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A Case of Type IIa Early Gastric Cancer Developed in Pernicious Anemia

Pernicious anemia is an autoimmune disease characterized by a gastric mucosal defect which results in an insufficiency of intrinsic factor to facilitate the absorption of the physiologic amount of cobalamin. Increased risk of cancers of the stomach has been reported for patients with pernicious anemia. We report here a case of a 65 year old woman who had been diagnosed as having pernicious anemia 16 months previously, was receiving monthly vitamin B12 injections, and developed early gastric cancer type IIa by routine follow-up gastroscopic examination. This patient underwent endoscopic mucosal resection for an early gastric cancer lesion with a free resection margin.

Key Words : *Pernicious anemia, Early gastric cancer*

Myung-Ju Ahn, Dongsoo Han, Young-Joon Park, Geun-Tae Park, Dong-Hyun Sohn, Young-Yeul Lee, Tae-June Jung, Il-Young Choi, In-Soon Kim, Se-Jin Jang*

Department of Internal Medicine, Department of Pathology*, Hanyang University College of Medicine, Seoul, Korea

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Address for correspondence
Myung-Ju Ahn, M.D.
Department of Internal Medicine, Hanyang University KURI Hospital, 249-1, Kyomun-dong, Kuri-si, Kyunggi-do 471-701, Korea
Tel : (0346) 60-2236, Fax : (0346) 65-2258

INTRODUCTION

It has long been claimed that patients with pernicious anemia are predisposed to the development of gastric adenocarcinoma (1-4). Intestinal metaplasia, achlorhydria, and formation of carcinogenic N-nitroso compounds are suggested to be pathogenic factors (5, 6). However, the prevalence of gastric adenocarcinoma does not exceed 1-3% in patients with pernicious anemia, and only 2% of gastric adenocarcinomas are associated with pernicious anemia (7-9). Therefore, the need for gastroscopic follow-up in pernicious anemia patients is still debated (10, 11). We report a case of a patient with pernicious anemia who developed early gastric cancer. We assume that this is the first case in Korean literature.

CASE REPORT

A 65 year old woman was admitted to the hospital on February 24, 1996 complaining of dizziness, loss of appetite, numbness of both hands and feet, and unexplained weight loss which had lasted for several months. She had no history of alcohol ingestion or gastrectomy. Physical examination showed anemic conjunctiva and mild icteric sclera but there was no hepatosplenomegaly. Peripheral blood count showed the following: white blood cells 2,300/mm^3, Hb 4.3 g/dl, Hct 15%, (MCV 122.3 fl, MCHC 35 ng), platelet 144,000/mm^3 and reticulocyte count 0.4%. Laboratory findings revealed total protein 6.2 g/dl, albumin 4.2 g/dl, total bilirubin 3.1 mg/dl (0.2-1.2), direct bilirubin 0.4 mg/dl (0-0.4), LDH 1405 U, AST/ALT 27/31 U, serum iron 196 μg/dl, TIBC 272 μg/dl, ferritin 211 ng/ml (10-240), serum VB12 122 pg/ml (200-1,000) and folate 11.4 ng/ml (3-15). A peripheral blood smear showed macroovalocytes of red cells. Hypersegmented neutrophils were also found (Fig. 1). Bone marrow aspirates showed megaloblastic changes in erythroid and myeloid lineage cells (Fig. 2). In stage I of the Shilling test, 1.7% of CN-[^{57}Co] Cobalamin was excreted in the urine within 24 hours (normal: 7-8%) and after giving intrinsic factor exogenously with CN-[^{57}Co] Cobalamin (stage II test), 10% of CN-[^{57}Co] Cobalamin was excreted, suggesting pernicious anemia. Although we did not check the anti-intrinsic factor (IF) antibody, anti-parietal cell antibody was positive in this patient. Gastroscopic examination also showed a severe degree of gastric atrophy in fundus suggesting atrophic gastritis (type A), but no other mucosal changes including malignancy were suggested at that time (Fig. 3A). Based on

