Journal of Gastroenterology and Hepatology (2001) **16**, 107–111

CASE REPORT

Acinar cell carcinoma with hypervascularity

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Abstract Acinar cell carcinoma is an uncommon malignancy with a reported incidence of 1% among exocrine tumors of the pancreas. The case of a 60-year-old Taiwanese man who presented with obstructive jaundice, abdominal pain, and body weight loss is described here. A mixed clinical picture of islet cell tumor and ductal carcinoma of the pancreas was shown to be a hypervascular tumor at the pancreatic head region with an irregular stricture at the common channel of the common bile and pancreatic ducts. The patient had normal levels of plasma carcinoembryonic antigen, carbohydrate antigen 19–9, α-fetoprotein, but an increase in plasma levels of insulin and C-peptide. Immunohistochemical stains and electron microscopic examination of the tumor was consistent with acinar cell carcinoma.

Key words: acinar cell carcinoma, pancreatic tumor.

INTRODUCTION

Acinar cell carcinoma of the pancreas is rare, accounting for approximately 1% of pancreatic exocrine tumors.[1,2] Clinical presentation is usually non-specific unless syndromes associated with excessive production of lipase into serum exist.[3–6] The differential diagnosis among islet cell tumor, ductal cell carcinoma, and acinar cell carcinoma is mostly based upon immunohistochemistry and electron microscopy.[1,3] It remains a highly invasive neoplasm and the survival rate is only slightly better than ductal carcinoma of the pancreas.[7,8] Mixed and combined ductal or endocrine components in acinar cell carcinoma of the pancreas have been described.[8–13] We report a Taiwanese patient with acinar cell carcinoma presenting with a mixed picture of islet cell and ductal carcinoma of the pancreas.

CASE REPORT

A 60-year-old male teacher presented with a 2-month history of vague epigastric discomfort. Tea-coloured urine without clay-coloured stool passage ensued 1 month later. He lost 10 kg of body weight before visiting our clinic. Because a firm abdominal mass was palpated by himself, he was admitted.

He was a habitual smoker and drinker since his youth. He denied having any major systemic diseases including hypertension, diabetes, pancreatitis, hepatobiliary lithiasis, and peptic ulcer disease before this illness. He did not experience fever, diarrhoea, dermatosis, flushing of the face, or symptoms of hypoglycaemia. His medication history was not remarkable. A familial history of malignancy and endocrinopathy was denied.

On admission his skin and sclera exhibited a yellowish appearance. His consciousness was clear and he was alert. The patient's blood pressure was 130/70 mmHg, his heart rate was 72 b.p.m. (beats per minute), and his respiratory rate was 20 breaths per minute. There was no fever. His conjunctivae were pink. The patient's chest and heart were unremarkable. No wheezes could be heard. A deeply seated firm mass was palpated at the patient's right subcostal region. Murphy's sign was negative. There was no hepatosplenomegaly, ascites, peripheral lymphadenopathy or pitting oedema of the lower legs.

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Accepted for publication 3 March 2000.

Laboratory data gave the following results. The red blood cell count was 5 090 000/μL, the haemoglobin was 11.7 g/dL, the haematocrit was 36.3%, the leucocyte count was 9250/μL (neutrophil 70%, lymphocyte 20%, eosinophil 3%, and monocyte 7%), and platelets were 453 000/μL. Biochemistry study showed albumin 3.9 mg/dL; globulin 3.5 mg/dL; total bilirubin 11.1 mg/dL; direct bilirubin 8.3 mg/dL; alkaline phosphatase 844 U/L (normal: 64–238 U/L); γ-glutamyltranspeptidase 541 U/L (normal: 27–76 U/L); aspartate aminotransferase 90 U/L (normal: 5–31 U/L); alanine aminotransferase 193 U/L (normal: 0–31 U/L); fasting serum glucose 119 mg/dL; serum amylase 114 U/L (normal: 35–118 U/L); and lipase 262 U/L (normal: 0–190 U/L). Tumor marker studies including carcinoembryonic antigen (CEA), α-fetoprotein (AFP), and carbohydrate antigen 19–9 (CA19–9) were all within normal limits. Hormone assay revealed normal levels of plasma adrenocorticotropin and growth hormone, but an increase in fasting serum levels of insulin (26.5 μU/mL; normal: 6–26 μU/mL), and C-peptide (8.3 ng/mL; normal: 0.15–0.65 ng/mL).

