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CASE REPORT

다른 시기에 식도와 위를 침범한 원발성 점막 연관 림프종

변승주, 강현우, 차주경, 류수령, 이정현, 김도연, 김어진[1]
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Primary Mucosa-associated Lymphoid Tissue Lymphoma Metachronously Involving Esophagus and Stomach

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Mucosa-associated lymphoid tissue (MALT) lymphoma is found in various organs as extranodal B cell lymphoma. The gastrointestinal tract is the most commonly involved extranodal site in MALT lymphoma. However, primary esophageal MALT lymphoma is very rare. In addition, few cases with metachronous gastric involvement have been reported. A 55-year-old man was diagnosed with MALT lymphoma by surveillance esophagogastroduodenoscopy. A 5 cm esophageal submucosal tumor-like lesion was incidentally revealed by screening esophagogastroduodenoscopy two years prior. Esophagogastroduodenoscopy showed a cylindrically elongated submucosal mass with normal overlying mucosa in the mid esophagus. He underwent surgery to confirm the diagnosis. The pathologic diagnosis was esophageal MALT lymphoma. He was treated with radiation, which achieved complete remission. Esophagogastroduodenoscopy and chest computed tomography were performed every three to six months, with no evidence of recurrence for 18 months. After 21 months, several elevated gastric erosions were found on the great curvature and posterior sides of the midbody and confirmed as MALT lymphoma pathologically. Here we report a case with MALT lymphoma metachronously involving the esophagus and stomach. **(Korean J Gastroenterol 2016;67:257-261)**

Key Words: Marginal zone B-cell lymphoma; Esophagus; Stomach; Metachronous

INTRODUCTION

Primary extranodal malignant B cell lymphomas of mucosa-associated lymphoid tissue (MALT) develop from the mucosal organs, mainly from those of the gastrointestinal tract.[1] Gastrointestinal tract MALT lymphoma comprises 5% of all lymphomas and 35-40% of primary gastrointestinal tract lymphomas.[2,3] Esophageal lymphoma is a rare condition, accounting for less than 1% of all gastrointestinal lymphomas.[4] Esophageal lymphoma is usually seen secondary to mediastinal lymph nodes invasion or continuous spread from gastric lymphoma.[5] A few case reports describe sequential involvement of the esophagus and stomach. Here we report a case with MALT lymphoma metachronously involving the esophagus and stomach.

CASE REPORT

A 55-year-old man was diagnosed with esophageal submucosal tumor (SMT)-like lesion incidentally by screening esophagogastroduodenoscopy two years prior. He had a 10-year history of hypertension and diabetes mellitus. He

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had no subjective symptoms and signs, such as dyspepsia, fatigue, dysphasia, fever, or weight loss. A cylindrically elongated SMT- like lesion (Fig. 1A) was found on the esophagus 25-30 cm from the incisor teeth, and an erosive lesion (Fig. 1B) was found in the lesser curvature side of antrum by esophagogastroduodenoscopy. However, the endoscopic biopsy specimen did not show any abnormalities. Endoscopic ultrasonography revealed an ovoid homogenous hypoechoic mass located in the submucosal layers (Fig. 1C). Chest CT scan showed a homogenous soft tissue mass 5 cm in length located in the anterior portion of the mid-esophagus. Posterior displacement of the esophageal lumen by the mass was observed. There was no evidence of infiltration of significant size of adjacent tissues or lymph nodes in CT scan. To confirm the diagnosis and treat the lesion, surgery was performed. The surgeon only enucleated 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. Diffuse atypical lymphoid cells infiltrates were seen (Fig. 1D). Immunostaining was positive for CD20 (Fig. 1E) and Bcl-2, and negative for CD3, CD5, CD23, Bcl-6, and cyclin D1. The esophageal mass was diagnosed as MALT lymphoma.

