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☐ Case Report ☐

An Unusual Case of Gastric Carcinoma with Synchronous Non-Hodgkin's Lymphoma

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We report a case of synchronous gastric adenocarcinoma and abdominal non-Hodgkin's lymphoma in a 56-year-old man. An explo-laparotomy was performed for the purpose of palliative resection of the stomach and to evaluate the nature of splenic and peri-pancreatic mass lesions. The pathologic stage of the gastric carcinoma was stage IB ($T_2N_0M_0$) and the clinical stage of the diffuse large cell type lymphoma was II_{A2S}. Following surgery and chemotherapy, the patient is now in a disease-free state.

Key Words: Synchronous, gastric adenocarcinoma, non-Hodgkin's lymphoma

The adenocarcinoma of the stomach is still the most common type of cancer in the Far East including Korea and Japan (Aoki, 1993; Kim, 1993). However, there have not been many reports of other types of malignancies synchronously discovered with gastric adenocarcinoma (Ikeguchi *et al.* 1995). Wotherspoon and Issacson had reported cases of synchronous adenocarcinoma associated with low grade B-cell lymphoma of mucosa associated lymphoid tissue (MALT) of the stomach (Wotherspoon and Issacson, 1995). But there have been no case reports of gastric carcinomas synchronously discovered with non-Hodgkin's lymphoma. Here, we report a single case of gastric carcinoma with a synchronously discovered non-Hodgkin's lymphoma not involving the gastrointestinal tract.

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CASE REPORT

A 56-year old man was admitted to the Yonsei Cancer Center, Yonsei University College of Medicine, Seoul Korea. He had been well until one month previously, when he started having recurrent bouts of indigestion and epigastric pain unresponsive to any medications. He did not complain of fever or night sweats. He had lost 2 kgs of weight during the previous month. On examining the abdomen, there was a direct tenderness on the epigastric area. There were no palpable lymph nodes in the cervical, supra-clavicular, axillary or inguinal areas. There were no abnormal findings on rectal examination. UGI series showed an ulcero-infiltrative lesion on the lesser curvature side of the antrum (Fig. 1). Gastrofiberscopic examination showed the ulcero-infiltrative lesion (Borrman type III) at the lesser curvature side of the antrum. The biopsy of the lesion subsequently proved to be a poorly differentiated adenocarcinoma. The computed tomography showed

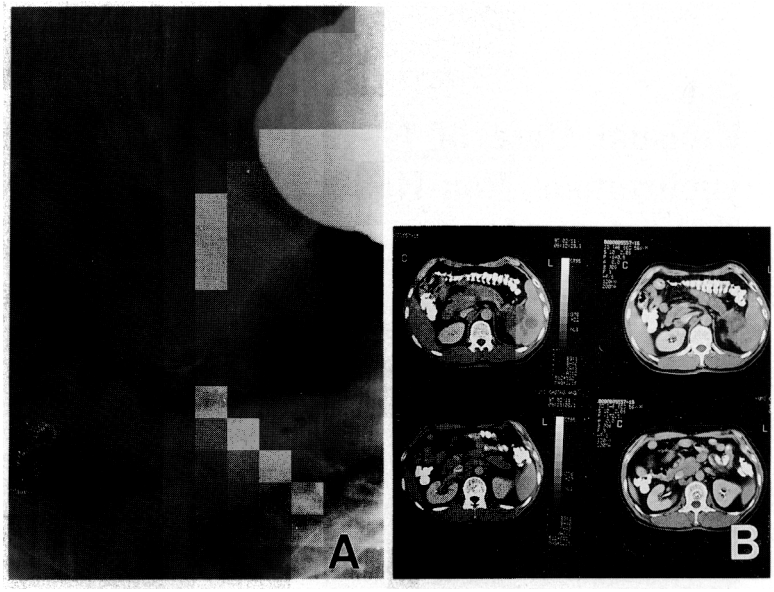

Fig. 1. A: UGI study shows the ulcero-infiltrative lesion in the antrum. B: Abdomino-pelvic CT shows retro-pancreatic, para-aortic, peri-splenic and splenic mass lesions.