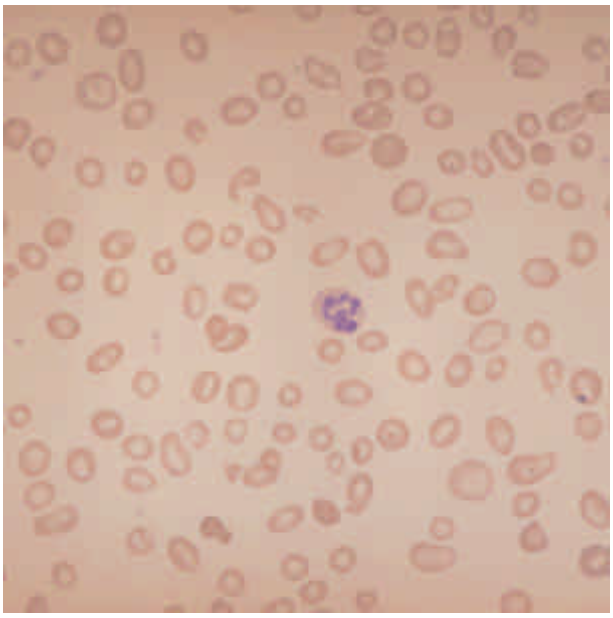

Fig. 1. Hypersegmentation of polymorphonuclear cells and macrocytosis with anisocytosis of red cells as peripheral blood evidence for an underlying megaloblastic process (×1,000).

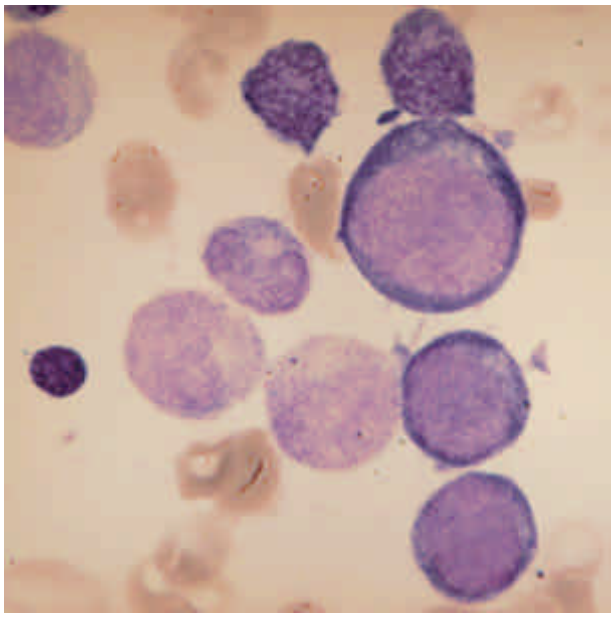

Fig. 2. Bone marrow aspirates reveal the megaloblastic feature in erythroid precursors (×1,000).

clinical diagnosis of pernicious anemia, 1,000 μg of cyanocobalamin monthly injection with oral folate was prescribed, and the hemoglobin level was normalized up to 12.5 g/dl after 3 months of treatment and her neurologic symptoms almost disappeared. During the next 16 months of the follow-up period, she was doing well, remained asymptomatic, and her hemoglobin level was stable. Even though she did not have any gastric symptoms, a routine follow-up gastroscopic examination was performed. Unexpectedly, on the gastroscopic examination, a 1 cm violet flat elevated lesion was noted in the lesser curvature of the antrum (Fig. 3B) and the lesion did not stain with methylene blue, suggesting type IIa early gastric cancer (Fig. 3C). Giemsa stain and the bacterial culture for *H. pylori* was negative. The biopsy of the mucosal lesion was adenocarcinoma. The gastric body mucosa showed marked atrophy of the fundic glands (Fig. 4). An abdominal computed tomography