In PET-CT, inflammatory change was evident, probably due to the recent operation and reactive mediastinal lymph nodes. There was no evidence of metastasis. Ann Arbor stage was IEA. The patient was treated 17 times with irradiation (mantle field 34 gray). Because of a positive *Campylobacter*-like organism (CLO) test, a *Helicobacter pylori* eradication regimen was begun, which consisted of clarithromycin 500 mg twice a day, esomeprazole 20 mg twice a day, and amoxicillin 1,000 mg twice a day for seven days.

After irradiation, esophagogastroduodenoscopy and chest CT was performed every three to six months. There was no evidence of recurrence for 18 months. After 21 months, laboratory data revealed a white blood cell count of 7,050/μL; hemoglobin, 14.1 g/dL; platelets, 213,000/μL; glucose, 105 mg/dL; total protein, 6.6 g/dL; albumin, 4.0 g/dL; serum aspartate transaminase, 57 IU/L; serum alanine transaminase, 28 IU/L; serum lactate dehydrogenase, 165 IU/L; BUN, 18.8 mg/dL; creatinine, 0.87 mg/dL; sodium, 135

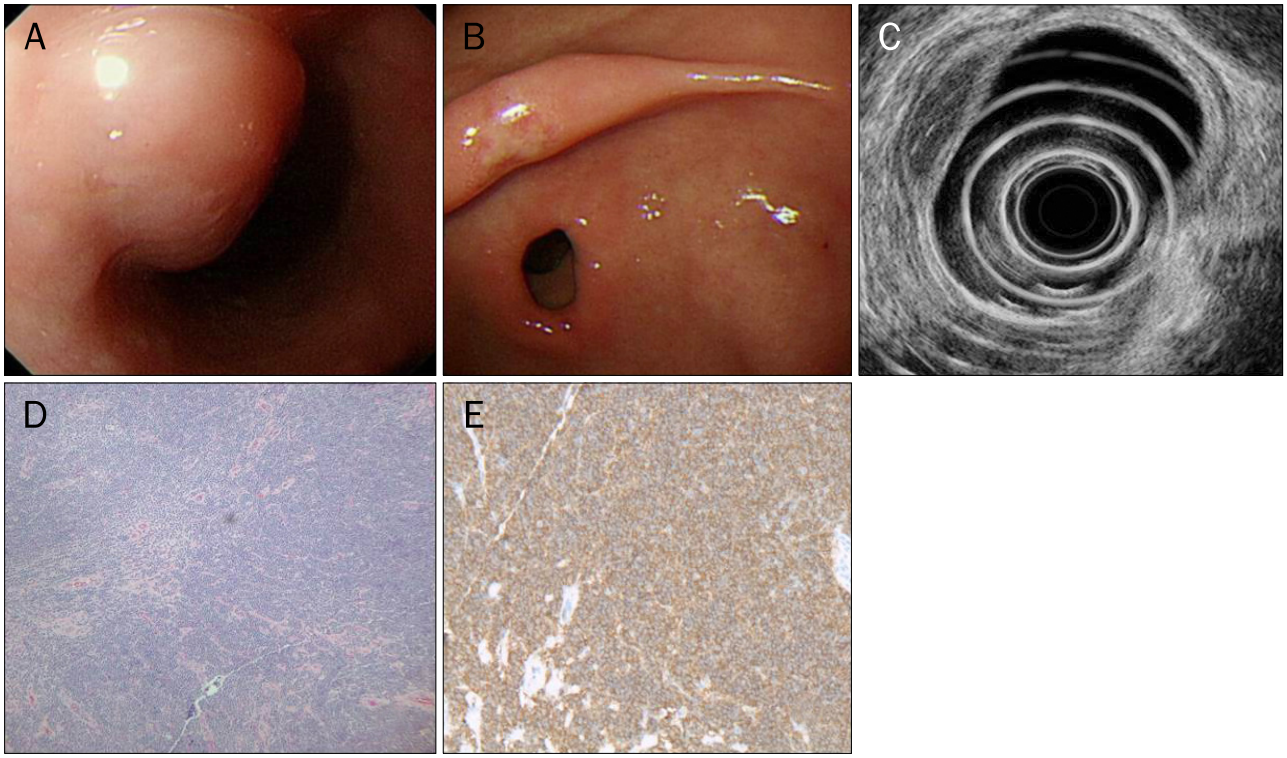

Fig. 1. Intial endoscopic and pathologic findings of the esophageal mass. (A) Esophagogastroduodenoscopy reveals elongated esophageal submucosal tumor-like lesion of the esophagus 25-30 cm from the incisor teeth. (B) Esophagogastroduodenoscopy reveals erosion on the antrum. (C) EUS shows an ovoid homogenous hypoechoic mass located in the submucosal layers. (D) Diffuse infiltration of atypical lymphoid cells (H&E,×100). (E) Positive immunoreactivity for the CD20 protein (immunohistochemistry, ×400).

