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Mixed adenoneuroendocrine carcinoma of the distal bile duct: A case report

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ABSTRACT

INTRODUCTION: Mixed adenoneuroendocrine carcinomas (MANECs) of the distal bile duct are extremely rare, and only a few cases have been reported in the English literature.
PRESENTATION OF CASE: An 82-year-old man was referred to our hospital for increasing biliary enzymes. Abdominal computed tomography (CT) showed enlargement of the intrahepatic bile ducts and stenosis of the distal bile duct. Endoscopic retrograde cholangiopancreatography showed stenosis of the distal bile duct and a high-density signal at the same site on diffusion weighted imaging. PET-CT showed increased FDG accumulation (SUVmax: 4.5) at the distal bile duct stenosis. Biopsy specimens obtained by endoscopic ultrasonography-guided fine-needle aspiration revealed adenocarcinoma. The patient was diagnosed with adenocarcinoma of the distal bile duct and underwent subtotal stomach-preserving pancreaticoduodenectomy with regional lymph node dissection. The resected distal bile duct tumor was $18 \times 14 \times 12$ mm in diameter. Hematoxylin and eosin staining revealed a composite carcinoma with adenocarcinoma and non-adenocarcinoma elements. The non-adenocarcinoma component stained positive for synaptophysin and chromogranin A. The Ki-67 labeling index was 37%. The non-adenocarcinoma component was therefore diagnosed as a neuroendocrine carcinoma. The two composite carcinoma was diagnosed as MANEC of the distal bile duct. The patient was treated with surgery alone and he remained disease-free for 7 months after the surgery.
DISCUSSION: The treatment of MANECs of the bile duct remains controversial and the prognosis is poor.
CONCLUSIONS: There is no standard treatment for MANECs of the bile duct. Larger studies are required to establish standard treatment regimens.

1. Introduction

The present work has been reported in line with the SCAREcriteria [1].

Mixed adenoneuroendocrine carcinomas (MANECs) are defined as composite carcinomas that consist of adenocarcinoma and neuroendocrine carcinoma elements, with each element occupying at least 30% of the tumor (World Heath Organization (WHO) classification 2010, neuroendocrine neoplasms in the digestive system) [2]. MANECs of the distal bile duct are extremely rare, and only a few cases have been reported. These tumors are seldom diagnosed preoperatively, and patients tend to have a poor prognosis. We report herein a case of MANEC of the distal bile duct.

2. Presentation of case

An asymptomatic 82-year-old man with a history of multiple myeloma treated with bortezomib and dexamethasone was referred to our hospital for evaluation of abnormal biliary enzymes. Laboratory analysis revealed hemoglobin, 10.2 g/dL; white blood cell count, $2.65 \times 10^3/\mu L$; platelets, $11.8 \times 10^4/\mu L$; serum total protein, 8.1 g/dL; serum albumin, 3.4 g/dL; total bilirubin, 0.9 mg/dL; aspartate aminotransferase, 261 IU/L; alanine aminotransferase, 256 IU/L; alkaline phosphatase, 838 IU/L; and serum amylase, 84 IU/L. The serum levels of various tumor markers were normal, including carcinoembryonic antigen, 1.4 ng/ml; carbohydrate antigen 19–9, 28.3 U/ mL; DUPAN-2, 25 U/ml; and SPAN-1, 6 U/ml.

Computed tomography (CT) demonstrated enlargement of the intra- and extrahepatic bile ducts and stenosis of the distal bile

Abbreviations: MANEC, mixed adenoneuroendocrine carcinoma; WHO, World Heath Organization; CT, computed tomography; ERCP, endoscopic retrograde cholangiopancreatography; IDUS, intraductal ultrasonography.

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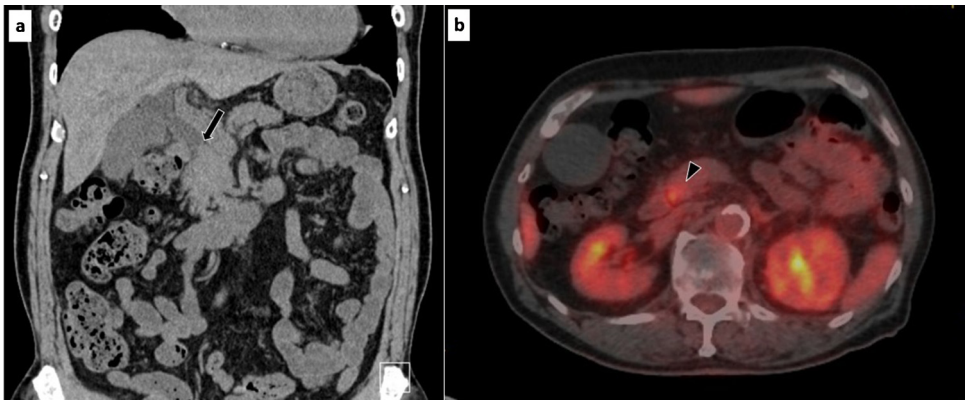

Fig. 1. Computed tomography (CT) showed diffuse enlargement of the common bile duct and a mass in the distal bile duct (black arrow) (Fig1a). PET-CT showed increased FDG accumulation (SUVmax: 4.5) in the distal bile duct mass (black arrowhead) (Fig. 1b).

