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조성범 · 박선영 · 주영은

Small Cell Carcinoma of Extahepatic Bile Duct Presenting with Hemobilia

Sung Bum Cho, M.D., **Sun Young Park,** M.D., and **Young-Eun Joo,** M.D.

Department of Internal Medicine, Chonnam National University Medical School, Gwangju, Korea

We report a case of small cell carcinoma of extrahepatic bile duct presenting with jaundice and hemobilia. A 59-year-old woman was admitted due to right upper quadrant pain and jaundice. An abdominal computed tomography revealed a 2 cm sized mass in the extrahepatic bile duct. Endoscopic retrograde cholangiopancreatography revealed bloody discharge coming out of the papillary orifice in endoscopic view and a dilated extrahepatic bile duct with multiple irregular filling defects in cholangiogram. A coronal T2-weighted image revealed a hyperintense mass at extrahepatic bile duct. Laparotomy was performed, and pathologic examination of resected specimen showed tumor cells having round to oval nuclei with coarsely granular chromatin and scanty cytoplasm, which were immunoreactive for synaptophysin and chromogranin A, compatible with the diagnosis of small cell carcinoma. The small cell carcinoma of bile duct, despite its rarity, should be considered in differential diagnosis of the causes for obstructive jaundice and hemobilia. **(Korean J Gastroenterol 2009;54:186-190)**

Key Words: Carcinoma; Small Cell; Bile duct; Extrahepatic; Biliary tract hemorrhage

Introduction

Neuroendocrine tumors of biliary tract are rare. Most of those occur in the gallbladder or in the ampulla of Vater, and such cases arising in common bile duct are extremely rare.[1-4] Among the neuroendocrine tumors, small cell carcinoma is high grade neuroendocrine carcinoma with an aggressive malignant potential including invasiveness and metastasis.[1-4] The usual symptoms of small cell carcinoma of bile duct were jaundice, biliary colic, weight loss resemble to those of ordinary bile duct cancer.[1] Hemobilia can occur when injury or disease causes communication between intrahepatic blood vessels and the biliary tract.[5,6] Causes of hemobilia include trauma, gallstones, inflammatory diseases, vascular disorders such as aneurysm, coagulopathy and malignant tumor.[5,6]

We, herein, report the case of small cell carcinoma of extrahepatic bile duct combined with hemobilia. Small cell carcinoma of bile duct is extremely rare case of hemobilia in the review of literature.

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연락처: 주영은, 501-757, 광주시 동구 학1동 8번지
전남대학교 의과대학 내과학교실
Tel: (062) 220-6296, Fax: (062) 228-1330
E-mail: yejoo@chonnam.ac.kr

correspondence to: Young-Eun Joo, M.D.
Devision of Gastroenterology, Department of Internal Medicine, Chonnam National University Medical School, 8, Hak-dong, Dong-gu, Gwangju 501-757, Korea
Tel: +82-62-220-6296, Fax: +82-62-228-1330
E-mail: yejoo@chonnam.ac.kr