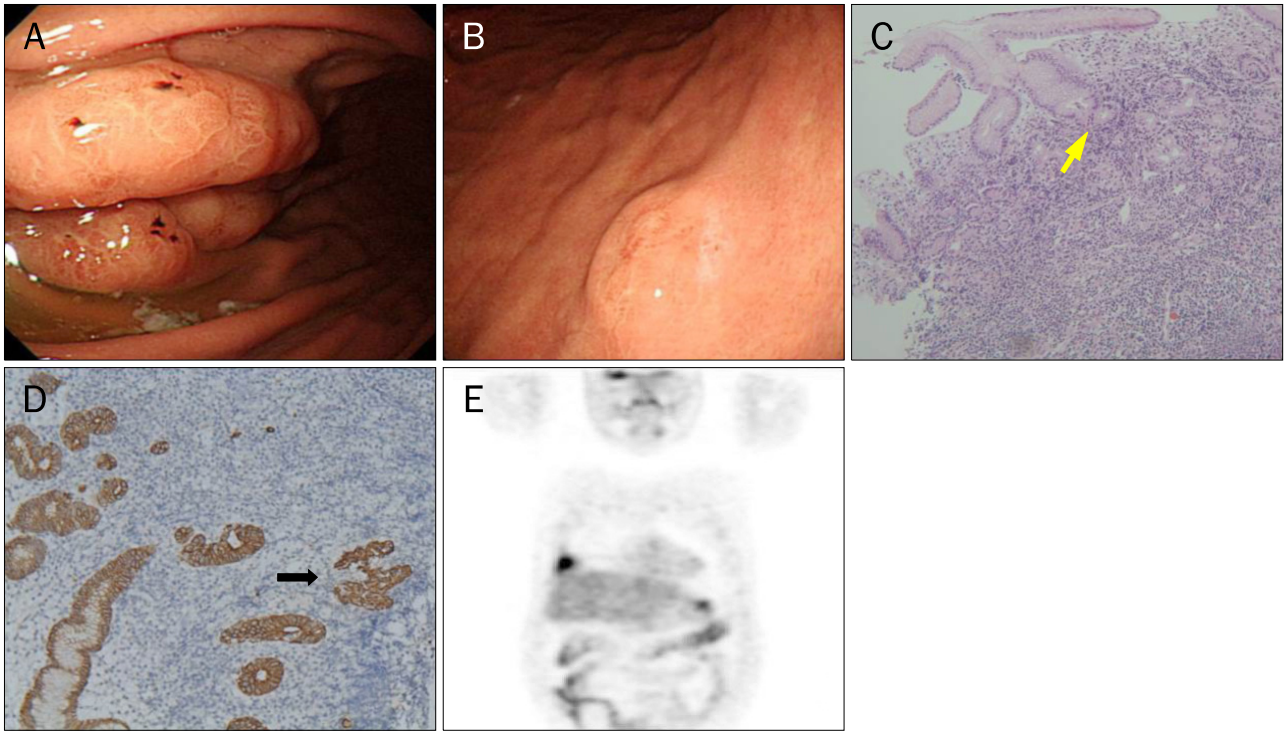

Fig. 2. Follow-up endoscopic, pathologic and PET findings of gastric lesion. (A) Esophagogastroduodenoscopy shows mucosal fold fusion on the greater curvature of the midbody. (B) Esophagogastroduodenoscopy shows erosion on the posterior wall of the midbody. (C) The lymphoid infiltrate in mucosa-associated lymphoid tissue (MALT) lymphoma extends deeper into the lamina propria (H&E, ×200; arrow, lymphoepithelial lesion). (D) Immunohistochemistry for CD20 shows many B-cells and contains lymphoepithelial lesions in which neoplastic B-cells infiltrated (immunohistochemistry, ×400; arrow, lymphoepithelial lesion). (E) Whole body PET-CT shows diffuse hypermetabolic lesion (maximum standardized uptake value=4.1) in the greater curvature side wall of body in stomach and hypermetabolic lesion (maximum standardized uptake value=5.4) in the right middle lung subpleural space.

mmol/L; potassium, 4.4 mmol/L; and chloride, 97 mmol/L. There were mucosal fold thickenings (Fig. 2A) on the greater curvature of the midbody and an erosion (Fig. 2B) on the posterior wall of the midbody on surveillance esophagogastroduodenoscopy. Biopsy was performed in the erosion and mucosal fold fusion. Endoscopic ultrasonography showed mucosal thickening with submucosal layer invasion on the anterior wall of the midbody. Histologically, diffuse atypical lymphoid cells infiltrating the lamina propria and lymphoepithelial lesions were seen (Fig. 2C). Immunohistochemistry for CD20 showed many B-cells and lymphoepithelial lesions (Fig. 2D). The CLO test was negative.

