Undifferentiated carcinoma of the extrahepatic bile duct with rapidly progressive course: Report of a case

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Abstract

We report a case of undifferentiated carcinoma of the extrahepatic bile duct. An 81-year-old woman was admitted with appetite loss and high fever. She was diagnosed with obstructive jaundice due to extrahepatic bile duct carcinoma with bulky lymph node metastases. High fever had continued after the effective percutaneous transhepatic biliary drainage (PTBD) and antibiotics administration. We performed a pancreateico-duodenectomy, and the patient became antipyretic immediately after the surgery. The histological findings revealed undifferentiated carcinoma with multiple lymph node metastases and infiltration of a large number of inflammatory cells in the stroma without abscess or necrosis. Two months after the surgery, high fever appeared together with intrahepatic bile duct recurrence, multiple lymph node metastases, and peritoneal metastases. The patient died 112 days after the surgery. Undifferentiated carcinoma arising from the extrahepatic bile duct is rare, and neoplastic fever was strongly suspected from the clinical course and the findings of examinations in this case.

Key Words: undifferentiated carcinoma, bile duct, neoplastic fever

Introduction

Undifferentiated carcinoma arising from the extrahepatic bile duct is rare. The incidence of undifferentiated carcinoma was reported to be about 0.3% among all extrahepatic bile duct cancers. We experienced a rare case of undifferentiated carcinoma arising from the extrahepatic bile duct with rapidly progressive course. We performed surgery for curative resection, considering as well that tumor resection was inevitable to relieve the patient from high grade fever.

Case report

An 81-year-old woman with appetite loss visited our hospital. She had a history of subarachnoid hemorrhage at 77 years of age and gastric cancer at 78 years of age. The histological diagnosis of gastric cancer was poorly differentiated adenocarcinoma and the histological findings were pT2N0M0, Stage IB according to the UICC classification. She had not received adjuvant chemotherapy for gastric cancer after the surgery. She had a high fever (over 40 degrees), and the laboratory tests performed on admission revealed the following: red blood cells (RBC), 2.82×10⁶ μl⁻¹ (normal range: 3.80-5.50×10⁶ μl⁻¹); white blood cells (WBC), 12200 μl⁻¹ (4500-9000 μl⁻¹); platelets (PLT), 30.7×10⁴ μl⁻¹ (13.0-37.0×10⁴ μl⁻¹); total bilirubin (T.bil), 2.26 mg/dl (0.30-1.20 mg/dl); aspartate aminotransferase (AST), 116 IU/l (13-33 IU/l); alanine aminotransferase (ALT), 76 IU/l (6-27 IU/l); lactate dehydrogenase (LDH), 197 U/l (119-229 IU/l); alkaline phosphatase (ALP), 3887 IU/l (115-359 IU/l); gamma-glutamyltranspeptidase (γ-GTP), 481 IU/l (0-47 IU/l); amylase (AMY), 45 IU/l (37-125 IU/l); C-reactive protein (CRP), 18.75 mg/dl (0.00-0.29 mg/dl); carcinoembryonic antigen (CEA), 6.4 ng/ml (0.0-5.0 ng/ml); and carbohydrate antigen 19-9 (CA19-9), 17 U/ml (0-37 U/ml). Multidetector-row computed tomography (MDCT) performed on admission revealed dilation of the intrahepatic bile ducts and a papillary mass (measuring 52×30×30 mm) in the extrahepatic bile duct (Fig. 1A, B). The patient was diagnosed with obstructive jaundice and cholangitis due to extrahepatic bile duct carcinoma. Percutaneous transhepatic biliary drainage (PTBD) was performed, and cholangiography via a PTBD catheter showed that the middle part of the extrahepatic bile duct was filled with a mass (Fig. 1C). Jaundice and hepatobiliary enzyme were improved by PTBD. However, the high fever continued, inspite of administration with several kinds of antibiotics (Meropenem hydrate, Cefazolin sodium hydrate, Tazobactam, Piperacillin hydrate, Levofloxacin hydrate). Blood and bile cultures were neg-
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Throughout the period, MDCT performed 1 month after admission revealed growth of the mass (measuring 69×35×35 mm) and bulky lymph node metastases. Although we diagnosed her with bile duct carcinoma, malignant lymphoma of the bile duct was considered as a differential diagnosis from the clinical course and imaging. We planned to perform a pancreaticoduodenectomy for curative resection. Although the patient had a high fever (over 38 degrees) on the day of the surgery, we performed the planned surgery. We resected pericholecdochal, periporal, peripancreatic head, and around superior mesenteric artery lymph nodes as systematic lymph node dissection, and we could perform curative resection macroscopically. Operative time was 460 minutes and intraoperative blood loss was 1168 ml. After the surgery, she was immediately antipyretic. She had a good operative course and was discharged on day 25 after surgery.

