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Case report

Primary acinar cell carcinoma of the ampulla of Vater

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Acinar cell carcinoma of the pancreatobiliary system is a relatively rare malignant neoplasm arising usually in the pancreatic parenchyma. We experienced a 68-year-old woman who presented with obstructive jaundice due to an ampullary mass 1.0 cm in diameter, detected by abdominal computed tomography and endoscopic examination. The patient underwent a curative surgical operation, and histopathological examination revealed that the tumor was confined to the ampulla of Vater with no continuity to the pancreatic parenchyma. The tumor cells showed acinar or tubular arrangement with eosinophilic to basophilic granular cytoplasm, findings identical to those of acinar cell carcinoma of the pancreas. Immunohistochemically, the tumor cells were positive for lipase. From these findings, we concluded that the tumor was primary acinar cell carcinoma arising in the ampulla of Vater, probably originating from heterotopic pancreatic tissue. This is the first reported case of primary acinar cell carcinoma in the ampulla of Vater.

Key words: ampullary neoplasms, pancreatic neoplasms, acinar cell carcinoma, ampulla of Vater, heterotopic pancreas

Introduction

Acinar cell carcinoma of the pancreatobiliary system is a relatively rare neoplasm that accounts for approximately 1%–2% of the exocrine pancreatic tumors in adults;[1–3] it usually arises in the pancreatic parenchyma, most commonly in the pancreatic head. Although the tumor has highly characteristic histologic features, the tumor cells produce pancreatic enzyme. Acinar cell carcinoma has two variant types, acinar cell cystadenocarcinoma and mixed acinar–endocrine carcinoma. Its definite diagnosis can be made on the basis of immunohistochemical and electron microscopic findings. Ectopic pancreatic tissue in the upper gastrointestinal tract is a relatively common finding, and is found in up to 15% of individuals at autopsy; the duodenum and stomach are the most common locations.[4] In most duodenal cases, the lesions are located in the portion several centimeters proximal to the ampulla of Vater, often in the submucosa beneath the minor duodenal papilla. In addition, the lesion can present in the ampulla of Vater.[5] Exocrine pancreatic neoplasms and endocrine tumors are very rare.[6,7]

Herein, we present a primary case of acinar cell carcinoma of the ampulla of Vater. To our knowledge, this is the first report of an acinar cell carcinoma in that location, except a previously reported mixed acinar–endocrine carcinoma in the ampulla of Vater.[8]

Case report

A 65-year-old woman was hospitalized because of fatigue persisting for about 3 months. Two months earlier, she had been diagnosed as having jaundice (serum direct bilirubin level at 15.0–17.4 mg/dl) by her primary physician. Percutaneous biliary drainage was performed. She also underwent endoscopic examination, which revealed a tumor in the ampulla of Vater. On admission, she showed no signs of jaundice. She had no personal or family history of pancreatic or biliary disease. Her abdomen was soft; no mass was palpable. Results of laboratory tests were as follows: serum direct bilirubin, 0.8 mg/dl (normal range, <0.3 mg/dl); alkaline phosphatase, 622 IU/l (103–335 IU/l); serum amylase, 74 IU/l (43–131 IU/l); lipase, 74 U/ml (13–49 IU/l); trypsin, 403 ng/ml (101–480 ng/ml); elastase-I, 685.69 ng/

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dl (<400 ng/dl); and white blood cell count, 6300/μl (3500–9300/μl). Her fasting blood glucose level was 107 mg/dl (<110 mg/dl). Tumor marker values were as follows: carcinoembryonic antigen, 1.5 ng/ml (1.0–6.5 ng/ml); carbohydrate-associated antigen 19-9, 11.4 U/ml (<37 U/ml); SPan-1, 6.7 U/ml (<30 U/ml); DUPAN-2, 28 U/ml (<150 U/m); and α-fetoprotein, 5.3 ng/ml (<10 ng/ml).

Ultrasonography demonstrated marked dilatation of the main pancreatic duct, by about 6 mm. There was no bile ductal dilatation. Portal venous phase-enhanced computed tomography showed a heterogeneously enhanced mass of 1.2 × 1.0 cm in the ampulla of Vater (Fig. 1A). No other lesion was detected in the liver or other organs. Endoscopic examination revealed a polypoid, exophytic mass in the ampulla of Vater (Fig. 1B). Endoscopic ultrasonography revealed a heterogeneous hypoechoic mass of about 1.0 cm in the ampulla of Vater without evidence of infiltration into the pancreas or muscularis propria of the duodenum, and dilatation of the main pancreatic duct (Fig. 1C, D). On percutaneous cholangiography, interruption of the bile duct was noted in the distal bile duct.