multiple lymphnode enlargements of the supra-pancreatic, perigastric and the splenic hilar area. Also shown was a 2.0 cm-sized hypodense lesion in the spleen and pancreas (Fig. 1). An explo-laparotomy was performed for the purpose of palliative resection of the stomach and also to evaluate the nature of the splenic and pancreatic mass lesions. In the operation field, there were no evidence of metastatic lesions in the liver or the peritoneum. There was no evidence of invasions of the primary gastric lesion to the pancreas, spleen, transverse colon or the mesentary. The main lesion of the stomach was an ulcero-infiltrative mass lesion measuring 6×5 cm in size and located at the lesser curvature side of the antrum. There were also multiple lymph node enlargements at the hepato-duodenal, retro-pancreatic and the para-aortic lymph nodes. There was a $7 \times 5 \times 4$ cm-sized multiple, pink, nodular mass lesion located at the spenic hilum. On the cut surface of the spleen, there also was a $2.3 \times 2 \times 1$ cm-sized well demarcated homogenous, solid mass lesion. The distal pancreas contained an ovoid, mass measuring $3 \times 2 \times 1$ cm in size. Total gastrectomy, Roux-en-Y esophago-jejunostomy with end to end anastomosis, splenectomy and distal pancreatectomy was performed on the remaining enlarged para-aortic lymph nodes (R_2 dissection). The pathology of the specimen showed the lesion of the stomach to be a poorly differentiated adenocarcinoma extending to the inner proper muscle with lympho-vascular permeation and cytokeratin stain positivity (Fig. 2). The proximal and distal resection margins were all free of the tumor and all of the dissected lymph nodes were negative for adenocarcinoma. The tumor cells found in the lymph nodes, spleen and pancreas expressed leukocyte common antigen, L26 and CD79a on special immunostaining (Fig. 3) but they did not express cytokeratin, UCHL1 and CD3. These findings were compatible with the diagnosis of non-Hodgkin's lymphoma diffuse large cell type (B-cell). But the gastric mass did not express leukocyte common antigen but expressed cytokeratin. Bone marrow biopsy showed 30% cellularity of the marrow with relative myeloid hyperplasia and without any evidence of malignant or immature cells. Chest computed tomography showed that the lymphoma did not involve the lung or the mediastinum. Post-operative gallium scan showed an increased uptake at the para-aortic area. The final diagnosis of this patient turned out to be a synchronous manifestation

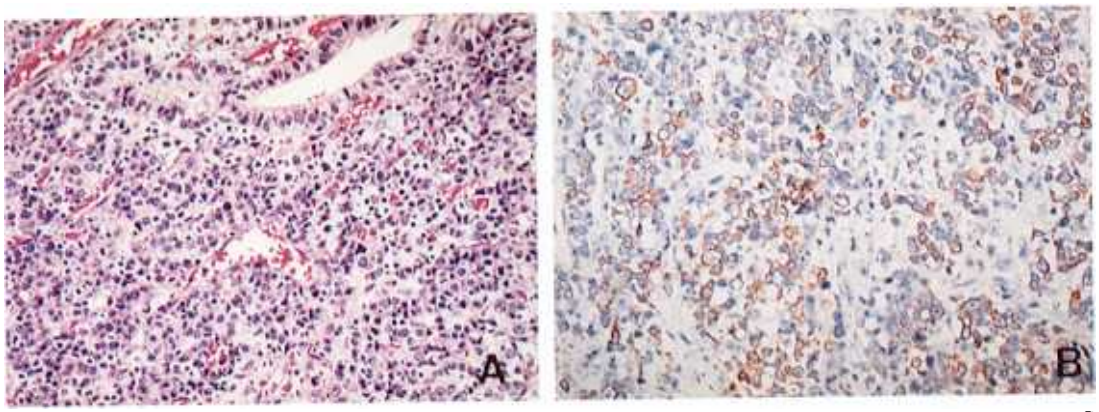

Fig. 2. Pathologic findings of the stomach lesion. A: H & E stain shows poorly differentiated adenocarcinoma. B: cytokeratin stain positivity of the cancerous lesion of stomach.

