A malignant nonfunctioning pancreatic endocrine tumor with a unique pattern of intraductal growth

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Abstract
The intraductal growth of nonfunctioning pancreatic endocrine tumors (NFPTs) is considered to be rare, and in our survey of the English-language literature, we found only three cases to have been described previously. We herein report the case of a 36-year-old man with a malignant NFPT that uniquely grew within the lumen of the main pancreatic duct (MPD) and completely obstructed the MPD, as shown by endoscopic retrograde pancreatography (ERP). Endoscopic ultrasonography clearly detected the tumor with intraductal growth. In addition, positron emission tomography (PET), using 18F-fluorodeoxyglucose (FDG) and computed tomography (CT) with the same scanner (FDG-PET/CT) showed enhanced uptake of FDG in the tumor. A pylorus-preserving pancreaticoduodenectomy and regional lymphadenectomy were performed under the preoperative diagnosis of an NFPT. Microscopically, positive immunoreactions for synaptophisin and vasoactive intestinal peptide indicated neuroendocrine differentiation of the tumor, while in addition, metastasis to a lymph node along the common hepatic artery was also observed. The patient has survived for 6 months after the surgery without any evidence of recurrence or metastasis. Both ERP and FDG-PET/CT were thus found to be useful for predicting the malignant potential of an NFPT in the preoperative diagnosis.

Key words Pancreas · Nonfunctioning endocrine tumor · PPPD · FDG-PET/CT

Introduction
Endocrine tumors of the pancreas are relatively rare, and the majority of clinically relevant pancreatic endocrine tumors are functional.1 Nonfunctioning pancreatic endocrine tumors (NFPTs) are found in 15%–35% of all surgical patients with pancreatic diseases, and they are usually associated with signs of an expanding mass.1,2 NFPTs are thus generally detected at rather advanced stages, with invasion of the surrounding structures or metastases to the liver and lymph nodes. Recent advances in diagnostic imaging modalities, including endoscopic ultrasonography (EUS) and endoscopic retrograde pancreatography (ERP) have contributed to the diagnosis of pancreatic disorders. During ERP, stenosis and complete obstruction of the main pancreatic duct (MPD) are occasionally observed, and these findings are generally suggestive of pancreatic malignancy. Although these findings are often demonstrated in pancreatic cancer, they are uncommon in pancreatic endocrine tumors.3–13 In addition, rarely, NFPTs may also show intraductal growth, and in our survey of the English-language literature, we found that only three such cases had been described.10,12 We herein report a patient demonstrating a malignant NFPT with a unique pattern of intraductal growth in the head of the pancreas and an obstruction of the MPD.

Case report
A 36-year-old man was referred to our hospital for the evaluation and treatment of a pancreatic mass. He had epigastric pain, and dilatation in the body and tail of the MPD was detected by ultrasonography (US). He had no past history of any pancreatic disorders. A laboratory examination on admission showed normal serum levels of amylase, lipase, and pancreatic hormones, including gastrin, insulin, and glucagons. In addition, carcinoembryonic antigen, carbohydrate antigen 19-9, and elastase-I levels showed normal ranges, while DUPAN-2 (220 U/ml) was slightly elevated. Abdominal computed tomography (CT) demonstrated an enhanced mass in the head of the pancreas, with dilatation of the
MPD in the body and tail (Fig. 1A). On positron emission tomography (PET) using 18F-fluorodeoxyglucose (FDG) and CT with the same scanner (FDG-PET/CT), this pancreatic lesion showed enhanced uptake of FDG; standardized uptake value (SUV), 4.67 (Fig. 1B). EUS revealed a well-defined isoechoic mass, measuring about 15 mm in size, within the lumen of the MPD (Fig. 1C). On ERP, an interruption of the MPD in the head of the pancreas was noted (Fig. 1D). We could not detect any malignant cells in the pancreatic juice. Magnetic resonance cholangiopancreatography (MRCP) showed dilation of the MPD in the body and tail (Fig. 2). On MR imaging, the lesion demonstrated low signal intensity on the T1-weighted image and high signal intensity on the T2-weighted image, with good contrast enhancement (Fig. 3A,B). No tumor was detected in the parathyroid glands or the pituitary gland.

Although acinar cell tumors or combined tumors could not be ruled out, a pylorus-preserving pancreatocoduodenectomy (PPPD) with a pancreaticogastrostomy and a regional lymphadenectomy were performed, under the preoperative diagnosis of an NFPT. Neither extrapancreatic invasion nor metastases to lymph nodes was observed during the operation. The resected specimen of the pancreas showed the presence of an intraductal yellow mass, which measured 16 × 15 mm in size (Fig. 4A,B). Microscopically, the tumor consisted of small nests and cords of uniform cuboidal cells arranged in a trabecular pattern (Fig. 4C). Immunohistochemically, the tumor was negative for insulin, gastrin, glucagon, somatostatin, and pancreatic peptide. Positive immunoreactions for synaptophysin (Fig. 4D) and vasoactive intestinal peptide (Fig. 4E) indicated neuroendocrine differentiation of the tumor. In addition, metastasis...