CASE REPORT

총담관으로 전이되어 폐쇄성 황달을 유발한 폐선암

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Metastatic Common Bile Duct Cancer from Pulmonary Adenocarcinoma Presenting as Obstructive Jaundice

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We report an extremely rare case of metastatic common bile duct cancer from pulmonary adenocarcinoma presenting as obstructive jaundice. The patient was a 76-year-old male, who presented with generalized weakness and right upper quadrant pain. Plain chest X-ray noted multiple small nodules in both lung fields. Abdominal computed tomography scan showed a stricture of the mid common bile duct along with ductal wall enhancement. Endoscopic retrograde cholangiography revealed a concentric, abrupt narrowing of the mid-common bile duct suggestive of primary bile duct cancer. However, pathology comfirmed metastatic common bile duct cancer arising from pulmonary adenocarcinoma with immunohistochemical study with thyroid transcriptional factor-1 (TTF-1). (Korean J Gastroenterol 2013;61:50-53)

Key Words: Common bile duct neoplasms; Neoplasm metastasis; Lung adenocarcinoma; Obstructive jaundice; TTF-1

INTRODUCTION

Malignant distal biliary obstruction is mostly caused by primary bile duct cancer or metastasis of other tumors to the peripancreatic, periportal, peribiliary lymph nodes, and head of the pancreas.[1] Common malignant tumors that could cause metastatic distal biliary obstruction are stomach cancer and colon cancer, but lung cancer rarely causes it.[1-3] Furthermore, biliary obstruction associated with metastasis to the common bile duct is even rarer in non-biliary cancers, especially in lung cancer.

CASE REPORT

A 76-year-old man presented with generalized weakness, poor oral intake and right upper quadrant pain of 2 months' duration. He was a never smoker. Since he had a history of Billroth-II operation for stomach cancer 12 years ago, surveillance esophagogastroduodenoscopy and screening colonoscopy were performed to rule out gastrointestinal cause of patient's symptoms. However, there was no evidence of stomach cancer recurrence and only one 1.2 cm sized lateral spreading tumor was found on the cecum, which was removed with snare electrocautery. On physical examination, the patient was chronic ill-looking and showed right upper quadrant tenderness. Laboratory evaluation revealed ane-

mia with hemoglobin of 10.5 g/dL (normal 12.0-16.0), obstructive jaundice with total bilirubin of 6.8 mg/dL (0.2-1.3), direct bilirubin of 4.5 mg/dL (0-0.4), alkaline phosphatase of


Fig. 1. Plain chest X-ray. Multiple small nodules were found in both lung parenchyma.

