CASE REPORT

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Synchronous Primary Low-grade Mucosa-associated Lymphoid Tissue Lymphoma of Colon and Stomach

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Gastrointestinal tracts are the most frequently involved sites of mucosa-associated lymphoid tissue (MALT) lymphoma. Stomach is the most common site of involvement among the gastrointestinal tract. Simultaneous occurrence of primary gastric and colonic MALT lymphoma is rarely reported. We report a case of synchronous double primary MALT lymphoma of the colon and stomach in a healthy subject. A 62-year-old male underwent an esophagogastroduodenoscopy and colonoscopy for medical checkup. An endoscopic examination of the stomach showed an erythematous mucosa in the great curvature of the lower body. The endoscopic finding of the colon was a flat elevated lesion in the sigmoid colon. Microscopic examinations revealed MALT lymphoma and gastric *Helicobacter pylori* infection. We performed imaging studies to evaluate distant metastasis and confirmed that there is no other metastasis. The patient was treated with *H. pylori* eradication therapy and CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy. He had not experienced any recurrence since the treatments, and reached a complete remission state after six months. **(Intest Res 2013;11:204-207)**

Key Words: Lymphoma, B-cell, marginal zone; Colon; Stomach

INTRODUCTION

A marginal zone B-cell lymphoma (MZBL) is the second most common subtype of non-Hodgkin's lymphoma in Korea,[1] and mucosa-associated lymphoid tissue (MALT) lymphoma is the most common form of extranodal lymphomas.[2]

MALT lymphoma can develop in almost any organ as a result of exposure to a persistent stimulus, such as chronic infection or certain autoimmune processes.[1] With the introduction of MALT lymphoma by Isaacson and Wright, more and more MALT lymphomas have been diagnosed.[3] MALT lymphoma is thought to be a multifocal disease, and most MALT lymphomas arise from the gastrointestinal organs, as well as from the extragastrointestinal organs, such as the salivary gland, thyroid gland, lung, bladder and skin.[3] The most common site of MALT lymphomas is the stomach (50%), and other sites of the gastrointestinal tract involved are small intestine (20-30%) and colon (10%).[4] Sometimes MALT lymphoma arises from different organs simultaneously. A few cases of primary gastrointestinal lymphoma that involve both stomach and colon are reported.[5,6] Here, we describe a rare case of synchronous primary gastric and colonic MALT lymphoma in a healthy subject.

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CASE REPORT

In October 2010, a 62-year-old male visited Konyang University Hospital for general medical checkup. He has no specific medical and surgical past history. In 2008, he underwent endoscopy of the stomach and colon for medical checkup, and there were no specific findings. On admission, he was not talking about any complaints. Vital signs (blood pressure 110/70 mmHg, pulse rate 70 beats/min, respiratory rate 20 beats/min, body temperature 36.6°C) and physical examination were normal. The results of serologic test, chest X-ray and simple abdomen X-ray were also normal. An esophagogastroduodenoscopy was performed. There was a erythematous mucosa that had a distinct margin from the adjacent mucosa in great curvature of the lower body (Fig. 1A). Histological evaluation of the biopsy samples showed *Helicobacter pylori*

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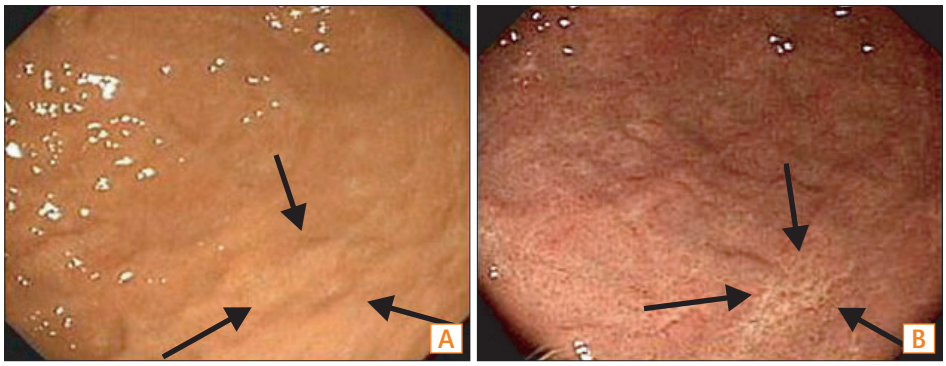

Fig. 1. Esophagogastroduodenoscopic findings. (A) The picture shows erythematous mucosa with distinct margin (arrows) in great curvature of the lower body. (B) After treatment, the following esophagogasroduodenoscopy shows mild erythematous mucosa (arrows) in great curvature of the lower body.

