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CASE REPORT

점막하 종양으로 발현한 원발성 식도 점막 연관 림프조직 림프종 1예

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Primary Mucosa-associated Lymphoid Tissue Lymphoma of the Esophagus, Manifesting as a Submucosal Tumor

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We report a case of primary mucosa-associated lymphoid tissue (MALT) lymphoma in the esophagus that manifested as a large submucosal tumor (SMT). Primary esophageal lymphoma is very rare, occurring in less than 1% of all patients with gastrointestinal lymphoma. Only a few cases of MALT lymphoma in the esophagus have been reported in the English literature. A 53-year-old man was referred to Dongguk University Ilsan Hospital (Goyang, Korea) in July 2012 for further evaluation and treatment of an esophageal SMT. Endoscopy showed a cylindrically elongated submucosal mass with normal overlying mucosa in the mid esophagus, 25-30 cm from the incisor teeth. He underwent surgery to confirm the diagnosis. Pathologic findings showed diffuse small atypical lymphoid cells which were stained with Bcl-2, CD20, but not with CD3, CD5, CD23, Bcl-6, or cyclin D1. These cells showed a positive monoclonal band for immunoglobulin heavy chain gene rearrangement. Based on the pathological, immunohistochemical, and molecular biological features, the esophageal mass was diagnosed as extranodal marginal zone B-cell lymphoma of the MALT type. **(Korean J Gastroenterol 2013;62:117-121)**

Key Words: Esophagus; Lymphoma; B-Lymphocytes; Marginal zone B-cell lymphoma

INTRODUCTION

In 1983, Isaacson and Wright[1] described a new type of extranodal B-cell lymphoma, which they called mucosa-associated lymphoid tissue (MALT) lymphoma. This entity is clinically and morphologically different from more frequently found nodal lymphomas.

Approximately 24-48% of all non-Hodgkin's lymphomas manifest extranodally.[2] The gastrointestinal tract is the most commonly involved extranodal site in non-Hodgkin's lymphoma.[3,4] Within the gastrointestinal tract, the stomach is the most common site for extranodal non-Hodgkin's lymphoma, but it is a rare site for primary esophageal lymphoma, accounting for less than 1% of patients with gastrointestinal lymphoma.[3-5] Due to their rarity, only a few cases of MALT lymphoma of the esophagus have been reported in the English literature. Here we report a case of primary esophageal MALT lymphoma presenting as a large submucosal tumor (SMT).

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CASE REPORT

A 53-year-old man was referred to Dongguk University Ilsan Hospital (Goyang, Korea) in July 2012 for further evaluation and treatment of esophageal SMT that had been detected incidentally by screening endoscopy. The patient denied dysphagia and any systemic symptoms. He had a history of hypertension and diabetes mellitus for 7 years. He also had a history of alcohol abuse for 10 years. Physical examination revealed no marked features; the liver, spleen, and superficial lymph nodes were not palpable. The patient's main laboratory data showed no abnormalities except mildly elevated liver transaminases, possibly due to alcoholic liver disease. Hepatitis B surface antigen, hepatitis C virus antibody and autoimmune antibodies were all negative.

Endoscopic examination revealed a cylindrically elongated SMT-like lesion of the esophagus 25-30 cm from the incisor teeth (Fig. 1A). However, the endoscopic biopsy specimen did not show any abnormal finding. Findings relevant to reflux esophagitis or Barrett's changes at the esophageal-gastric junction were not detected. Endoscopic ultrasonography showed an ovoid homogenous hypoechoic mass which was located in the deep mucosal and submucosal layers (Fig. 1B). Chest computed tomography showed a homogenous soft tissue mass of 5 cm length located in the anterior portion of the mid esophagus. Posterior displacement of the esophageal lumen by the mass was observed (Fig. 2). There were no signs of infiltration of significant size of adjacent tissues or lymph nodes.

To confirm the diagnosis and treat the lesion, surgery was performed. During the surgical process, surgeon decided to only enucleate the lesion, presuming that the mass was a benign lesion, such as a leiomyoma, based on the surgical findings. The surgical specimen was fragmented and consisted of grayish pink soft tissue, measuring 3.5×2.5×0.7 cm.