Abdominal ultrasonography showed a mass lesion at the pancreatic head and dilated biliary tracts. Endoscopic retrograde cholangiopancreatography (ERCP) demonstrated an irregular stricture at the junction of the pancreatic duct and lower common bile duct with proximal dilatation of both ducts, which was also shown on magnetic resonance cholangiopancreatography (Fig. 1). Abdominal computed tomography (Fig. 2) and magnetic resonance imaging (MRI) showed a lobulated homogenous mass at the pancreatic head accompanied with dilatation of the common bile duct and main pancreatic duct. Major vessels such as the portal vein, superior mesenteric vessels and splenic vessels were not invaded nor encased. A well-enhanced nodular lesion with high signal intensity on T2-weighted pulse sequence imaging was noted in the right lobe of the liver. Bilateral adrenal enlargement was also disclosed. A hypervascular tumor with neovascularity, supplied from the gastroduodenal and superior mesenteric arteries, was shown by arterial angiography (Fig. 3). The venous phase showed a patent portal vein. Three small hypervascular stains supplied by the right hepatic artery were also noted. Whipple's operation was performed for islet cell tumor of the pancreas with obstructive jaundice. Atypical hepatectomy was simultaneously done for a hepatic lesion found by intraoperative ultrasonography.

During the operation an encapsulated mass, 6.5 × 5 × 3 cm, with yellowish-white fragile contents was found at the pancreatic head. The pancreatic duct was obliterated, while the common bile duct was compressed. Regional lymphadenopathy was noted at groups 12 and 14. The liver was not cirrhotic, but had a marked

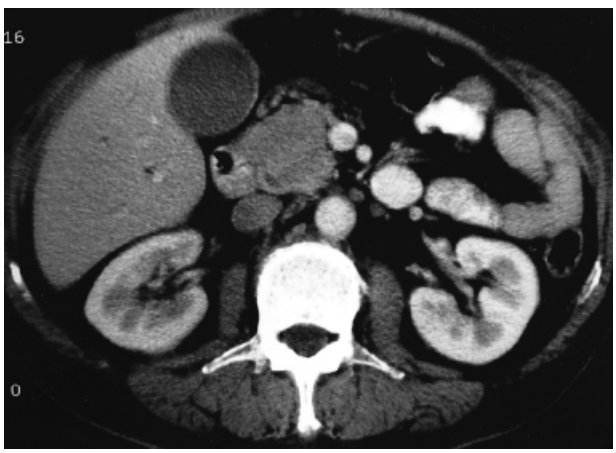

Figure 2 A 3.5 × 3-cm well-circumscribed tumor is located at the pancreatic head by computed tomography following contrast enhancement.

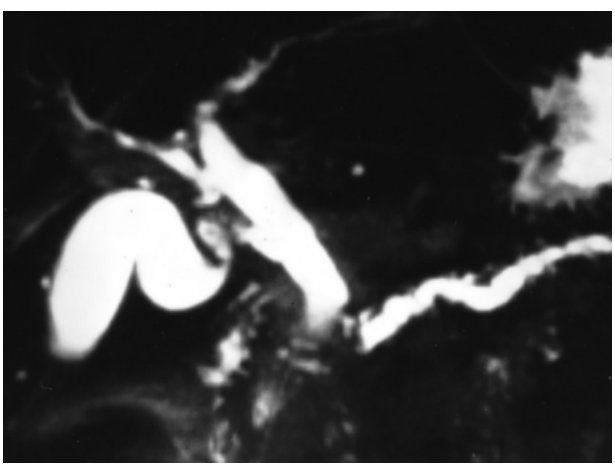

Figure 1 Magnetic resonance cholangiopancreatography shows a dilated main pancreatic duct and common bile duct. A stricture is noted at the junction.