Macroscopic analysis of the resected specimen revealed a nodular infiltrating type tumor measuring 7×4×4 cm with central ulceration at the middle part of the extrahepatic bile duct (Fig. 2A, B). Histological examination revealed that the tumor consisted of spindle-shaped, giant-shaped, pleomorphic atypical cells with large eosinophilic nucleioli, hyperchromatic bizarre nuclei, and abundant cytoplasm (Fig. 2C, D). Squamoid differentiation was also found in a small part (Fig. 2E). Infiltration of chronic inflammatory cells including lymphocytes and plasma cells, and to less extent, neutrophils were observed in the stroma. Any micro-abscesses or necrotic foci were not seen in the tumor. Immunohistochemical examination revealed that the tumor cells were positive for AE1/AE3 (Fig. 2F) and vimentin (Fig. 2G), but they were negative for granulocyte-colony stimulating factor (G-CSF) (Fig. 2H). Therefore,
the histological diagnosis was undifferentiated carcinoma of the spindle and giant cell type. Lymph node metastases were found in the pericholedochal, peripancreatic head, and around superior mesenteric artery. The postoperative histological findings were pT2N1M0, Stage IIB according to the UICC classification. The patient was not given surgical adjuvant chemotherapy. She was admitted to our hospital again with high fever 2 months after surgery. MDCT revealed intrahepatic bile duct recurrence, multiple lymph node metastases, and peritoneal metastases. She died 112 days after surgery.

Discussion

Well- to moderately differentiated adenocarcinomas are the most common malignant tumors of the extrahepatic bile duct, and undifferentiated carcinoma of the extrahepatic bile duct is rare. It was reported that the incidence of undifferentiated carcinoma of the bile duct was 0.38% by Albores-Saavedra et al. and it was 0.31% (10/3240 cases) by biliary tract cancer statistics registry in Japan from 1988 to 1997. Characteristically, glandular structures are absent in undifferentiated carcinomas, and the World Health Organization histological classification of tumors of the gallbladder and extrahepatic bile duct defines four histological variants of undifferentiated carcinoma: spindle and giant cell type, undifferentiated carcinoma with osteoclast-like giant cells, small cell type, and nodular or lobular type. Undifferentiated carcinomas are more common in the gallbladder than in the extrahepatic bile duct. Fourteen cases (including the present case) of undifferentiated carcinoma of the extrahepatic bile duct in the English literature were reviewed (Table 1). Although many cases had large tumors (9 of 14 reported cases were over 3 cm), most of them were early stage. Only 2 of 12 reported surgical cases, including the present case, resulted in the unfortunate outcome of recurrence. Generally, the prognosis of undifferentiated carcinoma is poor. It was reported that the 1-year survival rate of undifferentiated carcinoma of thyroid was 18% and that of gallbladder was 18%. The prognosis of undifferentiated carcinoma of the extrahepatic bile duct might not be so poor as the other undifferentiated carcinomas. Uchinami et al discussed that surgery might be effective if the undifferentiated carcinoma was localized to bile duct, but multidisciplinary treatment, including chemotherapy and radiotherapy, should be performed if involving lymph node metastases or vascular invasion. Although we did not perform histological examination before the surgery, if this case had been found to undifferentiated carcinoma preoperatively, we might consider other treatment.

Neoplastic fevers, well-recognized phenomena occurring in patients with neoplasms, are often observed with hematopoietic tumors and are sometimes observed with solid tumors. When considering neoplastic fever, we should exclude fevers due to infection, allergy, therapeutic side effects, and other causes. Chang proposed criteria for the working diagnosis of neoplastic fever as the following: temperature over 37.8 degrees at least once per day, duration of fever over 2 weeks, lack of evidence of infection, absence of allergic mechanisms, and lack of response of the fever to an adequate antibiotic therapy for at least 7 days. Interleukins, tumor necrosis factor and other factors that are induced or produced by neoplastic cells have been suggested to be mediators responsible for neoplastic fever. Infections, including cholangitis,
were ruled out in this patient because various cultures were negative and she had had a high fever after effective PTBD and administration with broad-spectrum antibiotics. The fever had met Chang’s criteria. Microscopic examination revealed no findings of abscess formation in the resected tumors. Furthermore, she was antipyretic immediately after the surgery, and a high fever developed again with tumor recurrence. The clinical course suggested that the neoplasm per se was the cause of her high grade fever.

In summary, we reported a case of undifferentiated carcinoma of the extrahepatic bile duct with rapidly progressive course, presenting increased fever in parallel with tumor growth. The biologic growth behavior of undifferentiated carcinoma arising in the extrahepatic bile duct is considered very aggressive. Although there is no consensus on indication for surgical treatment of undifferentiated carcinoma of the extrahepatic bile duct, a good prognosis might be possible if the surgery is performed at an early stage.

References