CASE REPORT

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Distal Cholangiocarcinoma with Gastric Metastasis Mimicking Early Gastric Cancer

Eun-Mi Kim*, Byung Seok Lee*, Hee Seok Moon*, Jae Kyu Sung*, Seok Hyun Kim*, Heon Young Lee*, and Dae Young Kang†

*Departments of *Internal Medicine and †Pathology, Chungnam National University Hospital, Chungnam National University College of Medicine, Daejeon, Korea*

We report an unusual case of distal cholangiocarcinoma with gastric metastasis mimicking early gastric cancer. A 67-year-old woman presented with a 4-month history of abdominal pain after eating. Computed tomography showed a malignant tumor of the common bile duct located just above the intrapancreatic segment, and endoscopy revealed a 2-cm, flat, elevated lesion with convergence of the surrounding folds, situated at the gastric angle. Based on the endoscopic biopsy results, an adenocarcinoma, thought to be an early gastric cancer, was diagnosed. The patient underwent Whipples's operation. Histopathological findings showed that the adenocarcinomatous tissue was clearly demarcated and infiltrated the gastric mucosa and submucosa, leaving the gastric superficial mucosa intact. Both tumors showed similar pathological features and were positive for cytokeratin (CK)-19 and CK-7. These finding suggest distal cholangiocarcinoma with gastric metastasis. **(Gut and Liver 2009;3:222-225)**

Key Words: Cholangiocarcinoma; Stomach; Metastasis

INTRODUCTION

Cholangiocarcinoma is the primary cancer affecting the bile duct. Although it comprises only 10-15% of all hepatobiliary neoplasms, its incidence is increasing.[1] Frequent metastatic sites of biliary cancer are the liver, peritoneum, intra-abdominal lymph nodes, and lungs.[2] Here, we describe a very rare case in which metastatic cholangiocarcinoma of the stomach was mistaken for primary gastric cancer in a patient who underwent Whipple's operation. However, histopathologic and immunohistochemical findings suggested that the gastric tumor was a metastatic adenocarcinoma originated from a distal cholangiocarcinoma.

CASE REPORT

A 67-year-old woman presented with a 4-month history of abdominal pain after meals. Her past medical history included essential hypertension. Physical examination revealed mild epigastric tenderness. Laboratory findings was as follows: aspartate aminotransferase 141 IU/L (normal; 10-40 IU/L), alanine aminotransferase 161 IU/L (5-40 IU/L) and total bilirubin 0.9 mg/dL (0.2-1.0 mg/dL). Serum CEA and CA19-9 levels were within normal limits. Computed tomography showed a malignant tumor of the common bile duct (CBD), located just above the intrapancreatic segment, with consequent dilatation of the proximal biliary tree including the gall bladder (Fig. 1). The periportal, common hepatic, and portocaval lymph nodes were enlarged. Endoscopy revealed a 2-cm, flat, elevated lesion with convergence of the surrounding folds, situated at the gastric angle (Fig. 2). Based on the biopsy results, an adenocarcinoma, thought to be an early gastric cancer, was diagnosed. The patient underwent Whipples's operation.

The surgical specimen consisted of a whitish mass, 2.1×1.3 cm in diameter, removed from the distal CBD and showing invasion of the pancreas and peripancreatic fat. Pathologic examination of the resected stomach dem-

Correspondence to: Byung Seok Lee
Division of Gastroenterology, Department of Internal Medicine, Chungnam National University Hospital, 33, Munhwa-ro, Jung-gu, Daejeon 301-721, Korea
Tel: +82-42-280-7164, Fax: +82-42-254-4553, E-mail: gie001@cnuh.co.kr
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onstrated that the tumor was very clearly demarcated from the surrounding nontumorous gastric mucosa and submucosa, and also showed invading lymphovascular spaces. In addition, the adenocarcinomatous tissue had infiltrated into the gastric mucosa and submucosa, while the gastric superficial mucosa was intact (Fig. 3).

Immunohistochemical stains showed that the tumor tissue was strongly positive for cytokeratin (CK)-7 and weakly positive for CK-19, while the surrounding gastric mucosa was negative for both cytokeratins (Fig. 4). Based on these findings, we diagnosed distal cholangiocarcinoma with gastric metastasis.