At the previous biliary drainage, the drainage tube had been placed directly in the common bile duct, instead of via a transhepatic route. Thus, we attempted ampullary biopsy, and a transpapillary biliary drainage by the rendezvous technique. However, the patient suffered from abdominal pain, likely from biliary peritonitis, during the drainage, so we gave priority to transpapillary biliary drainage rather than biopsy.

Subtotal stomach-preserving pancreaticoduodenectomy was performed with the preoperative diagnosis of carcinoma of the ampulla of Vater morphologically. The pancreatogram of the specimen revealed total occlusion of the main pancreatic duct in the head of the pancreas.

In gross appearance, the resected specimen was a white nodular submucosal mass, measuring 1.2 × 1.0 cm in its greatest dimension, in the ampulla of Vater (Fig. 2). A cut surface of the tumor showed it to be an ill-defined whitish tumor with no continuity to the pancreatic parenchyma. Histologically, the tumor was mainly within the ampulla of Vater (Fig. 3A). It had invaded the duodenal muscular layer without extending into the parenchyma of the head of the pancreas (Fig. 3B). The

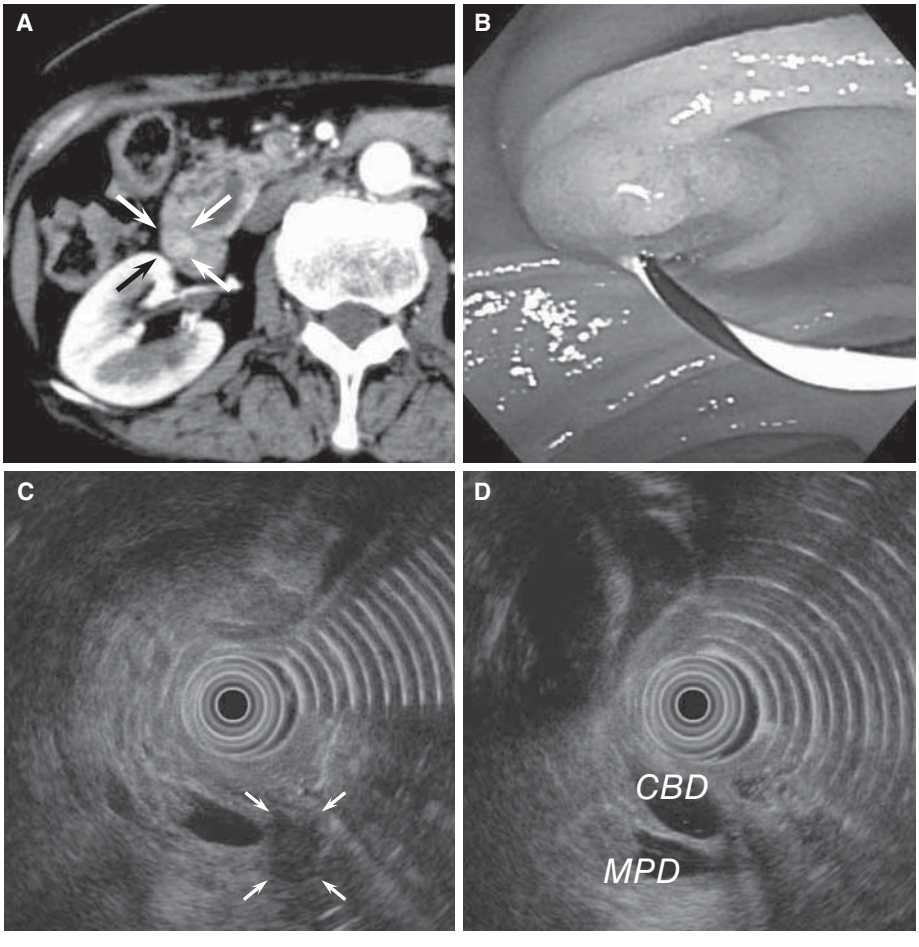

Fig. 1. A Computed tomography image showing a heterogeneously enhanced mass of 12 × 10 mm in the ampulla of Vater (*arrows*). **B** Endoscopic examination showed a polypoid, exophytic mass of the ampulla of Vater. **C, D** Transduodenal endoscopic ultrasonography showed a heterogeneous hypoechoic mass of about 10 mm in the ampulla of Vater without infiltration into the pancreas or muscularis propria of the duodenum (*arrows*). *CBD*, common bile duct; *MPD*, main pancreatic duct