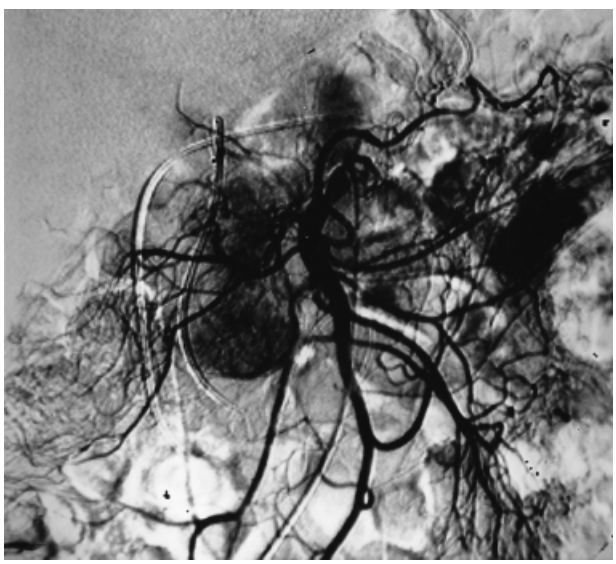

Figure 3 A hypervascular tumour with tumor stain supplied from the superior mesenteric artery is demonstrated by angiography.

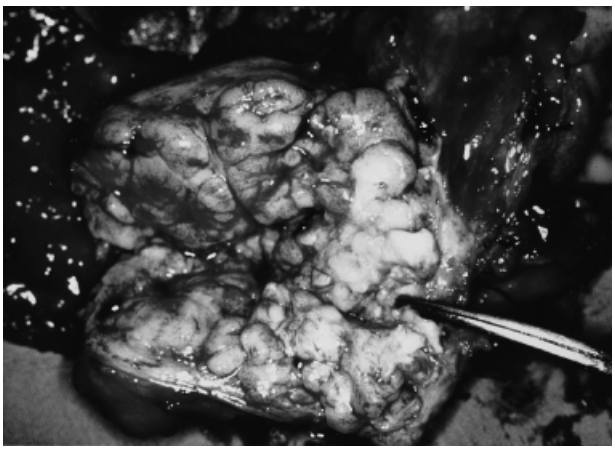

Figure 4 A well-encapsulated tumor with a yellowish-white fragile appearance is resected.

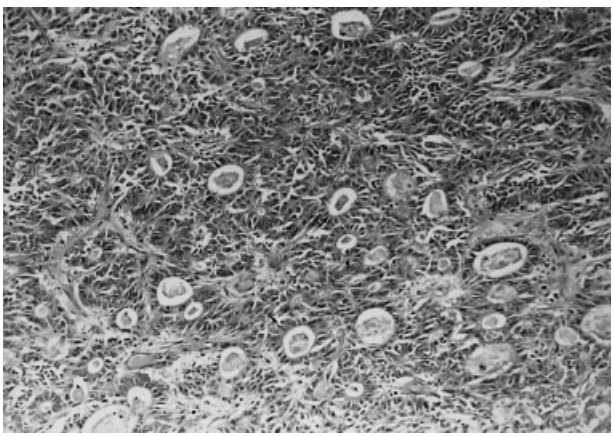

Figure 5 Light microscopy demonstrates an acinic arrangement of tumor cells (arrows) with abundant cytoplasm (H&E, ×150).

cholestatic appearance. A 1×1×1-cm yellowish-brown, but not well-encapsulated, tumor nodule at segment 8 of the liver was resected.