Case Report

A 59-year-old woman was admitted to our hospital with a 7-day history of right upper quadrant pain and jaundice. On admission, she was afebrile, blood pressure and pulse were normal, and she appeared well nourished. Scleral icterus was present. The abdomen was mildly distended, with tenderness in the right upper quadrant. Laboratory studies revealed white blood cell count 4,860/mm^3 (normal 6,000-10,000), hemoglobin 10.8 g/dL (normal 12-16), platelet count 383,000/mm^3 (normal 130,000-450,000) in CBC, serum albumin 3.5 g/dL (normal 3.0-5.0), AST 300 U/L (normal 5-37), ALT 504 U/L (normal 5-40), alkaline phosphatase 330 U/L (normal 39-117), γ-GTP 1,394 U/L (normal 7-49), amylase 324 U/L (normal 20-90), and lipase 450 U/L (normal 7-60). Total bilirubin was 9.7 mg/dL (normal 0.2-1.2) with 4.5 mg/dL of direct fraction (normal 0.05-0.3). Serum CEA and CA 19-9 were 1.2 ng/mL (normal 0-3.4) and 29.4 U/mL (normal 0-37) respectively. Coagulation profiles were within normal limits. An abdominal computed tomography (CT) revealed a 2 cm enhancing mass at extrahepatic bile duct (Fig. 1). There were no definite abdominal lymph node enlargement. Endoscopic retrograde cholangiopancreatography (ERCP) revealed blood coming out of the papillary orifice in endoscopic view (Fig. 2A) and a dilated extrahepatic bile duct with multiple irregular filling defects in cholangiogram (Fig. 2B). These findings were compatible with hemobilia. After endoscopic sphincterotomy, the choledochal blood clots were removed by the retrieval basket and balloon catheter. Endoscopic nasobiliary drainage was performed. On seventh hospital day, her liver enzymes and bilirubin level returned to normal. And she remained hemodynamically stable without tachycardia or hypotension. Before the laparotomy, an abdominal magnetic resonance imaging was performed after removal of endoscopic nasobiliary drainage catheter. A coronal T2-weighted image revealed an exophytic intermediate hyperintense mass at extrahepatic bile duct (Fig. 3). At laparotomy, bile duct tumor resection, cholecystectomy and Roux-en-Y hepaticojejunostomy were performed. Gross examination of resected specimen showed a nodular tumor measuring 3.0×3.0 cm located in extrahepatic bile duct (Fig. 4A). There were no stones within the gallbladder and common bile duct. Pathologic examination of resected specimen stained with hematoxylin-eosin showed small round tumor cells having round to oval nuclei with coarsely granular chromatin, inconspicuous nucleoli and scanty cytoplasm (Fig. 4B). These findings are compatible with those of small cell carcinoma. To clarify the nature of

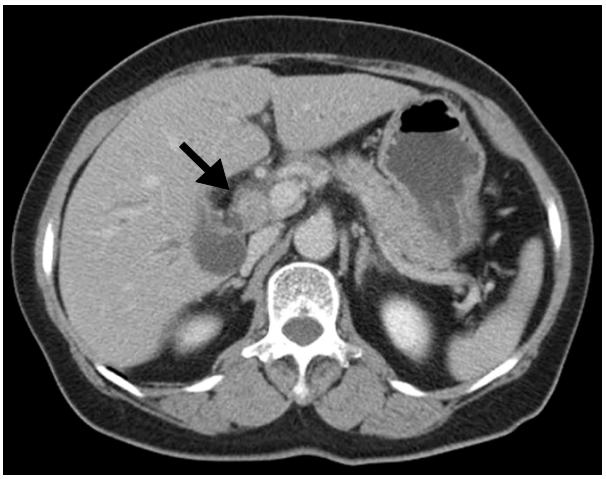

Fig. 1. An abdominal computed tomography revealed a 2 cm sized enhancing mass (arrow) in the extrahepatic bile duct.

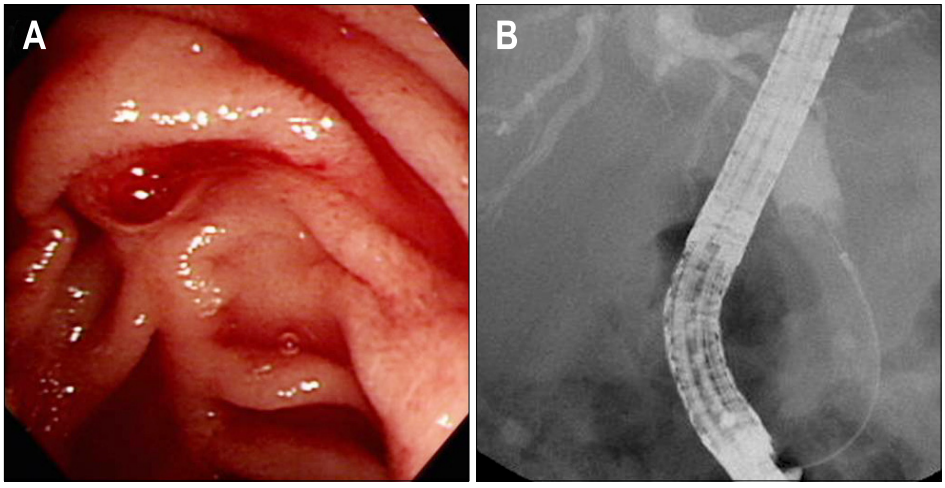

Fig. 2. Endoscopic retrograde cholangiopancreatographic findings. (A) It revealed bloody discharge coming out from the papillary orifice. (B) It showed a dilated bile duct with multiple irregular filling defects.