970 IU/L (39-117), aspartate aminotransferase of 237 IU/L (0-31), and alanine aminotransferase of 278 IU/L (0-31), and CEA of 10.2 ng/mL (0-5), CA19-9 of 2.7 U/mL (0-37). Multiple small nodules were found in both lung fields on plain chest X-ray (Fig. 1). Abdominal computed tomography scan showed a ductal wall enhancement on cross-sectional view, and a stricture of the mid-common bile duct along with shouldering on coronal view (Fig. 2). Chest computed tomography scan demonstrated obstructive pneumonia caused by lymphadenopathy compressing the bronchus of the left lower lobe additionally. Endoscopic retrograde cholangiography revealed a concentric, abrupt narrowing of the mid-common bile duct suggestive of primary bile duct cancer (Fig. 3A). However, biopsy specimen obtained at the strictured bile duct revealed clusters of columnar epithelial cells with immunoreactivity for Cytokeratin 7 and prominent nucleoli with strong immunoreactivity for thyroid transcriptional factor-1 (TTF-1) (Fig. 3B, C). The morphologic features and this immunohistochemical characteristic could make the diagnosis of metastatic adenocarcinoma from the lung. Additionally broncho-
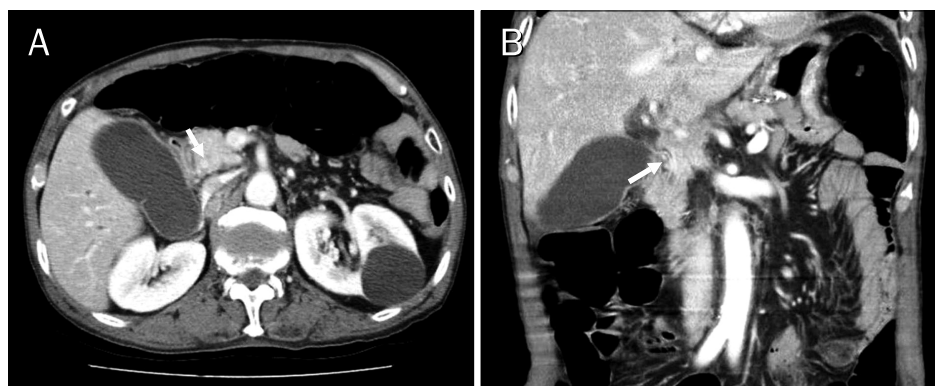
Fig. 2. Abdominal CT scan. (A) Ductal wall enhancement (arrow) was seen on axial image. (B) Note the stricture at the mid-common bile duct along with shouldering and ductal wall enhancement (arrow) on coronal image.
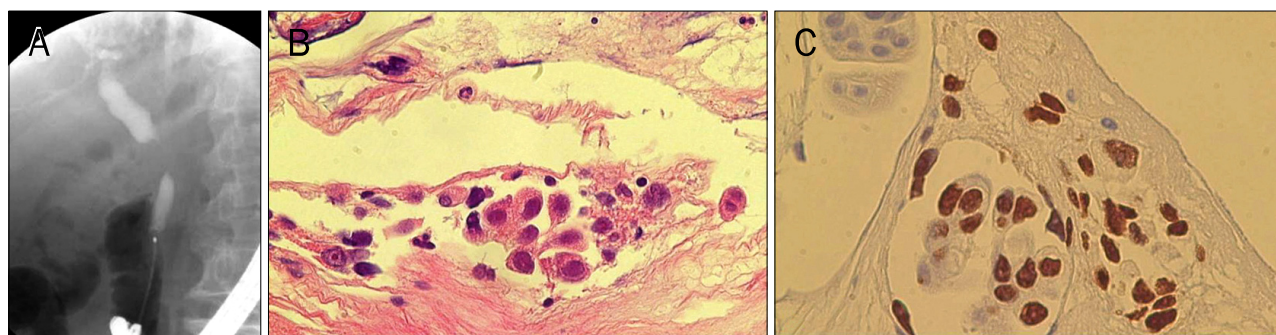
Fig. 3. Imaging and histologic findings of the common bile duct. (A) Endoscopic retrograde cholangiography revealed a concentric, abrupt narrowing of the mid-common bile duct. (B) Biopsy exhibited clusters of malignant columnar cells with prominent nucleoli and intracytoplasmic mucin vacuoles (H&E, ×400). (C) Adenocarcinoma cells demonstrated strong nuclear immunoreactivity for thyroid transcriptional factor-1 (×400).
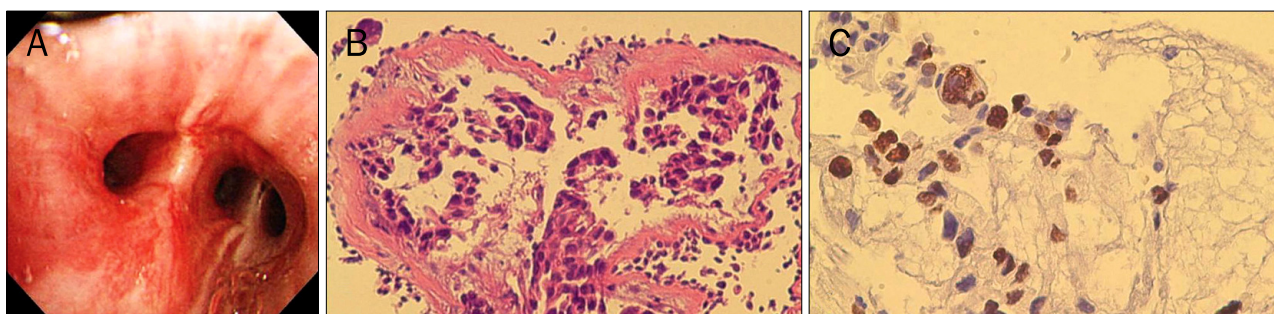
Fig. 4. Bronchoscopic findings and bronchial biopsy specimen. (A) Bronchoscopy showed hyperemic mucosal change, finding suspicious of cancer cell infiltration. (B) Biopsy revealed haphazardly infiltrating nests of adenocarcinoma cells with intracytoplasmic mucin production (H&E, ×200). (C) Adenocarcinoma cells were also reactive for thyroid transcriptional factor-1 (×400).