Histologically, the esophageal mucosa was unremarkable. The lamina propria and the submucosa were replaced by diffuse infiltration of atypical lymphoid cells (Fig. 3A). On

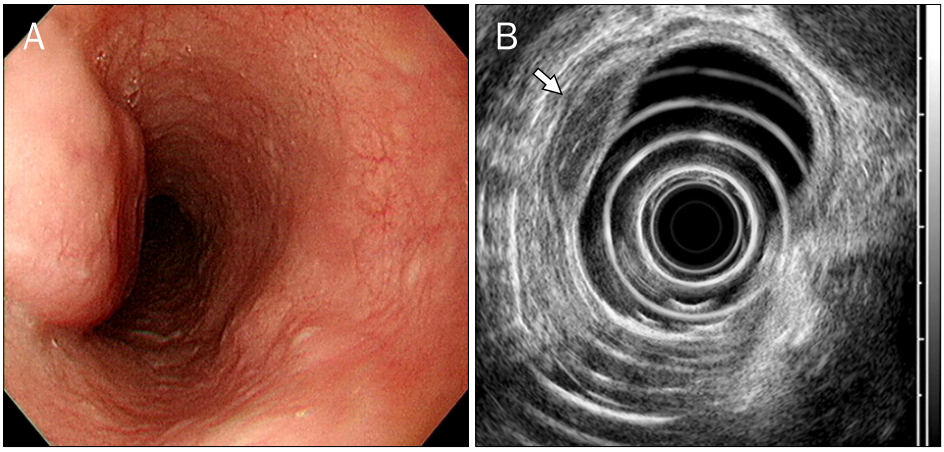

Fig. 1. Endoscopic findings. (A) Endoscopic observation shows a cylindrically elongated submucosal mass in the mid esophagus (25-30 cm from the incisor teeth). (B) Endoscopic ultrasonography shows an ovoid homogenous hypoechoic mass (arrow) originating from the third hyperechoic layer (submucosa).

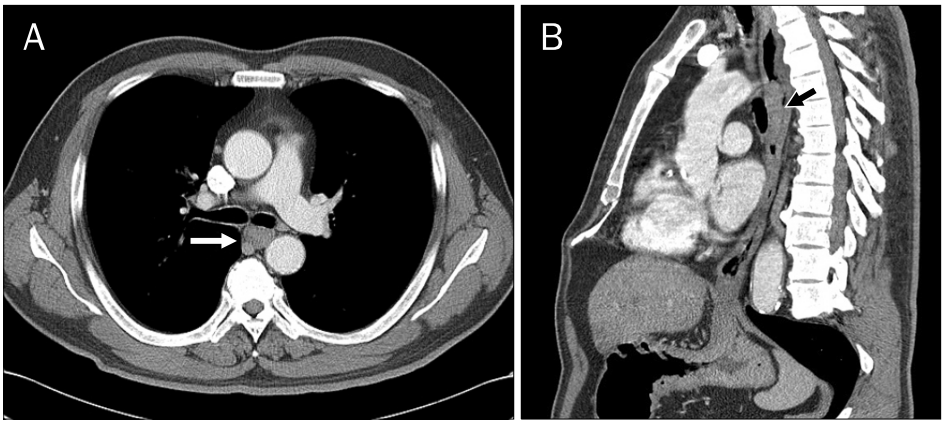

Fig. 2. Chest computed tomography findings. (A) There is a mediastinal solid mass arising from the esophagus wall (arrow). Its density is homogenous. (B) Sagittal reconstruction view shows a well-circumscribed longitudinal mass, following the path of the esophagus (arrow). There is a posterior displacement of the esophageal lumen by the mass.