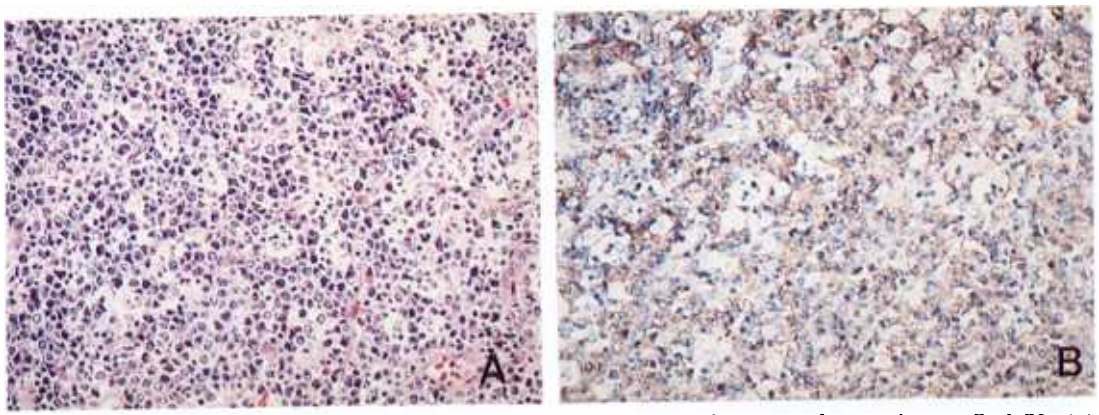

Fig. 3. Pathologic findings of the lymph-node lesion. A: H & E stain shows no adenocarcinoma. B: L-26 stain positivity of the cancerous lesion of the lymph node.

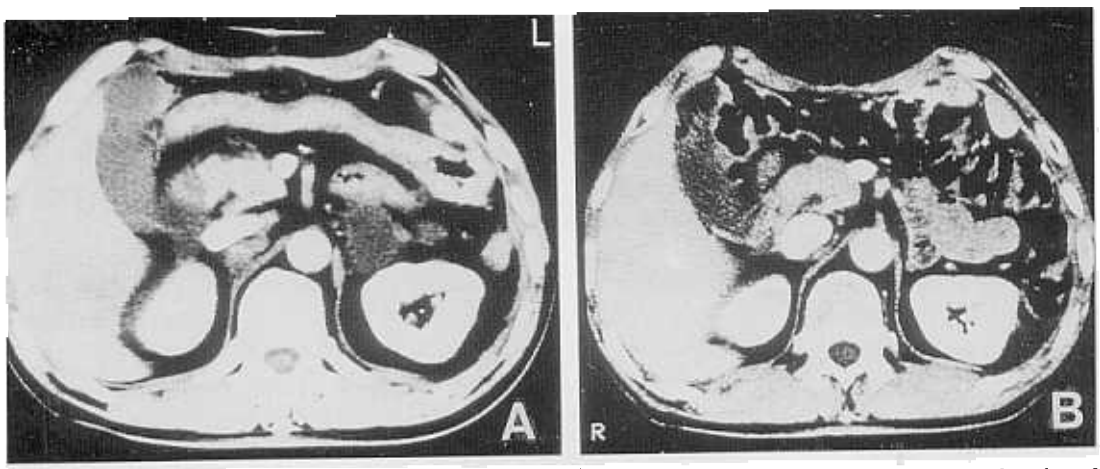

Fig. 4. Changes of the para-aortic lymph node before and after chemotherapy. A: enlarged para-aortic lymph node before chemotherapy B: complete remission of the lymph node after 6 cycles of BACOP chemotherapy.

of both gastric carcinoma and malignant non-Hodgkin's lymphoma. The pathologic stage of the gastric carcinoma was stage I_B ($T_2N_0M_0$). The clinical stage of the malignant lymphoma was stage II_{A2S} with multiple infra-diaphragmatic lymph nodes (hepatoduodenal, retropancreatic and para-aortic lymph nodes) and splenic involvements without any lesions involving the supra-diaphragmatic area. The patient finished 6 cycles of BACOP chemotherapy for the treatment of the lymphoma and is being followed up in a disease-free state for 12 months (Fig. 4). The patient is being checked every 6 months.

DISCUSSION

There have not been many case reports of other types of malignancies synchronously associated with gastric adenocarcinoma. In a study done on 890 early gastric carcinoma patients from 1963 to 1992, 97 cases had either synchronous or metachronous primary malignancies in organs other than the stomach (Ikeguchi *et al.* 1995). Among the 97 cases, synchronous primary malignancies were found in 32 patients. Of these 32 cases, there was mention of 2 cases of malignant lymphoma diagnosed with gastric adenocarcinoma. Unfortunately, the clinical outcome and the nature of the 2 lymphoma cases were not discussed in the article. According to this study, the most common types of synchronous malignancies associated with gastric adenocarcinoma were hepatocellular carcinoma, lung cancer and colorectal cancer.

