[症例報告]Small Cell Carcinoma of the Gallbladder Associated with an Ordinary Adenocarcinoma : A Mixed Type Tumor

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Small Cell Carcinoma of the Gallbladder Associated with an Ordinary Adenocarcinoma: A Mixed Type Tumor

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Abstract

A small cell carcinoma associated with an ordinary adenocarcinoma (mixed type tumor) of the gallbladder in a 49-year-old man is presented herein. Macroscopically, the gallbladder showed an annular, diffuse thickening of the body and fundus. The common bile duct distal to the cystic duct was also segmentally constricted by infiltration of carcinoma. Microscopically, the tumor of the gallbladder was composed of two neoplastc components; an ordinary adenocarcinoma and a small cell carcinoma. The ordinary adenocarcinoma replaced the mucosa with invasion to the muscularis, while the small cell carcinoma revealed extensive spread with vascular invasion into the common bile duct. Both tumors were partially intermingled with occasional transitional zones. Following pancreaticoduodenectomy, the patient had been placed on adjuvant chemotherapy, however expired with clinical manifestations of recurrence of carcinoma five months after surgery.

Introduction

Small cell carcinoma, a type of undifferentiated carcinoma, is a distinctive neoplasm resembling oat cell carcinoma of the lung in histological and clinical aspects. The tumors with this type of histological and highly malignant behavior have been reported in various organs[1-6]. Some of them are composed of the cells containing neurosecretory granules (NSGs). Only those of small cell type with NSGs have been considered as closely related to oat cell carcinoma of the lung[7,8].

We have recently observed a case of small cell carcinoma of the gallbladder associated with an ordinary adenocarcinoma. Although it was unfortunately unsuccessful to demonstrate intracytoplasmic NSGs in ultrastructural evaluation, the histological similarty to the reported cases[3-6]and so-called endocrine cell carcinoma, and the rarity of the tumors of this type in the gallbladder have prompted us to describe the present case.

Case Report

A 49-year-old man was admitted to the Hamamatsu Medical Center Hospital on January 29, 1982 with one week history of jaundice. He appeared somewhat ill. His bulbar conjunctivae and skin were mildly icteric. No mass was palpable in the abdomen.

The laboratory data on this admission were normal except the liver function tests. Serum total bilirubin was 8.0 mg/dl, GOT 201 (IU), GPT 358 (IU), Alkaline-phosphatase 41.9 (KAU), and r-GTP 945 (IU).

Ultrasonography (US) and computed tomography (CT) revealed the presence of a mass in the distal common bile duct (Fig. 1, left). Percutaneous transhepatic cholangiography (PTC) showed an annular stricture of the common bile duct distal to the cystic duct and outlined the small, deformed gallbladder (Fig. 1, right). A percutaneous transhepatic biliary drainage (PTBD) was also performed for biliary decompression. Two weeks after PTBD, the liver function tests almost recovered within normal limits. Selective hepatic arteriography revealed irregularities of the epicholedochal arterial plexus without any involvement of the hepatic artery and portal vein. From these data, he was diagnosed to have a carcinoma of the common bile duct.

At surgery, the gallbladder was hard in palpation, however appeared nearly normal on the peritoneal surface. The lymph nodes around the cystic duct, common bile duct and head portion of the pancreas were swollen in thumb's tip size. Pancreaticoduodenectomy through modified Child's procedure was carried out on February 15, 1982.

