in the middle gastric body.



Figure 1. (A, B) Enhanced abdominal computed tomography (CT) scan image of primary gastric follicular lymphoma; (C) Positron emission tomography-computed tomography (PET-CT) image of primary gastric follicular lymphoma.



Figure 2. Endoscopy images of primary gastric follicular lymphoma: (A) White-light; (B) Narrow-band; (C) Endoscopic ultrasound.

The lesion appeared firm, with poor elasticity, and originated from the submucosal layer (Figure 2). Due to the difficulty of diagnosis solely based on endoscopic findings, fine-needle aspiration (22G) biopsy was performed, and the pathology report confirmed follicular lymphoma, grade 2. Immunohistochemical staining showed CD21 (FDC network), CD20 (diffusely positive), CD3 (scattered positive), CD10 (positive), BCL-6 (positive), MUM1 (partially positive), BCL-2 (approximately 90% positive), CD5 (negative), CyclinD1 (negative), C-Myc (20%positive), PAX-5(positive), and CD19/CD22 (Figure 3). In situ hybridization for Epstein-Barr virus-encoded RNA (EBER) was negative. Due to financial reasons, the patient refused to undergo genetic testing. Based on the histopathological features observed with hematoxylin and eosin (H&E) staining, together with the immunohistochemical profile, a final pathology diagnosis of follicular lymphoma was established.

The patient was referred to the Hematology Department for further evaluation. Subsequently, he underwent positron emission tomography-computed tomography (PET-CT) (**Figure 1**), which demonstrated irregular thickening with high metabolic activity in the gastric body, consistent with follicular lymphoma, and a highly metabolic lymph node on the greater curvature of the stomach, suggesting lymphomatous involvement. The bone marrow biopsy revealed the absence of tumor cell infiltration. Although most primary gastrointestinal lymphomas are of the MALT type, they typically exhibit negative immunohistochemical staining for CD10, BCL6, and BCL2, which was inconsistent with our pathology findings [11]. Furthermore, PET-CT revealed no evidence of disease in other organs. Therefore, a diagnosis of primary gastric follicular lymphoma, stage II according to the Lugano classification, was considered. Given that gastric FL is not an indication for endoscopic submucosal dissection (ESD), and after excluding contraindications, we initiated R-CHOP chemotherapy, which consisted of rituximab 700 mg on day 0, cyclophosphamide 130 mg on day 1, doxorubicin 90 mg on day 1, vincristine 2 mg on day 1, and dexamethasone 16 mg on days 1-5. Prior to the administration of chemotherapy, hydration, alkalinization, and antiemetic treatments were administered. The patient tolerated the treatment well and did not report significant discomfort. He is currently under close outpatient follow-up.

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Figure 3. Immunohistochemistry: (A) Hematoxylin and eosin (H&E) staining, ×60; (B) CD10 expression, ×60; (C) CD20 expression, ×60; (D) BCL-2 expression, ×60; (E) BCL-6 expression, ×60; (F) Ki-67 expression, ×60.

#### Discussion

This case highlights several important clinical insights regarding the diagnosis and management of primary gastric follicular lymphoma (FL), a rare subtype of extranodal non-Hodgkin lymphoma. Due to its rarity, nonspecific symptoms, and often indolent course, primary gastric FL is easily overlooked or misdiagnosed, being particularly mistaken for mucosa-associated lymphoid tissue (MALT) lymphoma, which shares overlapping histologic features but differs significantly in pathogenesis, clinical course, and treatment strategy [12].

Follicular lymphoma is a common type of non-Hodgkin lymphoma, typically occurring in lymph nodes but also involving other organs such as the liver, spleen, and bone marrow. However, primary gastrointestinal FL is rare, accounting for only 1-3.6% of gastrointestinal non-Hodgkin lymphomas [1]. Primary gastric lymphomas are predominantly classified into 3 categories: diffuse large B-cell lymphoma (DLBCL), mucosa-associated lymphoid tissue (MALT) lymphoma, and FL [6]. In endoscopic examinations, DLBCL is characterized by the presence of ulcerative, nodular, or mass-like lesions. The most common endoscopic feature of DLBCL is ulceration, which typically presents as deep, irregular ulcers with necrotic bases and exudate [13]. The ulcer margins are often irregular, and the lesions frequently exhibit extensive invasion into the gastric wall. Occasionally, raised masses or nodular lesions are observed, with thickening of the gastric wall taking on a nodular or mass-like appearance [13]. In advanced stages, widespread mucosal erosion and hemorrhage may be seen on endoscopy [14].

MALT lymphoma is closely associated with *Helicobacter pylori* (Hp) infection and typically appears as chronic gastritis or erosive lesions under endoscopy. In contrast to FL, MALT lymphoma frequently presents with superficial or diffuse lesions in the gastric mucosa, and it is much more prevalent than FL [1]. Hp infection is frequently associated with MALT lymphoma, whereas FL is not typically linked to Hp infection [12]. These clinical and pathological differences are important for diagnosis, but the similar histological features of FL and MALT lymphoma in small biopsy samples often result in the misdiagnosis of FL as MALT lymphoma [15].

