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Acinar cell carcinoma of the pancreas eroding the pylorus and duodenal bulb

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Abstract
A 74-year-old woman presented at the National Defense Medical College Hospital in April 2001 with a chief complaint of upper abdominal pain. She had been diagnosed as having adenocarcinoma on the basis of results of examination of a biopsy specimen taken from an ulcer of the duodenal bulb at a local hospital. On admission, she showed no jaundice, but a hard mass, about 10 cm in diameter, was palpated in the right upper quadrant. Laboratory data showed high levels of serum carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) 19-9. Abdominal computed tomography (CT) and angiography demonstrated a giant enhanced mass in a pattern of eccentric gradation extending to the pylorus, duodenal bulb, and pancreatic head. She underwent pancreatoduodenectomy with combined resection of the transverse colon. The histologic diagnosis was acinar cell carcinoma (ACC), originating in the pancreatic head and extending to the stomach, duodenum, and transverse colon, without any lymph node involvement. In most reported cases of ACC, the preoperative diagnosis was a pancreatic mass or endocrine tumor of the pancreas. The correct diagnosis in those cases was made by postoperative or postmortem pathological examination. If criteria for detecting the slight differences between ACC and endocrine tumors on some images were to be established, the diagnostic skill for ACC would improve dramatically.

Key words Acinar cell carcinoma · Pancreatic tumor · Helical CT · Preoperative diagnosis

Introduction

Acinar cell carcinoma (ACC) is a rare neoplasm that accounts for fewer than 2% of all exocrine tumors of the pancreas.[1] The differential diagnosis of this lesion from other pancreatic tumors, especially endocrine tumor of the pancreas, has been discussed on the basis of findings on various images obtained by abdominal ultrasonography (US), abdominal computed tomography (CT), magnetic resonance imaging (MRI), and angiography. Some diagnostic points that differentiate ACC from other tumors have been described in previous reports,[2–5] but they were not definitive differences. We experienced a case of ACC of the pancreas head for which we failed to make a correct diagnosis.

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Case report

A 74-year-old woman presented at the National Defense Medical College Hospital in April 2001 with a chief complaint of upper abdominal pain that had persisted for about 2 months. She also had poor appetite and nausea due to a narrow pylorus. A local doctor had performed an endoscopic examination and discovered an ulcerative stenosis extending from the pylorus to the duodenal bulb, and examination of a biopsy specimen taken from the ulcer had revealed adenocarcinoma. On admission, she showed no signs of jaundice, paniculitis, or arthritis, but had a hard mass, of about 10 cm in diameter, in the right upper quadrant. Laboratory data showed low levels of serum cholesterol and high levels of serum carcinoembryomic antigen (CEA) and carbohydrate antigen (CA) 19-9 (33.9 ng/ml and 155 U/ml), respectively. Hypoglycemia, hyperlipasemia, or eosinophilia were not detected.

Abdominal US revealed a large round tumor, located in the pancreas head, with a clear margin, in which there was mainly a high-echoic area, and some low-echoic spots were included. The parenchyma of the pancreatic body was clearly delineated from the mass, with slight dilatation of the main pancreatic duct (Fig. 1a). Abdominal CT showed a large tumor extending from just under the abdominal wall to the pancreatic head, through which the pylorus and the bulb were penetrat-