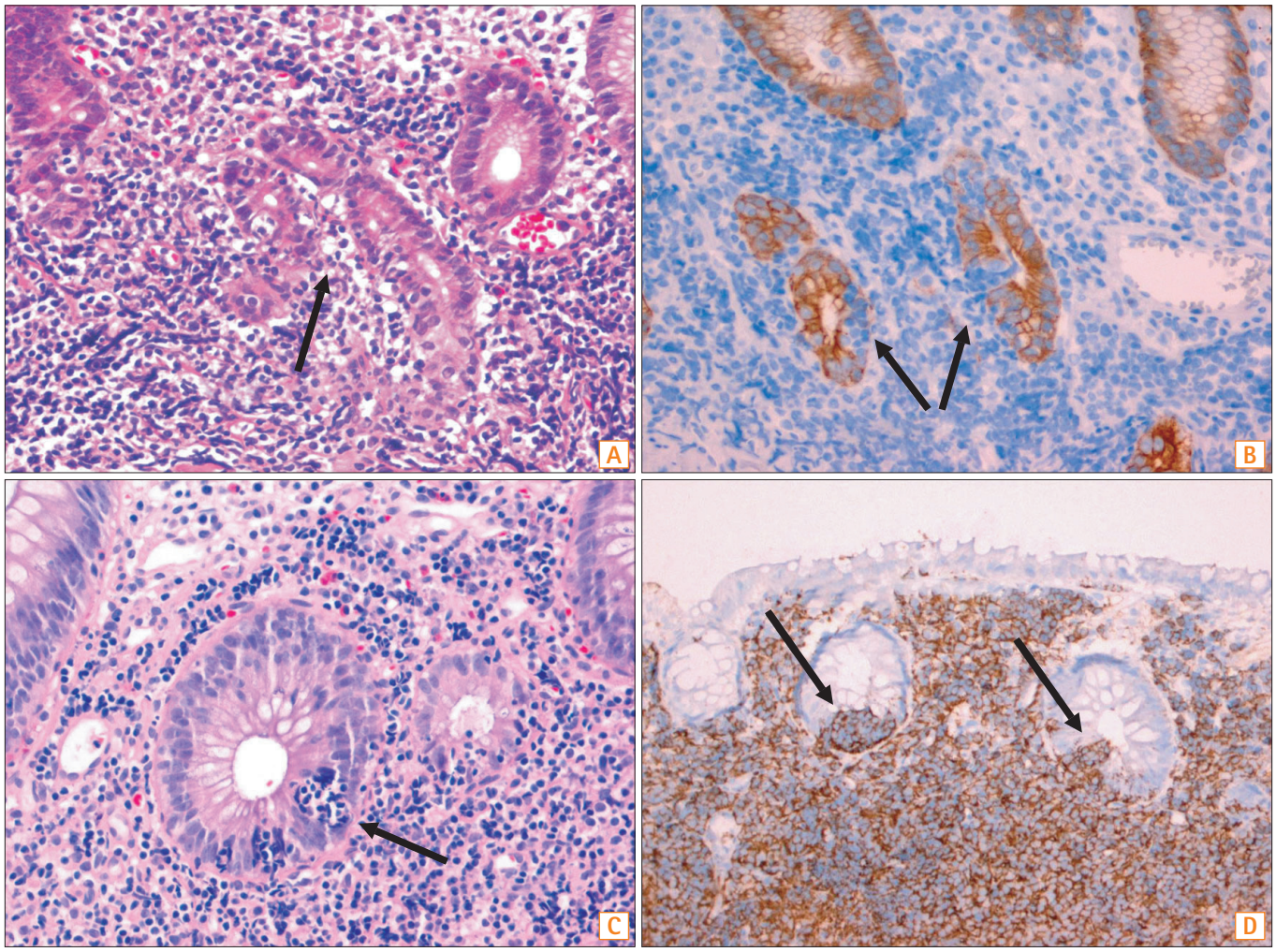

Fig. 2. Microscopic findings of stomach and colon. (A) The picture shows atypical lymphoid hyperplasia with some lymphoepithelial lesion (arrow; H&E stain, ×200). (B) Immunohistochemical staining with cytokeratin shows distinct lymphoepithelial lesions (arrows; ×200). (C) The picture shows diffuse lymphocytic infiltration and prominent lymphoepithelial lesion (arrow; H&E stain, ×200) (D) Immunohistochemical staining with CD20 shows diffuse infiltrative lymphocytes and lymphoepithelial lesions (arrows; ×200).