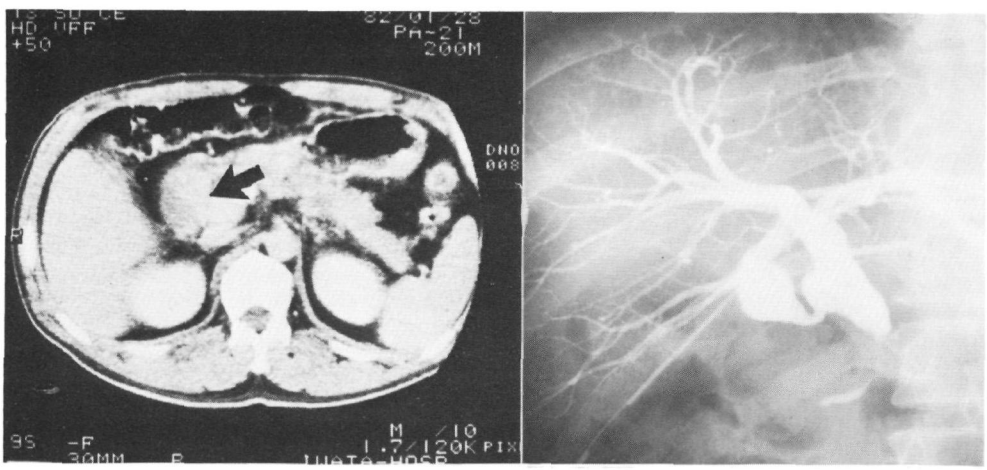

Fig. 1 Computed tomograph (left) demonstrates the presence of a mass in the distal common bile duct (arrow). Percutaneous transhepatic cholangiograph (right) shows an annular stricture of the common bile duct distal to the cystic duct. The gallbladder is seen to be shrunken and deformed in irregular shape.

Following surgery, he was placed on adjuvant chemotherapy with Mitomycin-C and Futraful (FT-207). Four months later he was readmitted with clinical manifestations including obstructive jaundice due to recurrence of carcinoma and finally expired five months after surgery.

Macroscopic findings

Opening the resected gallbladder, annular and diffuse thickening of the wall of the body and fundus, measuring 1 cm. in thickness was found. The lesion appeared gray-white, moist and rather hard (Fig. 2). The cystic duct lymph node was swollen. The distal common bile duct was also segmentally and annularly constricted with infiltration of carcinoma, 4 mm. in thickness and 2.5 cm. in length. The lymph nodes around the head portion of the pancreas were swollen in thumb's tip size, being considered as the mass in the distal common bile duct on US and CT (Fig. 3).

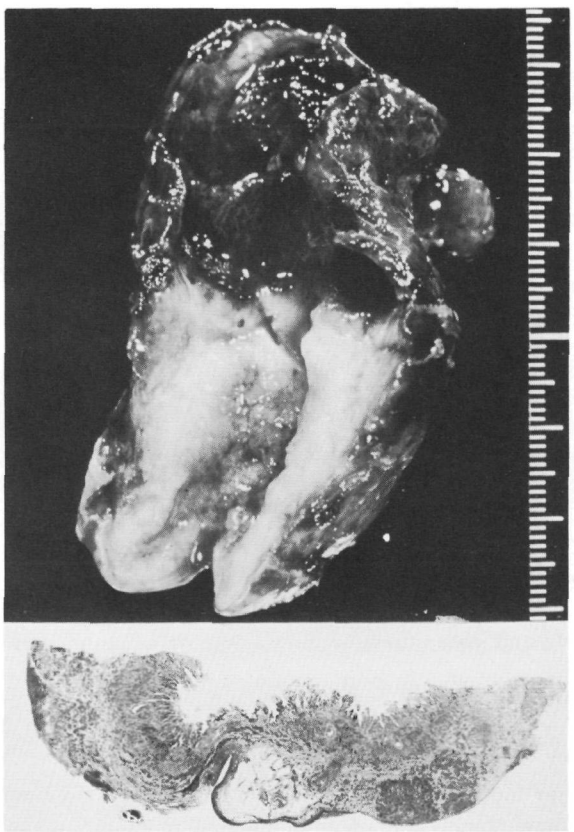

Fig. 2 Gross photograph of the gallbladder (top) showing a diffusely thickened lesion of the body and fundus. It appears gray-white, moist and hard. The cross section of the lesion (bottom) reveals extensive invasion of small cell carcinoma throughout the wall. The mucosa is replaced by ordinary adenocarcinoma (H & E. ×2).

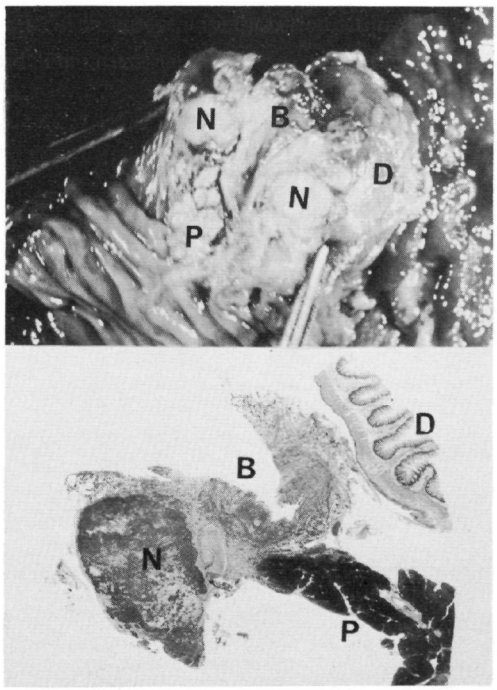

Fig. 3 Gross photograph of the common bile duct (top) showing an annular stricture of the common bile duct (B) and the swollen lymph nodes (N). P : pancreas, D : duodenum. The microphotograph of the common bile duct and lymph node (bottom) reveals diffuse involvement by small cell carcinoma (H & E. ×2).