scopy showed hyperemic mucosal change, finding suspicious of cancer cell infiltration (Fig. 4A). Biopsy also showed invasive nests of adenocarcinoma cells, which were strong positive for TTF-1 (Fig. 4B, C). Thus, the diagnosis of metastatic common bile duct cancer from pulmonary adenocarcinoma could be made. PET scan revealed metastasis to the bran, L2 lumbar spine, and left supraclavicular lymph node additionally. The patient was referred to the oncologist to undergo systemic chemotherapy after we inserted un-covered biliary metal stent.

DISCUSSION

Patients with primary bile duct cancers typically present with painless jaundice resulting from hilar or distal biliary strictures or with an intrahepatic mass causing abdominal pain. Common non-biliary malignancy that can cause distal biliary obstruction are stomach cancer and colon cancer. Biliary obstruction caused by lung cancer is rare and mostly due to the compression of the bile duct by metastasis to the surrounding the lymph nodes or to the pancreas head.

More than half of all lung cancer patients present with advanced stage at the time of diagnosis. Extrathoracic metastasis is found at autopsy in more than 50% of patients with squamous carcinoma, 80% of patients with adenocarcinoma, and more than 95% of patients with small cell lung cancer. The most frequent site of extrathoracic spread of lung cancer is to the liver and adrenal gland.[1] Patients with liver metastases may present with anorexia, weight loss, hepatomegaly, and right upper quadrant pain. However, liver dysfunction or biliary obstructions are rare. Metastasis to common bile duct-induced jaundice is very rare in lung cancer

and has not been reported in pulmonary adenocarcinoma in the English literature so far.

TTF-1 is a 38 kDa homeodomain-containing nuclear protein that plays a role in transcriptional activation during embryogenesis in the thyroid, diencephalon, and respiratory epithelium.[4-6] TTF-1 has been demonstrated to be expressed specifically in the lung or thyroid neoplasm.[7,8] TTF-1 expression varies according to the subtype of lung cancers. TTF-1 is expressed in 26% to 76% of adenocarcinomas, in 0% to 38% of squamous cell carcinomas, in 40% of large cell carcinomas, in 40% to 75% of large cell neuroendocrine carcinomas, and in 81% to 100% of small cell carcinomas.[8-10] Thus, it could serve as a reliable marker of primary lung cancer.[11] Roh and Hong[12] reported that TTF-1 was expressed in 69% of metastatic lung cancers in the cervical lymph nodes and had a specificity of 95% and a sensitivity of 69% for metastatic lung cancer.

When plain chest X-ray reveals multiple lung nodules and abdominal computed tomography scan shows solitary common bile duct stricture with shouldering and ductal wall enhancement without evidence of other intra-abdominal metastasis as is with the present case, it is necessary to differentiate between double primary cancer and common bile duct cancer with multiple lung metastasis. To make the diagnosis in our case, biopsy was performed at the strictured bile duct, but histopathology revealed adenocarcinoma cells with no biliary differentiation, i.e., no immunoreactivity for CA19-9. Since multiple pulmonary nodules were present, immunohistochemical study with TTF-1 was performed and it revealed strong positivity. Bronchoscopic biopsy also showed adenocarcinoma cells with strong immunoreactivity for TTF-1. Thus, we could confirm the diagnosis of metastatic common

bile duct cancer arising from pulmonary adenocarcinoma. Considering the patient's age, generalized condition, and advanced stage of malignancy irrespective of primary site, immunohistochemical study for localizing primary origin of bile duct stricture might not affect treatment modality and prognosis of the patient. However, If treatment modality such as surgery improves prognosis according to the bile duct histology, we should make every effort to identify the primary origin in patient with bile duct stricture and other lesion including lung. In summary, when it is necessary to differentiate between primary bile duct cancer and metastatic bile duct cancer from pulmonary adenocarcinoma, immunohistochemical study of the biopsy samples from bile duct with TTF-1 can be useful in differential diagnosis.

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