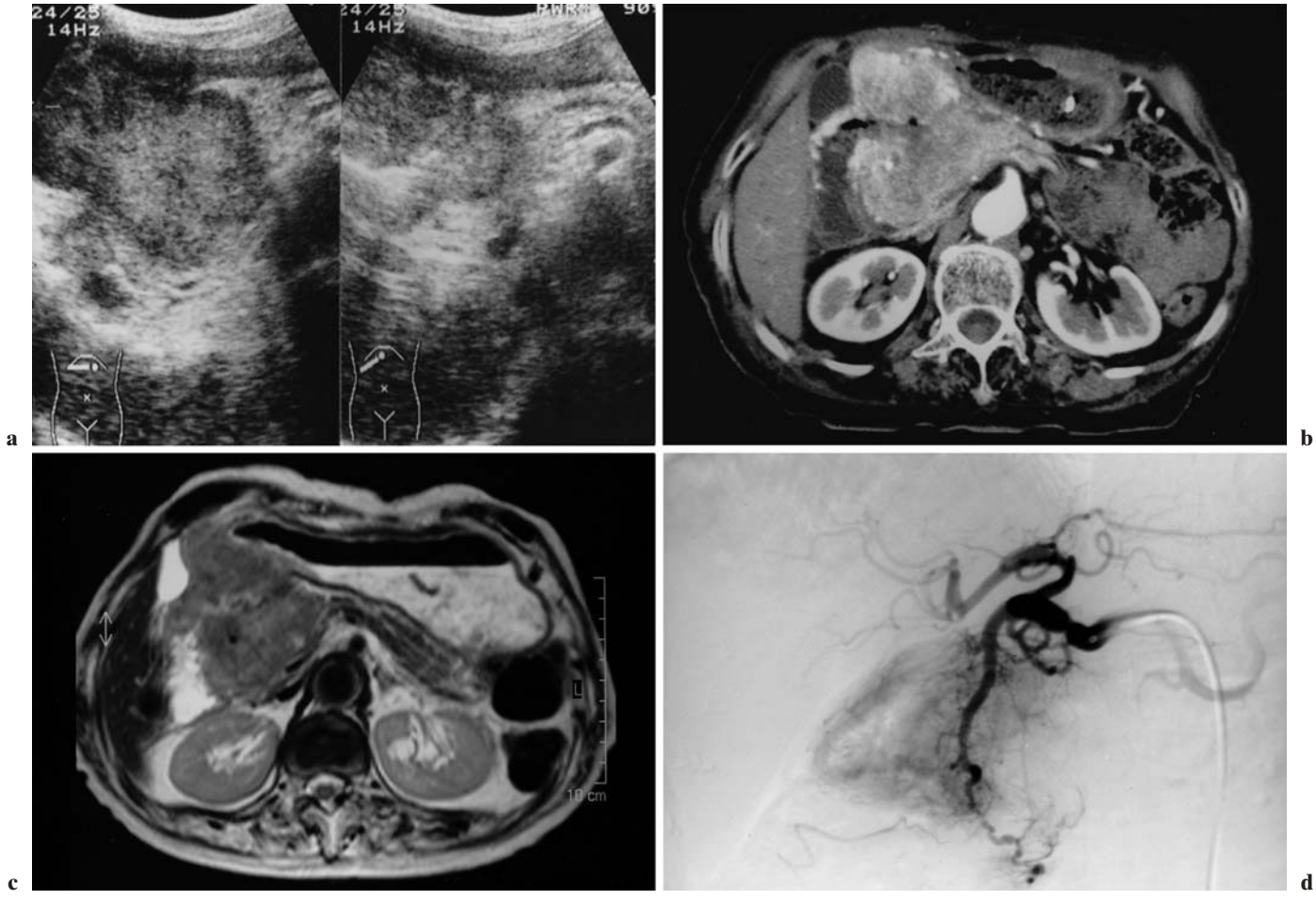

Fig. 1a–d. **a** Abdominal ultrasonography (US) revealed a large round tumor, located in the pancreas head, with a clear margin, in which there was mainly a high-echoic area, and some low-echoic spots were included. **b** Abdominal computed tomography (CT) showed a large tumor extending from just under the abdominal wall to the pancreatic head, enhanced in a pattern of eccentric gradation. **c** Magnetic resonance imaging (MRI) showed that the tumor had high-intensity regions on T2-weighted images, indicating that the tumor included necrotic parts. **d** Abdominal angiography demonstrated a giant, round-shaped area of staining supplied from the gastroduodenal artery. The portal vein was not invaded by the tumor

ing. The tumor was enhanced in a pattern of eccentric gradation (Fig. 1b). MRI showed that the tumor had high-intensity regions on T2-weighted images, indicating that the tumor included necrotic parts (Fig. 1c). Abdominal angiography demonstrated a giant, round-shaped area of staining supplied from the gastroduodenal artery (Fig. 1d). The portal vein was not invaded by the tumor. Neither liver metastasis nor paraaortic lymph node metastasis was detected on any images.