cells, immunohistochemical examination was performed. The tumor cells showed a strong reactivity for neuroendocrine cell marker, synaptophysin (Fig. 5A) and chromogranin A (Fig. 5B). Paraaortic lymph node enlargement was detected at 3 months after surgery. She had an uneventful postoperative course for follow up of 6 months.

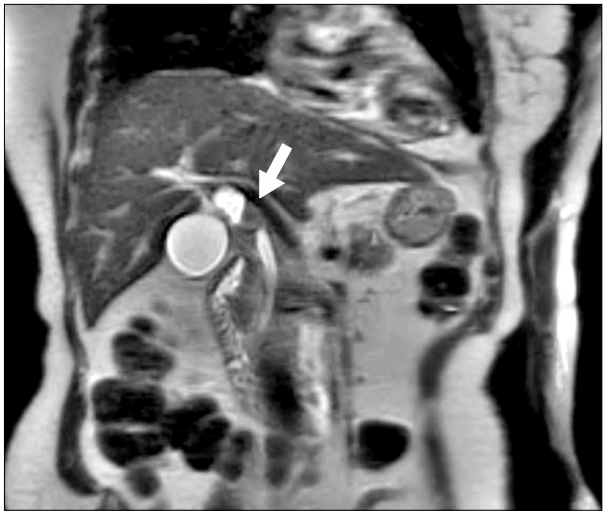

Fig. 3. A coronal T2-weighted image of magnetic resonance revealed an exophytic intermediate hyperintense mass (arrow) in the extrahepatic bile duct.

Discussion

Neuroendocrine tumors arise from embryonal neural crest cells, which migrate to the bronchopulmonary system and gastrointestinal tracts during development. Because of the paucity of these cells in bile duct, neuroendocrine tumor in this location is extremely rare and represent less than 0.4%.[1-4] Travis et al classified neuroendocrine tumors into three different categories: low-grade typical carcinoid; intermediate-grade atypical carcinoid, and high grade categories of large cell neuroendocrine carcinoma and small cell carcinoma.[7] At this report, a review of the medical literature disclosed a few cases of small cell carcinoma arising from the bile duct.[8-18] Most cases including this case present the features related to malignant

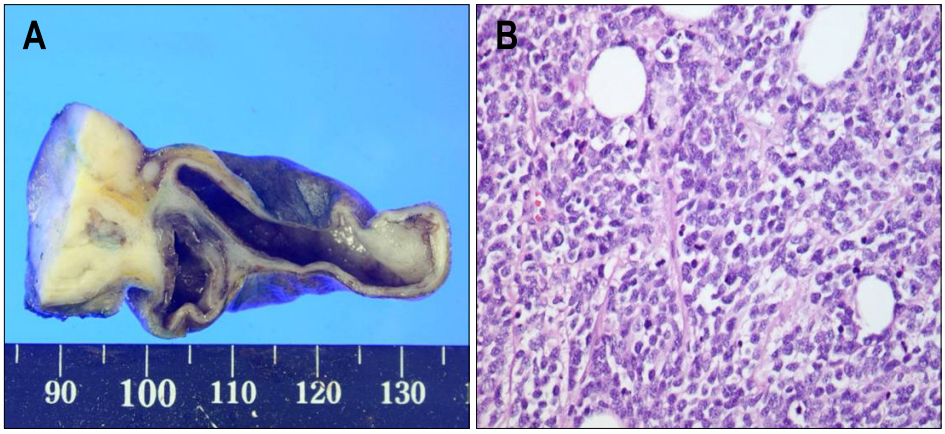

Fig. 4. Pathologic findings of resected specimen. (A) Gross specimen showed a hard tumor measuring 3.0×3.0 cm located in extrahepatic bile duct. (B) Pathologic examination of resected specimen, stained using hematoxylin-eosin showed tumor cells having round to oval nuclei with coarsely granular chromatin and scanty cytoplasm (H&E stain, ×400).