Fig. 1. Computed tomography demonstrated cancer of the common bile duct. The tumor was located just above the intrapancreatic segment, with consequent dilatation of the proximal biliary tree (white arrow).

DISCUSSION

According to a number of reports in the literature, metastasis to the stomach is a rare occurrence, with a reported incidence of less than 1%. The main primary metastatic tumors are those of the breast (33%) and lung (25%), and malignant melanoma (22%).[3]

In our patient, it was difficult to distinguish gastric metastasis of a cholangiocarcinoma from a primary gastric cancer on the basis of clinical, endoscopic, and radiologic features. Thus, results obtained from complete histo-

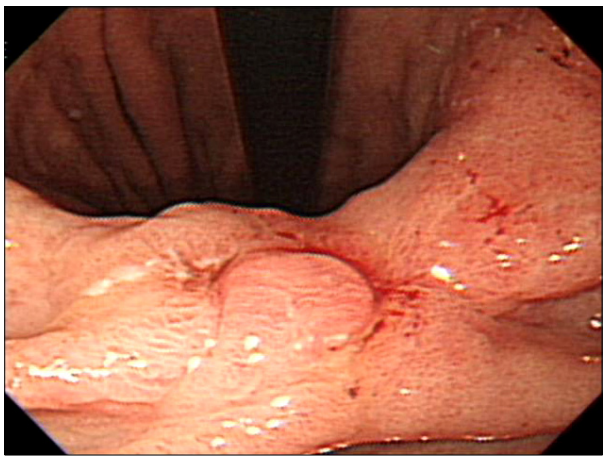

Fig. 2. Endoscopy revealed a 2-cm, flat, elevated lesion with convergence of the surrounding folds.

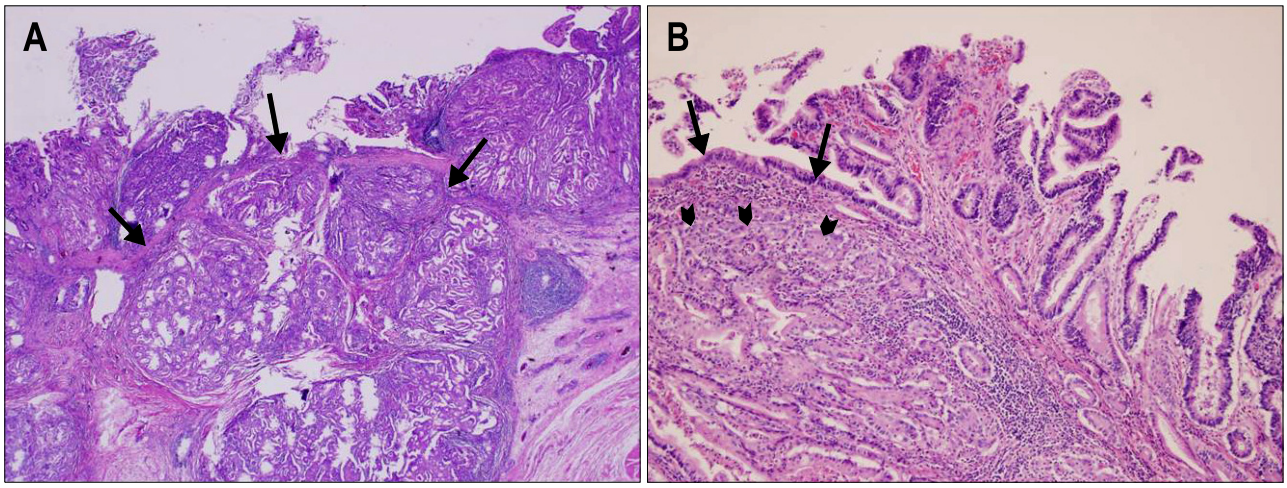

Fig. 3. (A) A stomach tumor in the resected specimen was very clearly demarcated from the surrounding nontumorous gastric mucosa and submucosa, and exhibited invading lymphovascular spaces (H&E stain, ×1). (B) The gastric wall of the resected specimen showed tumor cells (adenocarcinoma) infiltrating the mucosa and submucosa (arrow head), leaving the gastric superficial mucosa (arrow) intact (H&E stain, ×40).