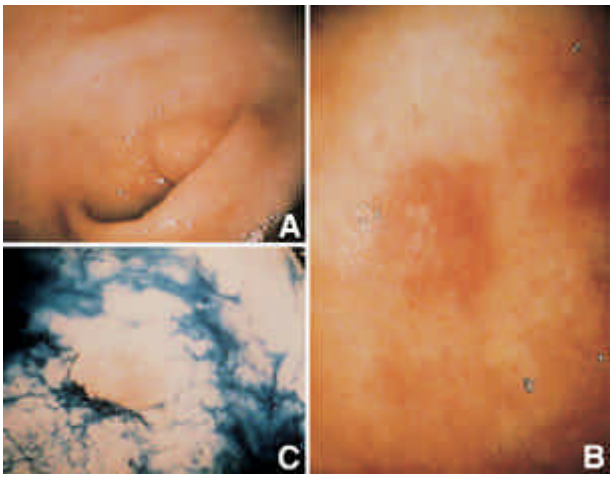

Fig. 3. Initial gastroscopic finding shows atrophic gastritis (A). Sixteen months later, a 1 cm sized flat elevated lesion was noted on the lesser curvature side of the antrum (B) and the lesion was not stained with methylene blue suggesting type IIa early gastric cancer (C).

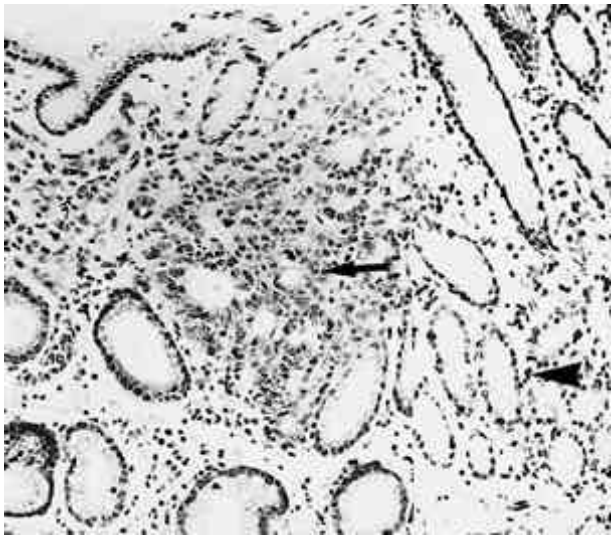

Fig. 4. The gastric mucosal biopsy shows moderately differentiated adenocarcinoma (arrow). Note marked atrophy of fundic glands (arrow head). Parietal cells were virtually absent.

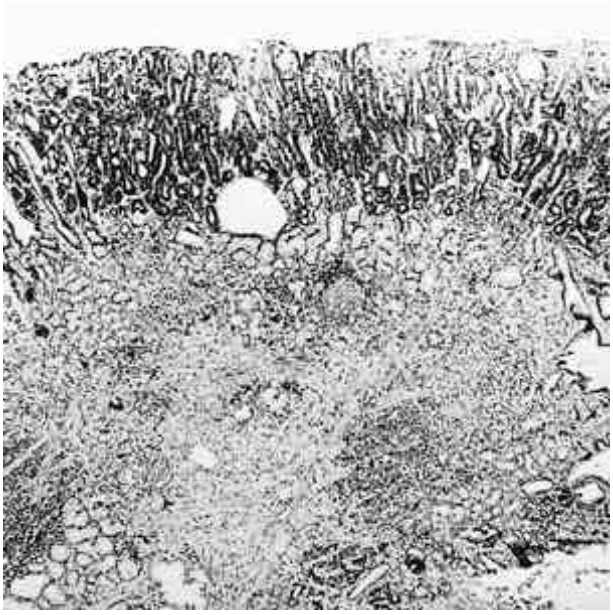

Fig. 5. Endoscopic mucosal resection shows adenocarcinoma confined in a superficial portion of the gastric mucosa.

scan did not show enlargement of the lymph nodes, or any evidence of organ metastasis. Therefore, she underwent endoscopic mucosal resection without any complications. Final biopsy results from the resected gastric lesion showed adenocarcinoma involving only the mucosal area with a clear resection margin (Fig. 5) and there was no evidence of nuclear atypia or megaloblastic changes in the adjacent mucosa. She is now well, but further meticulous examination, including a regular follow-up gastroscopic examination to detect the recurrence of disease, will be warranted.