A diffuse hypermetabolic lesion (maximum standardized uptake value=4.1) in the body greater curvature side wall of the stomach, and a hypermetabolic lesion (maximum standardized uptake value=5.4) in the right middle lung subpleural space were evident on PET-CT (Fig. 2E). Nonspecific fluoro-deoxyglucose colonic uptake was observed. A colonoscopy showed no abnormalities. There was no invasion of the bone marrow. There were no B symptoms. After confirmation as Ann Arbor stage IIIEA, the patient was treated with chemotherapy using a regimen consisting of cyclophosphamide, 750 mg/m^2; adriamycin, 95 mg/m^2; vincristine sulfate, 1.4 mg/m^2; and prednisolone sodium succinate, 100 mg. Complete remission was confirmed after six cycles of the chemotherapy on the basis of esophagogastroduodenoscopy, chest CT, and PET-CT. Esophagogastroduodenoscopy showed whitish scar change with the fusion of converging fold on the greater curvature of the mid body (Fig. 3A) and no erosive lesion on the posterior wall of mid body (Fig. 3B). Abnormal hypermetabolic lesions in the stomach and lung disappeared on PET-CT (Fig. 3C). Complete remission is being maintained for 12 months up to the present.

DISCUSSION

In 1983, Isaacson and Wright[6] described a new type of extranodal B-cell lymphoma, which they called “mucosa-asso-