Grossly, the pancreatic tumor was lobulated, and separated by fibrous strands with focal necrosis (Fig. 4). Microscopically, tumor cells were arranged in trabecular, glandular or solid patterns. Focal acinar arrangement was discernible (Fig. 5). The tumor cells were uniform in size with round nuclei, and abundant eosinophilic cytoplasm. Diasterase-treated periodic acid–Schiff (d-PAS) stain revealed diasterase-resistant cytoplasmic granules. Immunohistochemically, tumour cells were stained by cytokeratin and alpha-1-antichymotrypsin focally but not by neuron-specific enolase, chromagranin, insulin, glucagon and serotonin. Zymogen granules were noted under electron microscopy (Fig. 6). Acinar cell carcinoma was thus diagnosed. The tumor had invaded the papilla of Vater along the common channel of the pancreatic and common bile ducts. There was no discernible lymphovascular permeation or neural invasion. All the dissected lymph nodes were free from malignant cells, as were the resected duodenum, stomach, and omentum. The resected hepatic tumor, however, showed marked cholestasis and bile-plug formation, instead of infiltration by tumor cells.

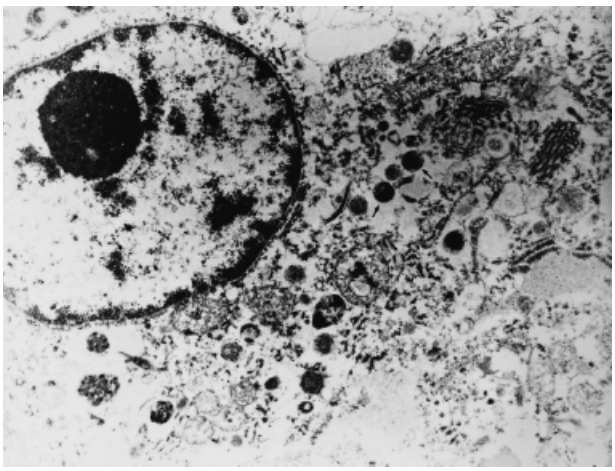

Figure 6 Electron microscopy reveals membrane-bound zymogen granules (arrows) with stacked rough endoplasmic reticulum in cytoplasm (7000X).

After the operation the patient had an uneventful course and the small tumors in the liver remained unchanged after a follow-up period of 2 months. Two months after operation, his serum insulin and C-peptide levels were 3 μU/mL and 1.9 ng/mL, respectively.

DISCUSSION

Acinar cell carcinoma is a rare pancreatic neoplasm that accounts for < 1% of pancreatic tumors.[1,2] The first large series of acinar cell carcinoma was that of Webb in 1977.[7] In 1992 Klimstra *et al*. reported the clinicopathological characteristics of 28 patients with acinar cell carcinomas of the pancreas.[8] The majority of them were Caucasian men with a mean age at presentation of 62 years. The presenting symptoms were nonspecific, but jaundice accounted for only 12%. Lipase secretion was reported at 16% in their series.

Functioning acinar cell carcinoma of the pancreas has been reported.[3–6] The common presentation was extensive subcutaneous fat necrosis resulting from excessive lipase production by the tumors. Such paraneoplastic syndromes including subcutaneous panniculitis, polyarthritis, intraosseous fat necrosis, and eosinophilia were not present in our patient, although his lipase level was mildly elevated.

In acinar cell carcinoma, if there is no change in the level of serum phospholipase A2 or lipase, no difference can be discerned between this and common type ductal adenocarcinoma. Although there was a mild increase in the level of serum lipase, we did not measure that of phospholipase A2. According to the initial presentation of jaundice, body weight loss, and a palpable mass at

the pancreas in an old man, ductal cell carcinoma of the pancreas is usually regarded as the most common diagnosis. But because no change was seen in the serum levels of tumor markers such as CEA and CA19–9, and a hypervascular lesion was seen in the pancreatic region on angiography, then clearly a difference from the common type of carcinoma was present, and this precludes a diagnosis of ductal cell carcinoma. Islet cell tumor, on the contrary, may present with such a clinical picture. Although the serum levels of insulin and C-peptide increased in the present case, the patient was free from symptoms of hypoglycaemia and his fasting plasma sugar level was within the normal range. An islet cell tumor, probably non-functioning, was thus suggested before operation.