Microscopic findings

The surgically removed specimens were fixed in a 10 percent formalin solution. The whole gallbladder and common bile duct were longitudinally sliced and stained with hematoxylin and eosin.

The tumor of the gallbladder was composed of two neoplastic components; an ordinary adenocarcinoma and a small cell carcinoma. The ordinary adenocarcinoma replaced the mucosa with invasion to the muscularis, while the tumor of small cell type was composed of sheets or loose aggregates of round to polygonal hyperchromatic cells which diffusely invaded the whole thickness of the wall with striking vascular invasion. The individual cells were small with scanty cytoplasm and indistinct cell margins. The nuclei possessed finely granular chromatin and indistinct nucleoli. Mitotic figures were frequent (Fig. 4). At the periphery of the tumor, the tumor cells of small cell type were pyknotic with dense hyperchromatic nuclei, rather resembling the lymphocytes. In some areas, the tumor of small cell type was closely adjacent to and intermingled with that of ordinary type. Cellular nests of small cell type appeared budding off from ordinary adenocarcinomatous acini. These transitional zones between both tumors were frequently evident (Fig. 5). The common bile duct and all of the lymph nodes were diffusely involved by small cell carcinoma.

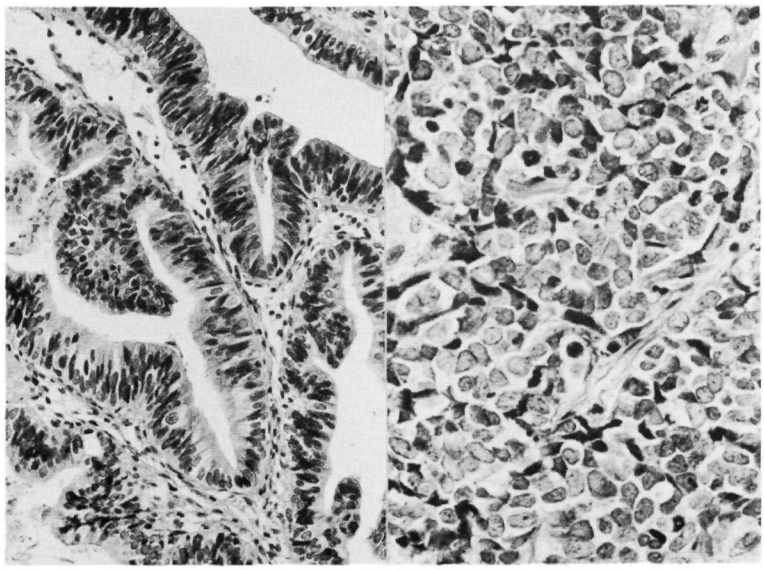

Fig. 4 Microphotograph of the mass of the gallbladder showing ordinary adenocarcinoma (left) (H & E. ×200) and small cell carcinoma (right) (H & E. ×400).