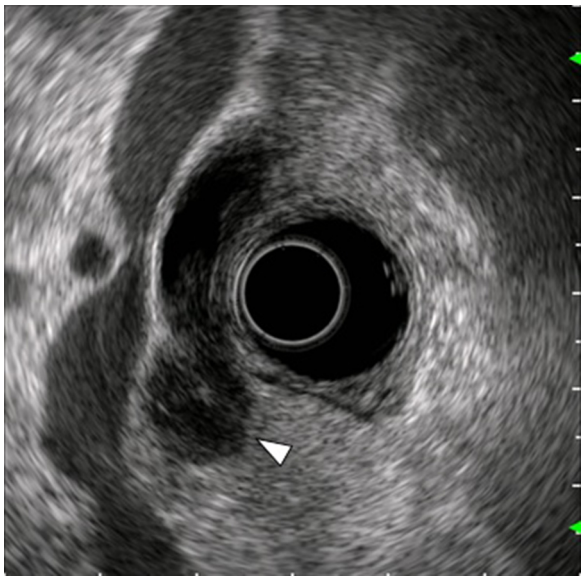

Fig. 2. Endoscopic ultrasonography showed a 10 mm hypoechoic mass in the stenotic region of the distal bile duct (white arrowhead).

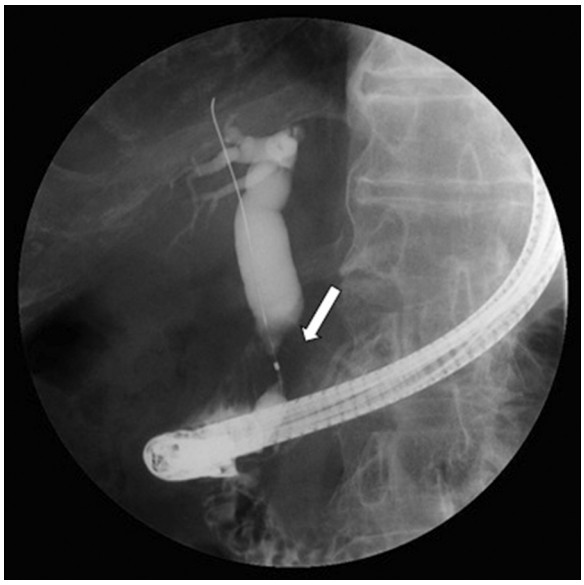

Fig. 3. Endoscopic retrograde cholangiopancreatography showed stenosis of the distal bile duct (white arrow).

duct (Fig. 1a). The para-aortic lymph nodes were enlarged to 10 mm due to multiple myeloma. Contrast enhanced CT revealed a replaced right hepatic artery. PET-CT showed increased FDG accumulation (SUVmax: 4.5) in the distal bile duct mass (Fig. 1b). Endoscopic ultrasonography showed a hypoechoic mass, 10 mm in diameter, at the distal bile duct (Fig. 2). Endoscopic retrograde cholangiopancreatography (ERCP) showed stenosis of the distal bile duct (Fig. 3). Intraductal ultrasonography (IDUS) showed thickening of the distal bile duct wall. The bile duct was drained with a 7Fr, 5 cm stent to prevent obstructive jaundice. A sample of the distal bile duct tumor was obtained using endoscopic ultrasonography-guided fine-needle aspiration and cytology revealed adenocarcinoma. The patient was diagnosed with distal bile duct carcinoma and underwent subtotal stomach-preserving pancreaticoduodenectomy with resection of the replaced right hepatic artery (non-revascularization) and regional lymph node dissection.

The cut surface of the surgical specimen demonstrated a nodular invasive tumor, measuring 18 × 14 × 12 mm, located in the distal bile duct (Fig. 4). Hematoxylin and eosin staining revealed a carcinoma composed of adenocarcinoma and non-adenocarcinoma elements, with each element occupying more than 30% of the tumor (Fig. 5a). The non-adenocarcinoma component stained positive for synaptophysin and chromogranin A (Fig. 5b,c). In addition, 37% of cells stained positive for Ki-67 (Fig. 5d). Based on these findings, the non-adenocarcinoma component was diagnosed as a neuroendocrine carcinoma. The patient was thus diagnosed with MANEC of the distal bile duct, Stage IIA (pT3N0M0) based on the 7th edition of the International Union Against Cancer tumor-node-metastasis classification.

The patient's postoperative course was complicated by a pancreatic fistula (ISGPF grade B) and delayed gastric emptying, but he was discharged on postoperative day 33. He remained disease-free for 7 months after surgery (Table 1).

3. Discussion

According to the WHO classification (2010), neuroendocrine neoplasms in the digestive system, including the gallbladder and extrahepatic bile ducts, are classed as NET G1 (carcinoid, mitotic count of <2 per 10 high powder fields (HPF) and/or ≤2% Ki67 index), NET G2 (mitotic count 2–20 per 10 HPF and/or 3–20% Ki67 index), or NET G3 (neuroendocrine carcinoma, mitotic count of >20 per 10 HPF and/or >20% Ki67 index). Moreover, composite carcinomas consisting of adenocarcinoma and neuroendocrine carcinoma elements, with each element composing at least 30% of the tumor, are