infection and diffuse lymphocytic infiltration of the centrocyte-like cells with a prominent lymphoepithelial lesion (Fig. 2A) and cytokeratin positiveness by immunohistochemistry (IHC), suggestive of MALT lymphoma (Fig. 2B). Also, colonoscopy was performed. At the sigmoid colon we found a flat elevated lesion, which had a loss of vascularity, and the color

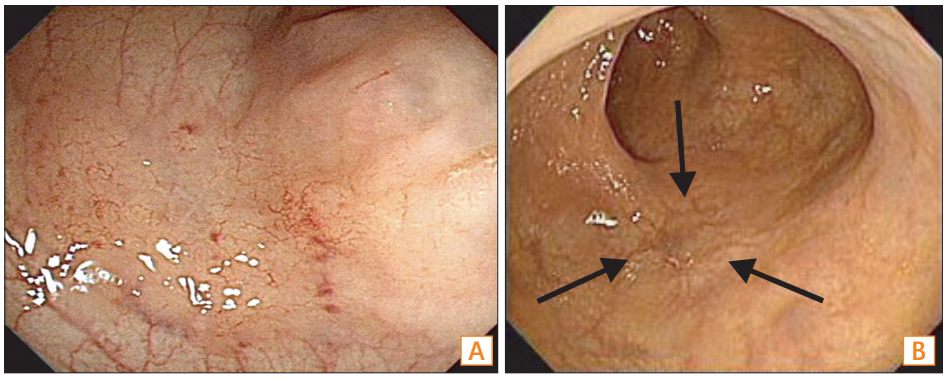

Fig. 3. Colonoscopic findings. (A) The picture shows slightly 1.5×0.8 cm sized flat elevated mucosal lesion with loss of capillary vascularity and tiny telangiectasia in sigmoid colon. (B) After treatment, the following colonoscopy shows healed scar of the colonic mucosa in sigmoid (arrows).

of mucosa of that lesion was changed to milk-white (Fig. 3A). Histological examination of the colonic samples showed diffuse lymphocytic infiltration and a prominent lymphoepithelial lesion as one of the stomach (Fig. 2C). Immunohistochemical stains demonstrated that the lymphocytes are CD3, CD20, CD5 and cytokeratin positive, and cyclin D1 negative (Fig. 2D). Ki-67 labelling index was 10%. At first, we considered a diagnosis of this endoscopic finding as gastritis and a nonspecific colonic lesion. However, after we confirmed the histological result, we diagnosed the case as simultaneous primary low grade MALT lymphoma of the stomach and colon. Then, we performed a CT of the abdomen and chest, positron emission tomography-CT and bone marrow biopsy for staging a work up. There were no other abnormal findings. The stage of this case was IV according to Ann Arbor classification. As there was so much persuasive evidence that gastric MALT lymphoma was related to *H. pylori*, eradication of *H. pylori* was recommended as the primary choice in the treatment of primary low grade gastric MALT lymphoma.[7] The patient was treated with a 7-day course of lansoprazole, amoxicillin and clarithromycin. Eradication of *H. pylori* was proved successful by a follow up ^{14}C-urea breath test. Following four cycles of CHOP (cyclophosphamide 750 mg/m^2, day 1; doxorubicin 50 mg/m^2, day 1; vincristine 1.4 mg/m^2, day 1; prednisone 100 mg, days 1-5) were performed, and these four cycles were repeated every 21 days. The patient was followed up closely with endoscopies, CT scans and complete blood count, as well as biochemistry in addition to biopsy after six months, but no evidence of tumor deterioration was detected. We found a scar of the former lesion, which had healed at a follow up endoscopy after six months (Fig. 1B, 3B). The patient reached a complete remission state after six months.