The diagnosis of acinar cell carcinoma would be mainly based on histological features of acinar arrangement, ultrastructural demonstration of zymogen granules, immunostaining for pancreatic enzymes, and occasional secretion of lipase into the serum.[4,8] Histologically, acinar cell carcinomas are sometimes difficult to differentiate from neuroendocrine tumors. Most of these tasks depend on immunohistochemistry and electron microscopy. Mixed exocrine and endocrine components, however, have been observed in some acinar cell neoplasms. In the series reported by Klimstra *et al.*, 42% of cases were shown to have a minor endocrine component detected by immunohistochemistry.[8] It was postulated that the neoplasms were derived from primitive, multipotential cells that would differentiate in several directions.[9] Such facts have been described as 'endocrine cells in ductal carcinomas',[10] 'acinar cell carcinoma with endocrine component',[11] or 'mixed duct–acinar and duct–acinar–islet cell tumors'.[12] Amphicrine characteristics such as an 'intermediate' cell containing both zymogen and endocrine granules was also demonstrated.[13] Two types of these tumors were therefore designated as 'mixed-cell population' and 'intermediate cell', respectively, but no endocrine markers could be demonstrated in this tumor despite an increase of serum levels of insulin and C-peptide. Postoperatively, plasma levels of insulin and C-peptide did decrease. But this phenomenon could be just a consequence of Whipple's procedure, which does not always indicate the existence of an endocrine component within the tumor.

Some acinar cell carcinomas may contribute to an increase of the circulating plasma CEA and AFP levels.[14] In the pathological examinations of the tumors gathered by Klimstra *et al*. 18% was positively stained by CEA and 6% was positively stained by AFP.[8] The serum levels of CEA, CA19–9, and AFP were all within the normal range in the present patient, although we did not perform such histological staining.

Histologically, this acinar cell carcinoma consisted of a solid and glandular pattern with an acinar arrangement. Immunohistochemically it originated from the exocrine pancreas, because of positive stainings of cytokeratin and alpha-1-antichymotrypsin, and negative stainings of neuroendocrine tumor markers, such as neuron-specific enolases, chromagranin, insulin, glucagon, and serotonin. In this patient, d-PAS staining was positive and zymogen granules were shown under electron microscopy; therefore acinar cell carcinoma was thus diagnosed. Although one hepatic tumor found by intraoperative ultrasonography was resected, serial histological section failed to document any tumor cells except evident cholestasis.

Aggressiveness was generally regarded as the clinical behaviour of acinar cell carcinoma. As Klimstra *et al*. reported, there were metastases at presentation in 50% of the patients, with an additional 23% developing metastatic disease later in their course.[8] Metastases, when present, were mostly limited to the liver and lymph nodes.[5,6,8] Metastases to spleen,[1] lung,[7] and adrenal gland[7] have also been described. Hepatic and adrenal tumors were suspected in our patient. Intraoperative ultrasonography disclosed only one suspicious hepatic tumor, but this 'tumor' failed to be verified histologically. Clinically suspicious adrenal tumors were not explored during this operation, but close follow up was mandatory.

Because acinar cell carcinoma of the pancreas is rare, strategy for management needs to be explored. Early diagnosis and resection remain the principal treatment, while other modalities of therapy, such as chemotherapy and hormone therapy, remain unsatisfactory. Although it was not statistically significant, an increase in survival rate was noted among those patients who underwent resection. A better prognosis would be anticipated among patients younger than 60 years, with a tumor size < 10 cm and whose tumors were not lipase-secreting.[8] The overall survival rate reported was 56.3% at 1 year, and 5.9% at 5 years, which was better than that for ductal cell carcinoma but lower than that from carcinoma of islet cell origin.[8]

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