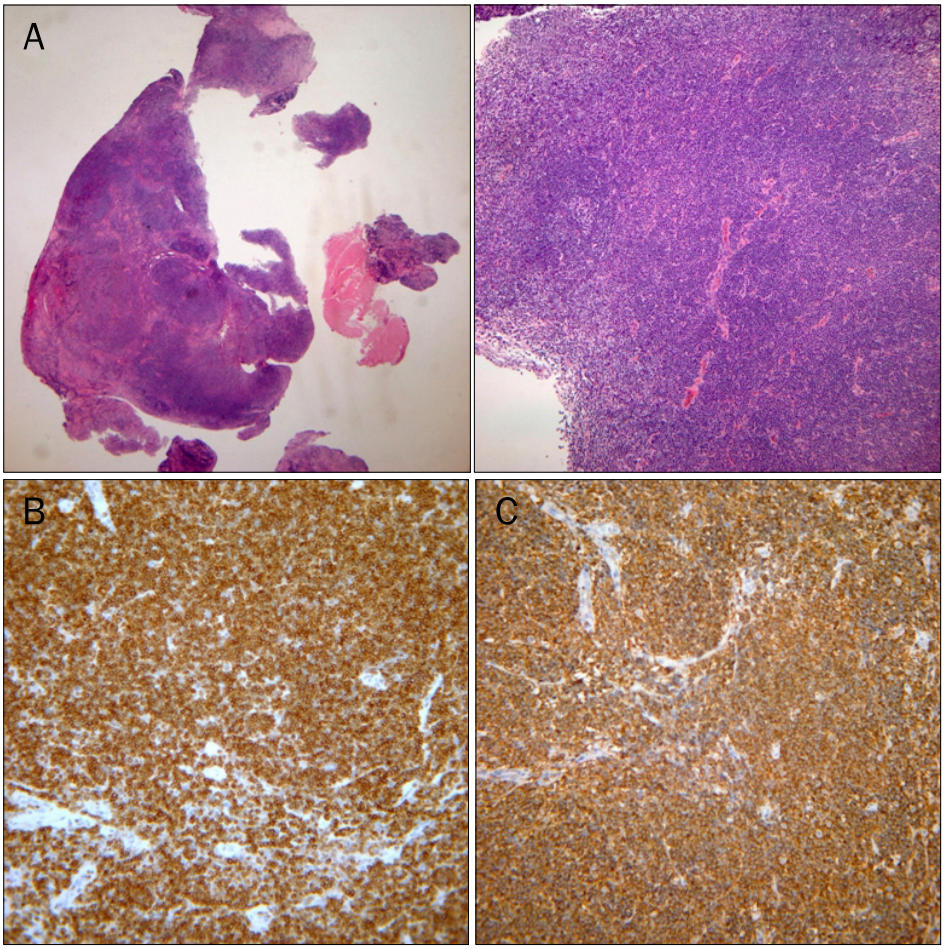

Fig. 3. Pathologic features. (A) Diffuse infiltration of atypical lymphoid cells occupying the marginal zone of the lymphoid follicle (H&E; left, ×12.5; right, ×100). (B) Positive immunoreactivity for the bcl-2 protein (immunohistochemistry, ×200). (C) Positive immunoreactivity for the CD20 protein (immunohistochemistry, ×200).

immunohistochemical staining, the tumor cells were positive for Bcl-2 (Fig. 3B) as well as CD20 (Fig. 3C), and negative for CD3, CD5, CD23, Bcl-6 and cyclin D1. Chromosomal abnormalities were not found. These cells showed a positive monoclonal band for immunoglobulin heavy chain gene rearrangement.

Based on the pathological, immunohistochemical, and molecular biological features, the esophageal mass was diagnosed as extranodal marginal zone B-cell lymphoma of the MALT type.

We performed bone marrow biopsy for the staging work-up of the esophageal MALT lymphoma, and the biopsy revealed no evidence of bone marrow involvement with the lymphoma. Follow-up endoscopy with the rapid urease test after surgery showed erosive gastritis with *Helicobacter pylori* infection. So the patient was treated with triple therapy (proton pump inhibitor, clarithromycin and amoxicillin for 1 week) successfully. We planned subsequent radiotherapy due to the possibility of remnant tumor. He is now alive and in good health.

DISCUSSION

According to the World Health Organization classification,[6] MALT lymphoma is a type of mature (peripheral) B-cell neoplasm, called "extranodal marginal zone B-cell lymphoma of the MALT type." MALT is physiologically distributed throughout the small intestine, appendix, colon and rectum, forming Peyer's patches, but is normally not found in the stomach mucosa or the esophagus. MALT lymphoma can develop from organs where lymphocytes are normally absent, by the acquisition of MALT. The acquired MALT develops in association with chronic inflammation induced by persistent infection or autoimmune disorders such as *H. pylori* infection, Sjögren's syndrome, or Hashimoto's disease.[7] In the esophagus, acquired MALT was detected in 5% of patients with Barrett's esophagus, and it was associated with *H. pylori* infection.[8] Although MALT lymphoma may arise from any organ, the esophagus is a rare site of origin.