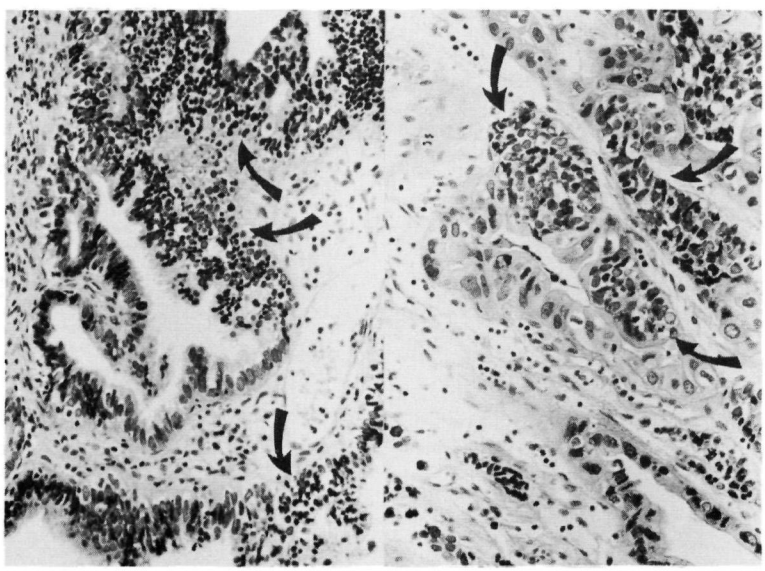

Fig. 5 Microphotograph of the mass of the gallbladder showing transitional zones. Nests of carcinoma of small cell type are seen to budd from the subcolumnar portion of ordinary adenocarcinomatous acini (arrows) (left , H & E. ×100) (right , H & E. ×200).

Small cell carcinoma was negative to argyrophilic reaction with Grimelius method and to argentaffin reaction with Fontana-Masson method. An ultrastructural study of the specimen to demonstrate intracytoplasmic NSGs was unsuccessful since the specimen fixed in a formalin solution was not available for the study.

Comments

Small cell carcinoma in the present case has characteristic microscopic features that are different from the ordinary types of carcinoma of the gallbladder. The tumor cells possess the hyperchromatic nuclei with minute nucleoli, scanty cytoplasm and indistinct cell margins. Tumors with microscopic feartures of this type are closely similar to malignant lymphocytic lymphoma or oat cell carcinoma of the lung. In addition to these morphological features, tumors of this type have been documented to have extensive spread with vascular invasion[3-6].Indeed, the present case showed extensive spread to the common bile duct and the regional lymph nodes. Because of such extension with vascular invasion it is nearly almost impossible to excise the lesions completely and it leads to poor clinical course.

On ultrastructural study, some of small cell carcinomas are composed of argyrophilic cells containing NSGs.[2-5]Unfortunately, the demonstration of intracytoplasmic NSGs was unsuccessful in this case. In the group of carcinoid tumors, histological spectrum ranges from a well-differentiated type to a poorly-differentiated or undifferentiated type. The former is histologically identical to typical carcinoid, the latter to oat cell carcinoma of the lung.[7]If the presence of intracytoplasmic argyrophilic granules and / or NSGs could be demonstrated in the present case, this tumor might gain membership in a family of carcinoid tumors or so-called endocrine cell carcinoma.[9]The diagnosis of carcinoid tumors may of course become more correct whenever it is possible to demonstrate intracytoplasmic argyrophilic granules. Neverthless, it is also true that argyrophilic granules cannot be shown in occasional instances of true carcinoid tumors with correct fixatives.

While, an ordinary adenocarcinoma was associated with the small cell carcinoma in the present case. In areas where the one was intermingled with the other, transitional zones between both tumors were frequently found. The nests of small cell carcinoma were seen to budd off from ordinary adenocarcinoma. The close association of small cell carcinoma with ordinary adenocarcinoma has been described to be characteristic of so-called endocrine cell carcinoma[9] or small cell carcinoma with intracytoplasmic argyrophilic granules and NSGs[2-5] which are identical to oat cell carcinoma of the lung. From these descriptions, the microscopic features of our case are closely similar to those of reported cases and it is strongly suggestive that the present case is also so-called endocrine cell carcinoma. These histological features described herein may lead us to believe that a small cell carcinoma originates in an ordinary adenocarcinoma. With regard to histogenesis of this rare tumor, however, it is generally accepted that the tumor cells may arise from the common precursor cells, the primitive cells of one sort capable of differentiating themselves into the tumor cells of each other,[5,6] while this possibility requires further investigations.

A mixed type tumor possessing two neoplastic components has been reported in the several organs[10-15]. There are two types of mixed type tumor. The one consists of the tumor with discrete areas of ordinary adenocarcinoma closely adjacent to areas of carcinoid tumor with or without transitional zones,[10,14,15] while the other comprises a more intimate admixture of ordinary adenocarcinoma and argentaffin and / or argyrophilic cells.[11,12] In spite of failure to demonstrate intracytoplasmic argentaffin and argyrophilic granules with silver impregnation and NSGs on ultrastructural study because of erroneous preparation of the specimen, the close relationship of a small cell carcinoma with an ordinary adenocarcinoma in the present case may represent a mixed type tumor, suggesting so-called endocrine cell carcinoma.

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