architectural pattern was acinal, with the tumor cells arranged in small glandular units. The tumor cells were similar to the normal pancreatic acinar cells. There was no component of ductal adenocarcinoma or endocrine tumor. Moderate to severe atypias were seen in the tumor cells, including nuclei with dispersed chromatin and central to eccentric prominent nucleoli (Fig. 3C). A moderate desmoplastic reaction in the stroma was also seen. The mitotic activity was in the range of 0–2 per high-power field. Periodic acid-Schiff stain after diastase digestion showed positive granules within the eosinophilic granular cytoplasm of the tumor cells (not shown). Immunohistochemical stainings with lipase (dilution 1:2000, Biodesign, Kennebunk, ME, USA) were strongly positive in the tumor cells (Fig. 3D), and negative for amylase (dilution 1:1000, Sigma, St. Louis, MO, USA), trypsin (dilution 1:10, Dako, Glostrup, Denmark), chymotrypsin (dilution 1:100, Zymed, San Francisco, CA, USA), μ1-antitrypsin (dilution 1:10, Dako), chromogranin A (dilution 1:150, Dako), neuron-specific enolase (dilution 1:200, Dako), synaptophysin (dilution 1:20, Dako), and α-fetoprotein (dilution 1:2,000, Dako). On the basis of these findings, a definitive diagnosis of acinar cell carcinoma of ampulla of Vater was made. The postoperative course was uneventful. At the 19-month follow-up, there was no clinical evidence of recurrence.

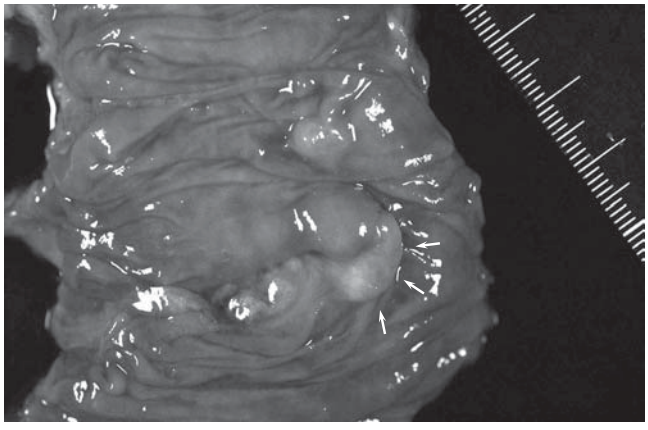

Fig. 2. Gross appearance of the resected specimen. The tumor was a white nodular mass (*arrows*)

Discussion

Heterotopic (ectopic, or aberrant) pancreatic tissue is found in 2%–15% of all autopsies.[4] The most frequent sites of heterotopic pancreas are gastric antrum (30%), duodenum (30%), jejunum (20%), and Meckel's diverticulum (5%). Recently, nine cases of ectopic pancreas located in the major duodenal papilla have been reported; among their summarized clinical features, it is interesting that five patients developed jaundice and six underwent excisions, including one who underwent pancreaticoduodenectomy.

The lesions of these patients were thought to have developed during rotation of the foregut, when frag-