From these results, our preoperative diagnosis was a nonfunctioning pancreatic endocrine tumor or gastric cancer invading both the duodenum and pancreatic head. The patient underwent laparotomy in June 2001. The tumor was found to involve the pylorus, duodenal bulb, pancreatic head, and transverse colon, exposing itself at the anterior wall of the antrum of the stomach and duodenal bulb. There was neither ascites nor liver metastasis. We therefore judged the tumor to have originated from the pylorus and the bulb. We performed pancreatoduodenectomy with combined resection of the transverse colon.

Findings of the resected specimen showed the size of the tumor to be $9.0 \times 5.2 \times 4.9$ cm (Fig. 2). Because the tumor was located mainly in the pancreatic head, its primary site was thought to be the pancreas. Both the choledochus and main pancreatic duct were intact. The tumor had grown grossly in a lobulated pattern, which is considered atypical for conventional pancreatic ductal carcinoma. Microscopic examination showed that the tumor cells had hyperchromatic round nuclei in a polarized arrangement, and that the cells had proliferated characteristically in an acinar configuration reminiscent of normal pancreatic acinar tissue (Fig. 3). Their eosinophilic cytoplasms showed faint granularity, which was

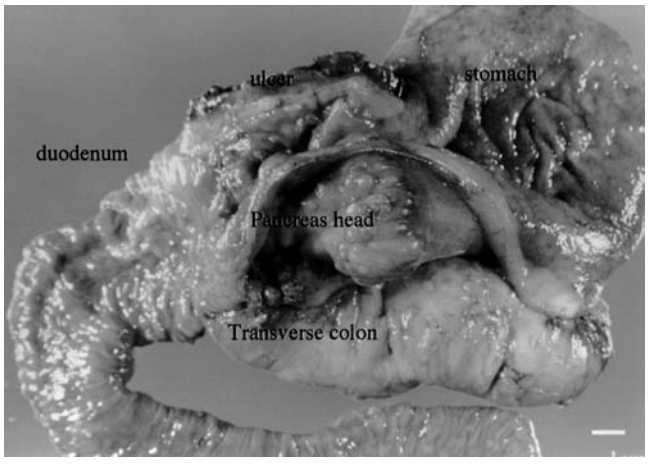

Fig. 2. The size of the tumor was 9.0 × 5.2 × 4.9 cm. The tumor involved the pancreas head, duodenum, stomach, and transverse colon

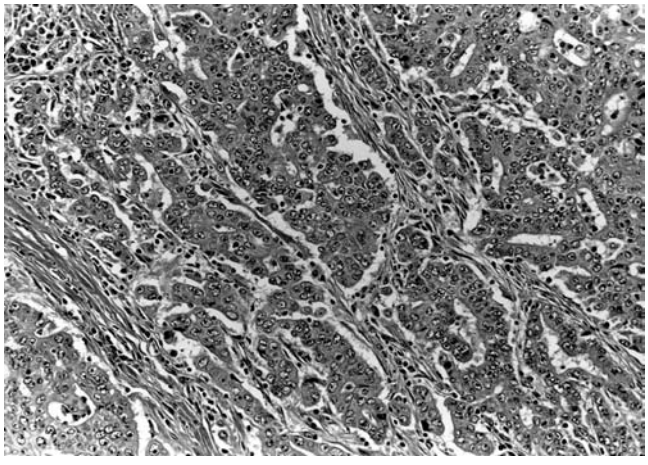

Fig. 3. Microscopically, the tumor cells had hyperchromatic round nuclei in a polarized arrangement. H&E, ×200

accentuated by diastase-resistant periodic acid-Schiff (d-PAS) stain. The tumor cells were weakly labeled by immunostaining for trypsin. The tumor also had duct-like tumor cell nests that were immunohistochemically positive for CEA. The possibility of neuroendocrine differentiation of the tumor was ruled out by negative results for chromogranin A staining. Based on these findings, the tumor was diagnosed as being ACC of the pancreas, extending to the stomach, duodenum, and transverse colon, with no lymph node involvement.