Our patient was initially admitted to hospital under the impression of advanced gastric carcinoma. The abdomino-pelvic computed tomography showed not only a mass involving the lesser curvature of the antrum but also masses involving the distal pancreas, the spleen and the para-aortic lymph nodes. If the mass lesions involving the pancreas, spleen and multiple lymphadenopathies were to be considered an extension of the gastric carcinoma, a curative resection of the stomach would not have been possible. However, an open laparotomy was done for two reasons. First, even a palliative resection of the primary lesion would be helpful in relieving the intractable epigastric pain and obstructive symptoms, as well as the fact that the general performance status of the patient was deemed adequate to undergo such an operation. According to Boddie *et al.* out of 1,887 patients diagnosed with gastric cancer from 1941 to 1981, 45 patients had undergone palliative total gastrectomies (Boddie *et al.* 1983). In this study, the patients who had undergone palliative total gastrectomy showed a modest improvement in survival over those who had undergone exploration alone (10.4 months versus 3.6 months). That our patient was in good general condition and the fact that a palliation of symptoms could be expected by palliative surgery justified an exploro-laparotomy. Second, although there are no exact data on the incidence of gastric carcinoma involving the splenic parenchyme, it is known to be very rare. In autopsy studies, 7% of autopsied patients with non-hematologic malignancies had splenic metastasis with breast cancer, lung cancer and malignant melanomas (Klein *et al.* 1987). The possibility of the splenic mass lesion being something other than a metastatic lesion from the stomach justified a splenectomy to determine the nature of the splenic tumor.

The final pathologic diagnosis of the gastric carcinoma was a poorly differentiated adenocarcinoma infiltrating to the muscularis propria, without any lymph node metastasis ($T_2N_0M_0$, Stage I_b). As a result, the R_2-type gastrectomy performed on the patient turned out to be a curative one for the adenocarcinoma. In Japan, 281 patients diagnosed with pathologic stage I_b who underwent radical gastrectomy with R_2 dissection had a 5-year survival rate of nearly 90% (Kinoshita *et al.* 1993). The excellent survival of stage I patients treated with surgery alone makes the consideration of postoperative adjuvant chemotherapy impractical in these patients.

The synchronously-discovered malignant lymphoma (diffuse large cell type of B cell origin) involved the hepatoduodenal, retropancreatic, splenic hilar and the para-aortic lymph nodes along with an involvement of the splenic parenchyme (stage II_{A2S}). A persistent controversy concerns the diagnosis of undifferentiated large cell tumors that frequently turn out to be undifferentiated carcinoma or high grade malignant lymphomas. A large part of this problem has been solved by the expression of leukocyte common antigen (LCA) on malignant lymphomas, and by the use of specific antibodies to keratin,

which detect cancers of epithelial origin. Some cases of large cell anaplastic cell lymphoma and Hodgkin's disease expressed keratin, but in most cases, LCA and keratin antibodies distinguish large cell lymphoma and anaplastic carcinoma (Gustmann *et al.* 1991). In our case, keratin was not expressed from lymph nodes but from the main gastric mass. Moreover, in lymph nodes, only B-cell specific surface markers such as L26 and CD79a were expressed (Jaffe, 1990). These findings of surface immunophenotyping markers made it easy to differentiate lymph node B-cell lymphoma and gastric adenocarcinoma.

The treatment principle for the early stages of intermediate and high grade non-Hodgkin's lymphoma is still controversial. The role of radiotherapy as the sole modality of treatment is for stage I non-Hodgkin's lymphoma. The role of radiotherapy in stage II non-Hodgkin's disease is still not resolved (Miller and Jones, 1983; Connors *et al.* 1987; Mauch *et al.* 1987; Longo *et al.* 1989; Fisher *et al.* 1993). In a retrospective analysis, patients with extended stage I-II diffuse large cell lymphoma (more than 3 sites involved or bulky mass of more than 10 cm in diameter) had a 6-year survival rate of 56% when receiving chemotherapy-based treatment(Mauch *et al.* 1987). Therefore, the treatment of extended clinical stage II of diffuse large cell lymphoma should be some forms of combination chemotherapy, but whether or not some form of radiotherapy should be added is still not resolved. In this particular case, the complete response was induced with BACOP combination chemotherapy.

In any type of advanced cancers, finding a tumorous lesion in the spleen should not result in an automatic assumption of metastasis to the spleen because of the rare nature of splenic metastasis by solid tumors. The nature of the splenic mass should always be investigated because of the profound impact it may have on the treatment and prognosis, as was the case with our patient.

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