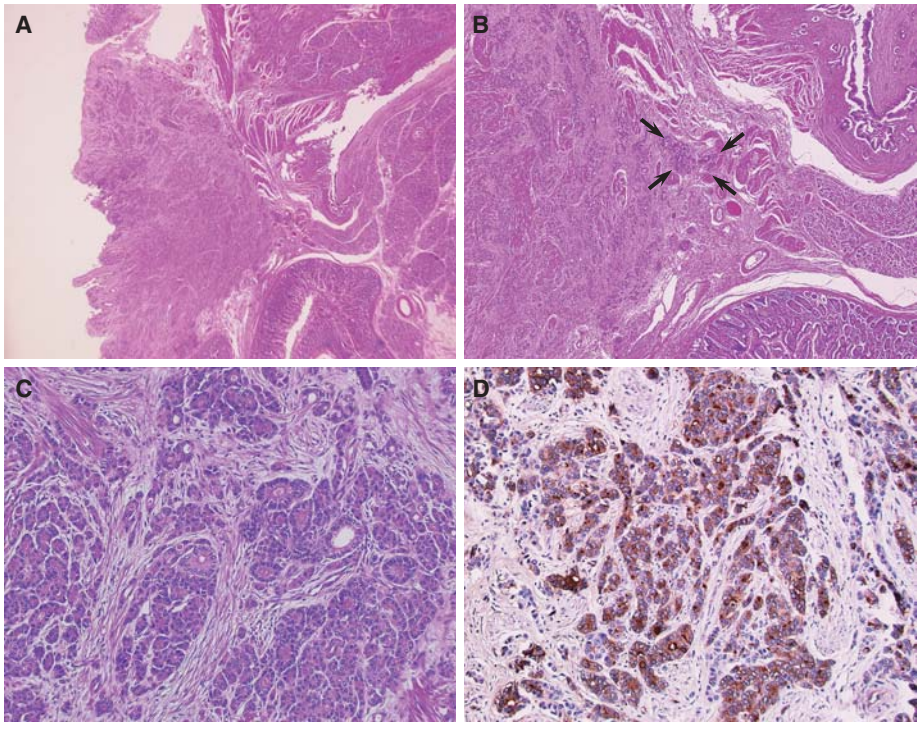

Fig. 3A–D. Photomicrographs of the resected specimen. **A** The tumor was located in the ampulla of Vater (hematoxylin and eosin, original magnification ×12.5). **B** It had invaded the muscularis propria of the duodenum (*arrows*) without parenchymal invasion (hematoxylin and eosin, original magnification ×40). **C** The tumor was hypercellular, consisting of cytologically uniform cells with cords, and granular eosinophilic apical cytoplasm. (hematoxylin and eosin, original magnification ×200). **D** It showed positive cytoplasmic immunoreactivity for the anti-lipase antibody (hematoxylin and eosin, original magnification ×100)

Table 1. Reported cases of acinar cell carcinoma originating from the heterotopic pancreas

First author and reference number	Age (years)	Sex	Symptoms	Location	Size (mm)	Operation	Outcome	Duration of follow-up (months)
Makhlouf[6]	71	M	None	J	35	SR	DOD, LM	12
Moncur[8]	78	M	Lower back pain	A	23	None[a]	Died	2
Sun[9]	86	F	None	S	50	PG	?	?
Present case	65	F	Jaundice	A	12	SSPPD	Alive, NED	19

J, jejunum; A, ampulla of Vater; S, stomach; SR, segmental resection; PG, partial gastrectomy with Billoth II reconstruction; SSPPD, subtotal stomach-preserving pancreaticoduodenectomy; DOD, died of disease; LM, liver metastases; NED, no evidence of disease
[a] An autopsy was performed

ments of pancreas became separated, or from pancreatic metaplasia of endodermal tissues.[6] Moreover, malignant change in heterotopic pancreas is very rare, and acinar cell carcinoma in heterotopic pancreas is thought to be even more rare. Makhlouf et al.[6] reported that of 109 cases of heterotopic pancreas in the gastrointestinal tract, 67 were in the stomach (62%) and 42 in the small intestine (38%).

According to their report, only two were carcinoma arising from heterotopic pancreas, both occurring in the jejunum; one was a ductal adenocarcinoma and the other an acinar cell carcinoma. Recently, two cases of acinar cell carcinoma arising in heterotopic pancreatic tissue have been documented.[8,9] One of these four cases and our case had the lesion in the ampulla of Vater (Table 1). The mean patient age was 75 years (range, 65–86 years). There was no sex difference. The mean tumor size was 30 mm (range, 12–50 mm). The median survival time was 11 months (range, 2–19 months).

For a carcinoma to be recognized as arising from heterotopic pancreatic tissue, three criteria have been proposed:[10] (1) the tumor must be found within, or close to, the ectopic pancreatic tissue; (2) a transition between pancreatic structures and carcinoma must be observed (i.e., duct-cell dysplasia or carcinoma in situ); and (3) the nonneoplastic pancreatic tissue must comprise at least fully developed acini and duct structures.

The lesion in the present case had no pancreatic tissues at the site in the ampulla of Vater. However, the pancreatic remnant tissue might have been totally replaced by the tumor.

In conclusion, we have described a case of primary acinar cell carcinoma arising in the ampulla of Vater, possibly originating from a heterotopic pancreatic tissue.

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