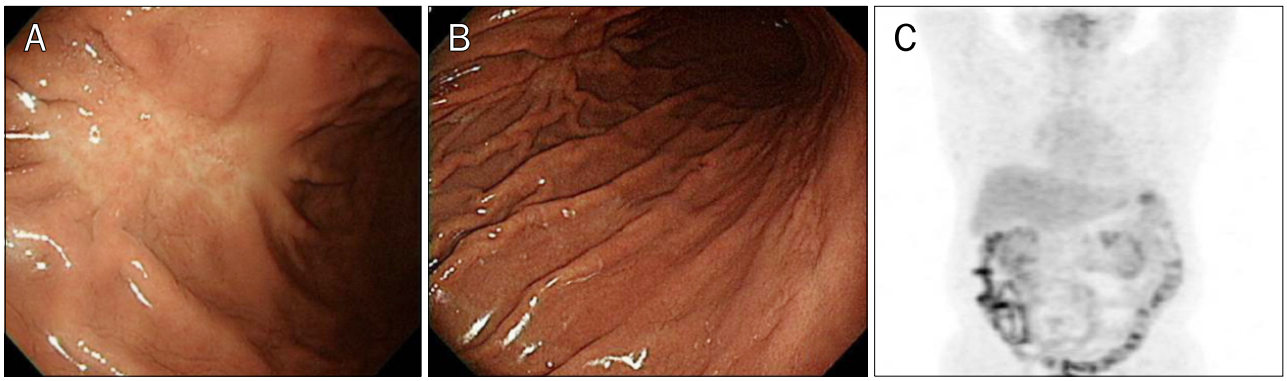

Fig. 3. Esophagogastroduodenoscopic and PET findings following chemotherapy. (A) Esophagogastroduodenoscopy shows whitish mucosal change by scar. (B) Esophagogastroduodenoscopy shows no mucosal change on the posterior wall of the midbody. (C) Abnormal hypermetabolic lesions are not detected in the stomach and lung using PET-CT.

ciated lymphoid tissue lymphoma". MALT lymphoma is the most common type of extranodal B cell lymphoma, and prevelance of low-grade MALT arising in MALT is the highest.[2] The gastrointestinal tract is the most commonly involved extranodal site in non-Hodgkin's lymphoma.[1,7,8] Primary extranodal B cell lymphomas of MALT develop from the mucosal organs, mainly from those of the gastrointestinal tract, including the stomach and colon.[9,10] They may also arise from the lung.[6] Although MALT lymphoma may arise from any organ, the esophagus is a very rare site of origin.[11]

The native type MALT consists of lymphoid tissue physiologically present in the gut (e.g., Peyer's patches), whereas acquired MALT develops in sites of inflammation in response to either infectious conditions, such as *H. pylori*-induced gastritis, or autoimmune processes, such as Hashimoto thyroiditis or Sjögren syndrome.[12] Acquired MALT in the esophagus has been reported in 5% of subjects with Barrett's esophagus and has been associated with *H. pylori*.[13]

When this case was first diagnosed as primary esophageal MALT lymphoma, we reported it in *the Korean Journal of Gastroenterology*[11] due to the rarity of this lymphoma. Because MALT lymphoma involving esophagus, stomach and lung metachronously is extremely rare, we report this case again. To our best knowledge, there was only one case report in English literature of MALT lymphoma arising in the esophagus with gastric and pulmonary metastasis.[14] In contrast with a previous reported case in which the CLO test was negative, the CLO test was positive in this case.

In this case, it was debatable whether MALT lymphoma in stomach represented metastasis or gastric MALT lymphoma. When first diagnosed, there was no evidence of MALT lymphoma in the stomach. Two years later, hypermetabolic lesions were evident in the stomach and right middle lung subpleural space using PET-CT. When first diagnosed, the patient had *H. pylori* infection and gastritis. MALT lymphoma can arise from an autoimmune response triggered by gastritis that is induced by *H. pylori* infection.[15] Thus, MALT lymphoma in the stomach is considered to be gastric MALT lymphoma. Based on the history of this case, since this new hypermetabolic lesion occurred in both locations, the MALT lymphoma in the stomach is considered to represent metastasis. To validate this, genomic alterations between esophageal and gastric MALT lymphoma should have been compared. Unfortunately, this was not done.

Esophageal MALT lymphoma is very rare, so natural history is not described and standard treatment is not established. In a case series, esophageal MALT lymphoma was reported to be of low-grade malignancy with an excellent response to both radiation and chemotherapy.[11] Although it is uncertain, the stomach and lung may be the most common site of esophageal MALT lymphoma recurrence considering the literature[14] including this case. Further studies with lengthy observation are needed to determine the biological and clinical characteristics and optimal treatment of esophageal MALT lymphoma. This patient underwent radiation therapy initially based on localized disease, and later underwent systemic chemotherapy later based on systemic disease (stage IIIEA).

In summary, we report a case of MALT lymphoma that was sequentially generated in the esophagus and stomach. Careful surveillance of gastric recurrence by esophagogastroduodenoscopy may be important after treatment of esophageal MALT lymphoma.

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