Primary gastric lymphoma is a rare gastric malignancy. Although the stomach is the most common site of primary gastrointestinal lymphoma, it accounts for only 1-5% of gastric malignancy.\(^1\)

Primary gastric lymphoma is not only uncommon, but complex in its diagnostic process.\(^2\) By endoscopic view, correct diagnosis of gastric lymphoma is unlikely, since it mimics gastritis, ulcer or erosion. Even after endoscopists take biopsies from benign looking lesions, pathologists need to make a differential diagnosis between neoplastic, and reactive, lymphoid infiltrations. Then, further differentiation of subtypes, with the aid of immunohistochemical staining (IHS), is required.

Because of its rarity and diagnostic complexity, pathological reports from endoscopic biopsy, revealing primary gastric lymphoma, can at times be unreliable. Such unreliability is even more likely when endoscopic biopsy indicates the rarest subtype of gastric lymphoma, while initial endoscopic presentation fails to raise the slightest suspicion of gastric lymphoma.

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**Key Words:** Lymphoma, B-cell, marginal zone; Neurilemmoma; Stomach neoplasms

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We report a rare case of a patient, presenting with a gastric submucosal tumor, whose initial diagnosis of CD5 positive primary gastric lymphoma was overturned to gastric schwannoma, by the histopathological report on the surgical specimen. We would like to establish clinical and pathological explanations, and to suggest options for prevention of such discordance of diagnoses.

CASE REPORT

A 53-year-old male was diagnosed with a gastric submucosal tumor, by endoscopic examination, during his annual health screening, in December 2010. A 2.5 cm sized round mass was located at the greater curvature of the antrum (Fig. 1). On EUS, the homogenous hypoechoic mass as originated from the fourth layer.

Fig. 1. Endoscopic and EUS images taken in its initial presentation. (A) A 2.5 cm sized round mass was located at the greater curvature of the gastric antrum. (B) On EUS, the homogenous hypoechoic mass originated from the fourth layer.

Fig. 2. Histopathological and immunohistochemical findings of specimen from deep endoscopic biopsy. (A) Multiple pieces of gastric mucosa show heavy infiltration of lymphoid tissue, without normal gastric mucosa structure (H&E, ×40). (B) Small round lymphoid tissue infiltrates in the gastric mucosa, and entraps a few small vessels (H&E, ×200). (C) Immunohistochemical stains show positive reaction for CD5 and CD20 (×100), but no reaction for CD23 and cyclin D1 (×200), in crushed lymphoid lesion.
from the fourth layer. Although gastrointestinal stromal tumors (GISTs) are the most common submucosal tumors of the gastrointestinal tract, the diagnosis was not to be confirmed without histological examination. Regular follow-ups were recommended for this asymptomatic submucosal tumor.

In December 2011, at the follow-up endoscopic examination, the tumor showed no interval changes. Upon request for histological confirmation from the patient, deep endoscopic biopsy after mucosal incision was attempted. Mucosa above the mass was incised, using electrocautery, and deep biopsy was performed, using endoscopic forceps through the mucosal opening, in an effort to acquire specimen from this submucosal tumor. The histological examination showed heavy infiltration of lymphoid tissue, which was consistent with malignant lymphoma (Fig. 2). IHS showed positive reaction for CD20 and CD5, but no reaction for CD23 or cyclin D1.

Abdominal CT showed a 2.5 cm sized round exophytic submucosal tumor, with two small lymph nodes in the gastroepiploic area (Fig. 3). PET-CT revealed mild fluorodeoxy-D-glucose (FDG) uptake, only at the gastric antrum.

Although the endoscopic appearance was odd, the initial histological diagnosis of gastric lymphoma was not to be neglected. In an effort to make histological confirmation, as well as offer treatment, a surgical treatment was recommended for this submucosal lesion, which might not have been suspected of gastric lymphoma, without the histological report. Laparoscopy assisted distal gastrectomy with lymphadenectomy was performed, in January 2012.

Macroscopic inspection of the tumor showed a firm white mass occupying the submucosal, muscular and subserosal layers, with intact overlying mucosal layer (Fig. 4). Microscopic examination revealed a well-circumscribed tumor, consisting of spindle cells, with peripheral lymphoid cuffing (Fig. 5). IHS showed a positive reaction for S-100 protein, but no reaction for CD34, CD117, desmin or DOG-1. Of the 65 lymph nodes harvested, no lymph node abnormality was observed. The final diagnosis was gastric schwannoma.

**DISCUSSION**

The endoscopic finding of gastric lymphoma is usually indistinguishable from benign gastric disease, such as gastritis, ulcer, or erosions. In such cases, diagnosis of lymphoma by the endoscopist is almost impossible. Thickened or irregular gastric folds, resembling classical gastric lymphoma, are less frequently detected. Detection of mass lesions is even more unusual. Our patient presented with a smooth round submucosal mass in the gastric antrum, and histological diagnosis of gastric lymphoma from endoscopic biopsy was never expected. Even after learning the result of endoscopic biopsy, clinicians were still unconvinced by the features appearing on endoscopy.

The histopathological diagnosis of gastric lymphoma is composed of two steps. The first step is to observe lymphoid infiltrate, and to make a distinction between neoplastic, and reactive. The second step is to define the subtype of gastric lymphoma, by IHS. Whereas our endoscopic findings were rather odd, the histological findings were consistent with gas-

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**Fig. 3.** Abdominal computed tomographic scan. A round exophytic submucosal mass was located in the gastric antrum (arrow). Effervescent granules were used for gastric distension.