Furthermore, DLBCL and MALT lymphoma are more frequently associated with lymph node involvement or systemic spread, whereas FL tends to remain localized, with fewer cases of widespread dissemination [16]. Most gastric FL presents as hypoechoic submucosal tumor-like lesions, with a few mucosal changes during EUS examinations [11]. Depressed and ulcerative lesions are rare compared with MALT lymphoma or diffuse large B-cell lymphoma. These findings were consistent with the endoscopic findings in the present case. Previous studies have shown that primary intestinal FL often presents with symptoms such as bowel obstruction, whereas primary gastric FL typically lacks the clinical symptoms such as abdominal pain, diarrhea, early satiety, bloating, or positive fecal occult blood tests [17]. This aligns with the clinical presentation observed in our patient, whose lesion was discovered during a routine health check-up, highlighting the potential benefit of early endoscopic screening in asymptomatic individuals.

From the pathological perspective, FL and MALT lymphoma have distinct immunohistochemical profiles. MALT lymphoma typically expresses CD20 and CD79a as B-cell markers and is associated with BCL-10 and MALT1 gene abnormalities [18]. Conversely, FL is often positive for BCL-2 and CD10, and is associated with the t(14;18) chromosomal translocation [19]. These immunohistochemical differences are of paramount importance in distinguishing these 2 types of lymphomas.

The patient underwent standard laboratory tests and an enhanced abdominal CT scan upon admission. However, because the lesion on imaging could be easily mistaken for gastric cancer or other malignant lesions, we arranged for electronic gastroscopy and endoscopic ultrasound (EUS). As in a previously reported case, narrow-band imaging (NBI) revealed a "treelike appearance" (TLA) phenomenon, which indicated significant lymphomatous infiltration and associated neovascularization [11]. Although TLA was initially studied and defined in MALT lymphoma [20], the presence of TLA during endoscopy does not necessarily rule out the possibility of follicular lymphoma. In our patient's NBI imaging, the typical TLA was not observed. We speculate that this may be attributable to the fact that he had grade 2 lymphoma. According to the guidelines, grade 3B FL (characterized by sheet-like blastoid cells) is considered an aggressive lymphoma, while grades 1, 2, and 3A are categorized as indolent diseases [21]. For indolent lymphomas, tumor cell infiltration and neovascularization are relatively less pronounced, which may explain the absence of typical TLA.

Due to the lack of specific endoscopic features for FL, early fine-needle aspiration biopsy and comprehensive pathological evaluation, including immunohistochemical analysis, are crucial for correct diagnosis [10]. In this case, the diagnosis of gastric FL was confirmed based on pathological and immunohistochemical findings. This case highlights that early tissue biopsy is a critical tool in avoiding misdiagnosis, and EUS-guided fineneedle aspiration biopsy is a safe and feasible method for obtaining tissue samples. For the diagnosis of primary gastric FL, a thorough upper-gastrointestinal endoscopic examination is necessary, as well as a comprehensive ultrasound evaluation of lymph nodes and bone marrow biopsy [22]. This is necessary to ascertain the disease stage, which is crucial for developing an appropriate treatment plan.

Immunochemotherapy is currently the most commonly used treatment option both in China and internationally [23]. Among

these, the combination of rituximab and chemotherapy has become the standard first-line treatment for patients with FL11/14/24 4: 20: 00 AM. Both the CHOP regimen and the CVP regimen (Cyclophosphamide + Vincristine + Prednisone) have been shown to improve both the short-term and longterm prognosis of patients. Of these, the R-CHOP regimen is one of the most frequently used standard treatments for FL patients, while the R-CVP regimen is more suitable for elderly patients or those with compromised cardiac function [21]. For patients in stage I-II FL without bulky disease (tumor diameter less than 7 cm), there is sufficient clinical evidence to support the use of involved-site radiation therapy (ISRT) [24]. However, in our patient, due to the specific location of the gastric FL and to minimize the risk of perforation and bleeding, we opted for systemic chemotherapy with the R-CHOP regimen, taking into account the patient's strong preference for treatment.

The Follicular Lymphoma International Prognostic Index (FLIPI) is widely used to predict the prognosis of patients with FL. With the increasing use of anti-CD20 monoclonal antibody therapy for FL, the FLIPI-2 model has become more commonly applied in clinical practice [25]. FLIPI-2 incorporates the following factors:  $\beta$ 2-microglobulin levels exceeding the upper limit of the normal range, the largest involved lymph node having a diameter greater than 6 cm, bone marrow involvement, hemoglobin levels <120 g/L, and age >60 years [26]. One point is assigned for each factor, resulting in a risk classification: a score of 0-1 point indicates low risk, 2 points indicates intermediate risk, and 3-5 points indicates high risk. The 2-year overall survival rates for these groups are 98%, 94%, and 87%, respective-ly, while the 2-year progression-free survival rates are 84%, 70%, and 42%, respectively [26].

## Conclusions

We report a rare case of primary gastric follicular lymphoma that presented as a submucosal tumor on endoscopy. In this case, EUS and NBI imaging were not sufficient for an accurate diagnosis, thus necessitating EUS-guided fine-needle aspiration biopsy, followed by pathological and immunohistochemical examination. The patient was subsequently treated with R-CHOP chemotherapy and is currently under close outpatient follow-up.

#### **Declaration of Figures' Authenticity**

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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