DISCUSSION

Primary extranodal MALT lymphoma, which was first introduced by Isaacson and Wright can arise in a variety of anatomical sites, such as the gastrointestinal tract, salivary gland, thyroid gland, lung, breast, bladder, and skin.[3] Most MALT lymphomas arise from gastrointestinal organs and the stomach is the most common site involved, accounting for about 50-60% of gastrointestinal tract lymphomas.[4] The most frequently observed non-gastric intestinal MALT lymphoma involvement site was the ileocecal region (40.7%). The rectal (15%) MALT lymphoma was observed more frequently than MALT lymphoma of the colon (4%).[8]

A clinical manifestation of the gastric MALT lymphoma is nonspecific. Symptoms are varied and include asymptom, dyspepsia and epigastric pain. Primary colonic MALT lymphoma is a very rare disease, and most symptoms are also nonspecific, and include asymptom, abdominal bloating and abdominal pain.[9] Endoscopic examinations of the gastric MALT lymphoma revealed various findings, such as geographic superficial ulcer, mucosal depressions or elevation, mucosal atrophy, erosion, and etc. Endoscopic findings of the colon MALT lymphoma were obtained from a configuration of a single polyp, or a flat elevated mucosal lesion.[10] It has been reported that low-grade MALT lymphoma is a neoplasm with a favorable clinical behavior and an excellent prognosis. However, the early diagnosis of MALT lymphoma is unsatisfactory, because of the very indolent course and various endoscopic patterns as already mentioned. When certain findings are disclosed by endoscopy, we should take lymphoma into consideration and biopsies at not only the abnormal mucosa, but also the normal mucosa, repeatedly. Moreover, it is necessary to try a biopsy of the submucosal layer. Histological features of the MALT lymphoma is a lymphoepithelial lesion caused by atypical lymphocytic infiltration, centrocyte-like cell and differentiation of the plasma cell. However, diagnosis cannot be made by only these features. Histologic evaluation, including IHC, represents the diagnostic procedure more reliably to detect the tumor. IHC finding shows CD 19, CD 20, CD 22 and Bcl-2 positive, and CD 3, CD 5, CD 10 and Bcl-1/cyclin D1 negative. MALT lymphoma can be differentially diagnosed with other lymphoma by these findings.

The acquisition of MALT lymphoma is induced by autoimmune disease or chronic inflammation. The relation between *H. pylori* infection and gastric MALT lymphoma is well established. Morgner et al.[7] reported that eradication of *H. pylori* infection is associated with complete remission in approximately

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80% of patients with low-grade MALT lymphoma in the early stage. Therefore, for low-grade gastric MALT lymphoma, the ideal treatment option should be an eradication of *H. pylori*. The role of *H. pylori* in colonic MALT lymphoma is unclear. However, in individual cases of lymphomas of the small intestine, rectum and salivary glands, eradication of *H. pylori* can lead to complete remission of the tumor.[11] Although treatment of colonic MALT lymphoma is not established, various treatment options, such as operation, chemotherapy, radiotherapy, eradication of *H. pylori* and endoscopic resection, have been reported with no consensus established on the most effective therapy.[12] Therefore, individual treatment is needed according to the stage of disease, age of patient, comorbidities, and etc. Gastrointestinal MALT lymphoma is a highly chemo-sensitive disease. Many recent studies show that chemotherapy alone can be effective for primary gastrointestinal MALT lymphomas.[13] Moreover, chemotherapy has the advantage of organ preservation and is effective for micro-metastases.[14] It is well-known that the CHOP chemotherapeutic regimen (cyclophosphamide, doxorubicine, vincristine and prednisone) remains the first line therapy for primary colorectal lymphomas.[15] Nowadays, new active drugs such as monoclonal antibodies like rituximab have been introduced and are used as part of chemotherapy treatment.[15] Several studies have shown that adding rituximab to the CHOP regimen resulted in higher response rates and better survival for some cancers, but there is little information about its effect in primary colorectal lymphoma.[16] Localized gastrointestinal MALT lymphoma can also be controlled with local modalities, such as surgery. However, surgical resection is disputed, because the incidence of late morbidity, such as malnutrition and dumping, is more common in patients treated with surgical resection.[17] In some cases, such as localized low-grade lymphomas, surgery alone with or without radiotherapy cannot be used, especially in patients at risk of complications such as hemorrhage, obstruction, and perforation. Therefore, in these cases, chemotherapy, with or without surgical excision, remains the basis of treatment.[15]

In conclusion, this report found a rare case of synchronous primary gastric and colonic MALT lymphoma in a healthy subject. Eradication of *H. pylori* was the first treatment given to the patient. Although the optimal management of primary lymphoma of the colon is not established, we treated the patient with chemotherapy and four cycles of CHOP for organ preservation and prevention of micro-metastases as mentioned above. He responded rapidly to the treatment and no evidence of tumor growth was detected after 6 months. In the future, adding new immunochemotherapies to the CHOP regimen may have an impact on primary colon lymphoma survival.

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