The patient was discharged from our hospital 30 days after the operation. She was followed at the outpatient clinic at the local hospital. She died of multiple liver metastases 6 months after the operation. There was no chance to perform chemotherapy because of the rapid growth of the metastases.

Discussion

Acinar cell carcinoma is rare, accounting for only 1% to 2% of all exocrine tumors of the pancreas.[1] It occurs predominantly in males (male/female ratio of 2:1) and the elderly, but can occur at ages ranging from 3 to 90 years.[6] The tumor arises from acinar cells in the peripheral parenchyma. Occasionally it secretes lipase, resulting in polyarthralgia and subcutaneous and lytic bone and fat necrosis.[6–8] Jaundice is infrequent.[9] Several cases with elevated serum alpha-fetoprotein (AFP) level have been reported,[10–12] but, to the best of our knowledge, a case such as ours, in which both CEA and CA19-9 levels were elevated, has never been reported.

Pathologically, ACC grows grossly in a lobulated pattern. Microscopically, the tumor cells have hyperchromatic round nuclei in a polarized arrangement and their eosinophilic cytoplasm is positive for d-PAS staining. Immunostaining for at least one of the exocrine pancreatic enzymes, such as trypsin, lipase, chymotrypsin, and phospholipase A2, is usually positive. Immunostaining for CEA or AFP is rarely positive. The positive CEA staining in our patient was compatible with the presence of duct-like tumor cell nests in part of the carcinoma. Immunostainings for synaptophysin and chromogranin have been reported to be positive in one-fourth of cases of this tumor.[9] Large electron-dense granules are identified in the tumor by electron microscopy, and neuroendocrine secretory granules may also be found.[6] Toyota et al.[13] reported that finger-print-like zymogen granules detected by electron microscopy could be an important factor in the genesis of ACC.[13]

Resection is usually selected for the treatment of ACC. An unresected patient has poor prognosis. Chen et al.[10] reported the effectiveness of concurrent chemoradiation therapy for a patient with AFP-producing ACC, and Kobayashi et al.[14] reported that intraperitoneal chemotherapy after en-bloc resection was effective for intraperitoneal recurrence of ACC. These reports included many suggestions for improving the prognosis of ACC patients. But, in most cases, chemotherapy and radiation therapy have small effects as primary treatment or as treatment to prevent recurrence after the resection of ACC.[15]

Differential diagnosis from endocrine tumors, solid pseudopapillary tumors, pancreatoblastoma, and ductal adenocarcinoma is difficult.[2] Usually, a correct diagnosis is not made preoperatively, but is made from postoperative or postmortem pathological findings.[4,16–18] Only patients showing some clinical symptoms that are peculiar to ACC have been diagnosed correctly.[7] This entity should be considered when encountering a case of pancreatic head tumor in which the bile duct and the main pancreatic duct are not obstructed despite the large size

of the tumor. However, such a tumor will usually be diagnosed as a pancreatic endocrine tumor. Unfortunately, it can be quite difficult to distinguish ACC from endocrine tumors only from images taken preoperatively.

Dynamic contrast helical CT and dynamic MRI are now available as diagnostic tools.[19,20] There have been some studies in which differences between helical CT images and dynamic MRI images of pancreatic duct cell carcinoma were examined,[3,5,19,20] but there have been no reports on imaging to identify ACC preoperatively. If criteria for detecting the slight differences between ACC and endocrine tumors on some images were to be established, the diagnostic skill for ACC would improve dramatically.

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