We were able to find 11 case reports of primary esoph-

Table 1. Clinical Findings of Reported Primary Esophageal MALT Lymphomas

Patient No.	Author	Age (yr)	Sex	Past medical history	Complaint	*Helicobacter pylori* infection	Tumor feature			Therapy	
							Site	Size (cm)	Endoscopic finding	Primary	Adjuvant
1	Chung et al.[9]	65	Male		Dysphagia	No	U-M	10×3×3	SMT	Chemotherapy (CHOP×6)	
2	Nishryama et al.[18]	63	Female		None	No	M	10	SMT	ND	
3	Hayashi et al.[10]	62	Female		None	No	ND		SMT	Chemotherapy (R-CHOP×3)	
4	Hosaka et al.[11]	83	Female		Heartburn	No	U	1 and 1	SMT	EMR	
5	Kishi et al.[12]	59	Male		Tarry stool	No	U-L	15×6.5×6	SMT	Radiotherapy (36 Gy)	
6	Kitamoto et al.[13]	74	Male	MCTD	None	No	M		SMT	Radiotherapy (36 Gy)	
7	Miyazaki et al.[14]	49	Male		None	No	L		SMT	Operation	
8	Shim et al.[15]	61	Male	Tbc, syphilis, autoimmune thyroiditis	None	Yes	M-L	2×8	SMT	Operation	*H. pylori* eradication
9	Soweid and Zachary[16]	61	Male		None	Yes (treated)	U	1×2 and 1×2	SMT	*H. pylori* eradication	Chemotherapy (regimen unknown)
10	Yano et al.[17]	70	Female		None	No	M	0.6×0.8 and 2.0×0.8	SMT	EMR	Radiotherapy (30 Gy)
11	Ogura et al.[19]	60	Female		Dysphagia		U-L		SMT	Chemotherapy (R-CHOP×6)	

MALT, mucosa-associated lymphoid tissue; MCTD, mixed connective tissue disease; Tbc, tuberculosis; U, upper; M, middle; L, lower; ND, no description in the original reports; SMT, submucosal tumor; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisolone; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone; EMR, endoscopic mucosal resection.

ageal MALT lymphoma in the English-language literature (Table 1).[9-19] Many of these cases were diagnosed surgically. However, only one case was diagnosed by endoscopic ultrasound-guided fine-needle aspiration.[19] The average age of these patients was 64.3 years (range, 49-83 years); there were six men and five women. Two patients had a history of autoimmune disease; the other nine had no notable medical history. No pattern was found among the tumor sites in the esophagus, but endoscopic findings were similar to those of SMTs. Two of the patients had dysphagia,[15,19] but the remainder had no associated symptoms, namely dysphagia. Although our patient had a large sized esophageal mass, he had no symptoms. Only one of the published cases presented *H. pylori* infection at the time of diagnosis.[15] Another case had an incidence of previous infection, but not at the time of diagnosis.[16] The other nine cases did not show *H. pylori* infection. Our patient was infected with *H. pylori* and received *H. pylori* eradication therapy.

It is known that gastric MALT lymphoma without chromosomal aberration of t(11;18) regresses completely after *H. pylori* eradication therapy.[20] However, esophageal MALT lymphoma is still rare and no standard treatment has been established. One patient underwent endoscopic mucosal resection only,[11] one underwent endoscopic mucosal resection followed by radiotherapy,[17] one underwent surgical resection only,[14] one underwent surgical resection followed by *H. pylori* eradication therapy,[15] three underwent chemotherapy only,[9,10,19] one underwent *H. pylori* eradication therapy followed by chemotherapy,[16] and two underwent radiotherapy only.[12,13] Our patient had surgical resection of the tumor and *H. pylori* eradication therapy; radiotherapy is subsequently considered for possible remnant tumor.

Barrett's esophagus may be associated with MALT. However, none of the cases of previous esophageal MALT lymphoma showed Barrett's esophagus. And only two cases of previous esophageal MALT lymphoma and our case were positive for *H. pylori*. We could not confirm a relationship between esophageal MALT lymphoma and Barrett's esophagus

or *H. pylori* infection.

The vast majority of esophageal MALT lymphomas appear to be of low-grade malignancy, showing slow growth and a low tendency to spread. Therefore, long term follow-up is needed to determine the biological and clinical characteristics of this disease. Thus, it is important to conduct further studies involving more patients with primary esophageal MALT lymphoma.

In summary, primary esophageal MALT lymphoma is a very rare disease. Our case was found incidentally during endoscopy. We report a case of esophageal MALT lymphoma without peripheral or mediastinal involvement which presented itself as a large SMT. This growth feature might be a characteristic of primary esophageal MALT lymphoma. Close attention should be paid to SMT-like esophageal masses.

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