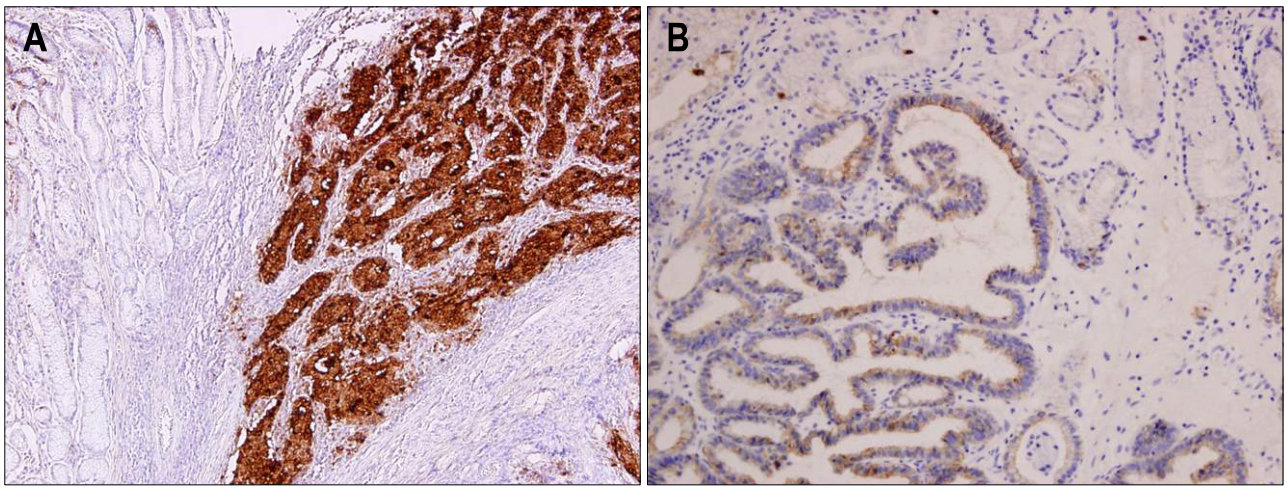

Fig. 4. Immunohistochemical staining of the gastric carcinoma showing that the tumor was strongly positive for cytokeratin (CK)-7 and weakly positive for CK-19, while the surrounding gastric mucosa was negative for both cytokeratins (A, CK-7 immunohistochemical staining, ×100; B, CK-19 immunohistochemical staining, ×200).

pathologic and immunohistochemical studies of gastric biopsies should be compared with the characteristic features of cancer of the CBD.

The anatomic distribution of CK-7 and CK-19 is generally restricted to epithelia of primary sites and their neoplasm. Most cholangiocarcinomas are positive for CK-7 and CK-19 as in our patient. Primary gastric cancer has the same staining pattern, because CK-7 and CK-19 expressions are reported to be positive in about 80% of stomach cancer cases. However, both the normal gastric mucosa surrounding the tumor and the gastric carcinoma, if it originates from the stomach, are positive for CK-7 and CK-19.[4,5] Metastasis to the gastrointestinal tract initiates from the serosa and submucosa and progresses to cause intraluminal lesions, as occurred in this case.[6] Based on these considerations, we diagnosed metastatic gastric carcinoma from a distal cholangiocarcinoma. Another important immunohistochemical marker, CDX-2 is a very useful marker to distinguish stomach cancers from bile duct cancers, because CDX-2 expression is reported to be positive in 61% of stomach cancer cases but only in 13% of bile duct cancers, however CDX-2 was not performed in our study.[7]

Until now, unusual metastastic sites from cholangiocarcinoma were reported to be the colon, adrenal gland, skull bone, epididymis, corneal limbus, meninges, ovary, skeletal musle, and skin.[2,8-15] Metastasis of a distal cholangiocarcinoma to the stomach has not been reported previously to our knowledge but, as in the above-mentioned sites, appears to be a rare site of metastasis of this tumor.

In conclusion, a careful histopathologic and immunohistochemical review is very important in diagnostic differentiation of metastatic tumors from primary sites in this case.

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