DISCUSSION

Pernicious anemia is interested in not only its hematologic abnormalities but also association of increased risk of gastric cancer (1-4). We presented a case of early gastric carcinoma developed in a patient during the clinical course of pernicious anemia. Although it is difficult to elucidate their relevance and sequential events during relatively short follow-up period of 16 months, there are some supportive evidences that the gastric carcinoma in this patient is associated with preexisting pernicious anemia. First, it has been already known that the risk of gastric carcinoma is increased several fold in pernicious anemia and in our case the gastric cancer was detected during endoscopic follow-up of pernicious anemia. Second, gastrofiberscopic examination revealed that the patient had type A gastritis, which is a main gastric pathology of pernicious anemia. Third, histopathologic examination showed mucosal adenocarcinoma of intestinal type on the background of atrophic gastritis and intestinal metaplasia, which is considered as pathologic sequence of gastric cancer development in not only most of old age in Korea but pernicious anemia patients. We assume that this might be the first report of gastric carcinoma developed in the patient of pernicious anemia in Korean literature, although causal relationship is not proven.

An excess risk of stomach cancer in pernicious anemia has been documented for many years (1-4), consistent with the underlying atrophic gastritis and histamine-resistant achlorhydria. It has been estimated that the risk of stomach cancer is increased 3 to 6 fold in pernicious anemia patients (12-15).

Although the exact pathophysiologic mechanism that predisposes patients with pernicious anemia to neoplasia has not been ascertained, achlorhydria, hypergastrinemia, and atrophic gastritis with intestinal metaplasia have all been postulated as playing a role. Chronic atrophic gastritis generally is considered a precursor lesion of stomach cancer (16-18). The high pH and concomitant presence of *H. pylori* in the stomach may enhance the conversion of nitrates to nitrites and consequently the formation of nitrosamines, which are potent carcinogens. The more prevalent chronic atrophic gastritis (Type B) mainly affects the antral mucosa; whereas, the autoimmune chronic atrophic gastritis (Type A) in pernicious anemia, leads to diffuse atrophy of the corpus mucosa, with loss of parietal cells and causes severe impairment of gastric secretion (19). The accompanying failure of intrinsic factor secretion and malabsorption of cobalamin usually ensues for many years before pernicious anemia is clinically manifested. This long standing gastritis may help explain the elevated risk of stomach cancer.

Although a recent investigation points to a threefold increase in the risk of gastric malignancy, the benefit of preventive endoscopic screening in patients with pernicious anemia is still controversial (8-9, 20-22). Borch et al. (23) reported that a continuing gastric screening programme of these patients would consume considerable medical, economic and administrative resources in view of the prevalence of the disorder. However, Sjoblom et al. (10) evaluated the findings of follow up gastroscopies performed three years after primary gastroscopic screening of 56 pernicious anemia patients revealing that two cases (3.6%) of early gastric cancer and two cases of small gastric carcinoid tumors (3.6%) were detected and it was reported that regular endoscopic surveillance for gastric cancer may be beneficial. Since gastric cancer is still one of the most common cancers in our country, follow-up endoscopic screening should be performed, especially in patients with pernicious anemia.

It has been also reported that the excess risk of cancers of the buccal cavity and pharynx was noted in patients with pernicious anemia (3, 4, 12) and other hematologic malignancies such as acute myelogenous leukemia (24-26), polycythemia vera (26), multiple myeloma (3, 27, 28), and other unspecified leukemia were also observed in pernicious anemia. The relationship between these hematopoietic malignancies and pernicious anemia needs further clarification because diagnostic misclassification of pernicious anemia is possible.

In summary, we present here a case of early gastric cancer developed in a patient with pernicious anemia on routine gastrofiberscopic examination. Since pernicious anemia is linked to many other malignancies other than gastric cancer, it is important to follow up patients with pernicious anemia for the early detection of other malignancies.

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