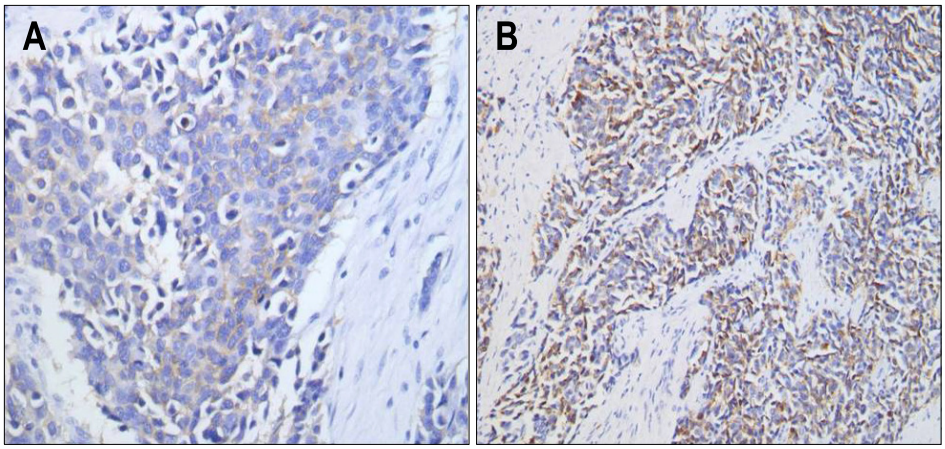

Fig. 5. In immunohistochemical staining, neuroendocrine cell marker, synaptophysin (A) and chromogranin A (B) were strongly positive.

biliary obstruction with jaundice, biliary colic and pruritus.

Hemobilia, defined as bleeding into the biliary tree, is a rare cause of upper gastrointestinal bleeding and jaundice.[5,6] Hemobilia can occur due to trauma, gallstone disease, inflammatory diseases including acalculous cholecystitis, cholangitis, hepatic abscess, hepatic artery aneurysm, coagulopathy or malignancies of the liver and pancreas and biliary tract.[5,6] Hemobilia cases present with a classic triad of biliary colic, obstructive jaundice, and gastrointestinal bleeding. However, only 22-40% of cases present with the triad.[5,6] On admission, this case did not present with gastrointestinal bleeding as primary symptom. This case presented with symptoms, signs, and laboratory studies that suggest biliary obstruction without overt gastrointestinal bleeding. But ERCP findings in our case were compatible with hemobilia. So far, there have been no case report of small cell carcinoma of bile duct combined with hemobilia. Therefore, hemobilia should be considered as one of clinical manifestations of this tumor.

The clinical or radiological findings of small cell carcinoma in bile duct resemble those of ordinary bile duct cancer. Therefore, differentiation of small cell carcinoma from other cancer of the bile duct is very difficult. The final diagnosis of this tumor in most cases relied on histopathologic and immunohistochemical examinations of resected specimen. Only 3 cases were diagnosed before treatment using percutaneous transhepatic cholangioscopy with biopsy,[12] ERCP with brushing[15] and endoscopic ultrasonography guided fine needle aspiration biopsy.[17]

In the review of medical literature, clinically, small cell carcinoma of bile duct is known to be highly aggressive and its prognosis is poor. Most cases died of metastases within 1 year after surgery. This case also showed early lymph node metastasis after surgery.

Surgery was performed in most cases. And chemotherapy and radiotherapy like in cases of pulmonary small cell carcinoma have been reported to show some effectiveness in few cases.[8,12,14,17] However, effective treatment modality for this tumor have still not been established because of its rarity. Further larger studies are needed to establish optimal management for this tumor.

In summary, first, small cell carcinoma of bile duct, despite its rarity, should be considered in differential diagnosis of causes of obstructive jaundice and hemobilia. Second, an early and accurate histopathologic and immunohistochemical diagnosis and surgical resection, if feasible combined chemotherapy and radiotherapy, may be the approach to offer a chance for cure.

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