**Fig. 4.** Cross-section of the tumor, showing a white firm mass below the intact mucosal layer. The mass originated from the muscularis propria, occupying the submucosal and subserosal layers, as well.
tric lymphoma, showing heavy infiltration of lymphoid tissue. However, results from IHS doubled its oddness, by showing a positive reaction, not only for CD20, but also for CD5.

CD20 is a B-cell marker, and its expression is associated with extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma), mantle cell lymphoma, chronic lymphocytic leukemia (CLL), or follicular lymphoma. Among these, mantle cell lymphoma and CLL are commonly known to be associated with CD5 expression. In our case, negative expression for cyclin D1 made diagnosis of mantle cell lymphoma less likely, and negative expression for CD23 made diagnosis of CLL less likely, as well.2

The emphasis must be placed on CD5 positivity. It has been generally known that CD5 positivity is occasionally associated with extra-gastric marginal zone lymphoma, but never with primary gastric MALT lymphoma.2 However, there was a recent report on CD5 positive MALT lymphoma, in which one case was associated with primary gastric MALT lymphoma.3 It appears that CD5 positivity is rare in MALT lymphoma, occurring in less than 1% of cases, and is often associated with involvement of nongastric sites, and with an increased tendency of disseminated disease. In our case, with no sign of disseminated disease, IHS led us to one of the rarest subtypes of gastric MALT lymphoma. Even if we disregard the oddness of endoscopic findings, IHS provided us with another peculiarity, of failing to convince with its diagnosis.

Historically, the primary choice for treatment of gastric lymphoma was surgery alone, or surgery followed by chemotherapy and/or radiotherapy.4,5 Some investigators have reported that gastrectomy with D2 lymphadenectomy alone provides excellent survival benefit, for patients with early stage gastric lymphoma. However, it has been reported that conservative treatment of *Helicobacter pylori* eradication, chemotherapy and/or radiotherapy could yield comparable results on survival to surgical treatment, and such a treatment could be a favorable approach, by preserving the stomach.6,7 The treatment choice for our patient was surgery. The conservative treatment may have been a choice.
However, we decided that the basis for conservative treatment was not solid enough, from the somewhat odd endoscopic findings, with a peculiarity in IHS.

The postoperative histopathological finding confirmed gastric schwannoma. Gastric schwannoma is a rare neoplasm, constituting 0.2% of all gastric tumors. It is a mostly benign submucosal tumor, composed of spindle cells, with a peripheral cuff-like lymphocytic infiltration. It is known to arise in the submucosa and muscularis propria, with an intact mucosal layer. Immunohistochemically, gastric schwannoma is strongly positive for S-100 protein, and frequently positive for glial fibrillary acidic protein (GFAP) with variability. On the other hand, it reacts negatively to CD117, CD34, smooth muscle actin (SMA) and desmin.

Regarding plausible causes of the disparity between preoperative and postoperative diagnoses, we would like to emphasize the methodology of the preoperative endoscopic biopsy. There is a recent report on deep biopsy following mucosal incision being useful, in a histological diagnosis of submucosal tumors. Upon suspicion of a submucosal tumor, a mucosal incision with deep biopsy was performed, since the conventional endoscopic biopsy is often inadequate for definite diagnosis of submucosal tumors. This specimen revealed heavy infiltration of lymphoid tissue, and gastric lymphoma was suspected. It seems that the deep biopsy was not deep enough, or did not reach the target, where spindle cells were to be retrieved. Instead, the deep biopsy was misdirected to the peripheral lymphoid cuff, sampling heavy infiltration of lymphoid tissue only.

An attempt to acquire specimen from a verified location of the tumor may be helpful. There is a report on EUS guided fine-needle aspiration (EUS-FNA), with IHS helping the differential diagnosis of gastric submucosal tumors. Another report, however, found that EUS-FNA was not able to make preoperative diagnosis of gastric schwannoma. We believe that deep biopsy, following mucosal incision and EUS-FNA, are two complementary strategies to improve the diagnostic accuracy of submucosal tumors.

Some may argue that another attempt for endoscopic biopsy should have been made. On review of this case, a successful acquisition of spindle cells may have altered the treatment plan. However, the chance of acquiring spindle cells is still doubtful, after failing at the initial attempt. Moreover, at the time of treatment planning, schwannoma was not even of the slightest concern. Our concerns were whether the initial findings were to be neglected, if the second biopsy showed negative findings; and whether conservative treatment was to proceed, ignoring the odd appearance, if the second biopsy showed similar findings to the initial biopsy. We concluded that, whatever the result from the second biopsy was, it would not alter the treatment plan, and surgery was conducted for both treatment and diagnosis, without another endoscopic biopsy.

Although relieved by the fact that the chemotherapy was not our initial choice of treatment, the extent of surgical resection may be a subject of debate. In clinical practice a false-negative finding at endoscopic biopsy is not uncommon for this submucosal tumor, and surgical resections, including all of wedge resection, subtotal gastrectomy and total gastrectomy, are the known choices available. The availability of preoperative diagnostic confirmation may be an important factor in reducing the extent of resection.

Clinicians should be aware that, in some instances, the peripheral lymphoid cuff of gastric schwannoma may mimic gastric lymphoma. Upon an unexpected pathological report of gastric lymphoma from endoscopic biopsy of clinically suspected benign submucosal tumor, having the slightest suspicion of gastric schwannoma is important. Such awareness may provide clinicians with valid reasons for additive procedures, such as EUS-FNA, or repeated deep biopsy with IHS of S-100, upon such encounters.

REFERENCES