

Main Pancreatic Duct Obstruction due to a Small Nonfunctioning Endocrine Tumor of the Pancreas

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ABSTRACT

A 65-year-old Japanese male was referred to our hospital for evaluation of a main pancreatic duct obstruction. Two months previously, he had suffered an attack of acute pancreatitis that was resolved with conservative treatment. Dynamic contrast-enhanced study by multidetector row computed tomography revealed a well-enhanced 5 × 5 mm mass in the head of the pancreas with dilatation of the main pancreatic duct in the body and tail. On endoscopic retrograde pancreatography, obstruction of the main pancreatic duct in the head of the pancreas was noted. Pancreatic juice cytology was nondiagnostic. Endoscopic ultrasonography demonstrated a well-defined hypoechoic mass, about 5 mm in size, with distal main pancreatic duct dilatation. The patient underwent elective pylorus-preserving pancreaticoduodenectomy. Pathological examination revealed a well-differentiated endocrine tumor of the pancreas of uncertain behavior, 5 mm in size. Immunohistochemically, the tumor was diffusely positive for chromogranin A and synaptophysin, and focally it was positive for insulin, glucagon, and CA19-9; it was negative for gastrin. The final diagnosis was main pancreatic duct obstruction secondary to a nonfunctioning endocrine tumor of the pancreas of uncertain behavior.

Of note, a small nonfunctioning endocrine tumor of the pancreas is important in the differential diagnosis of main pancreatic duct obstruction demonstrated by radiographic examinations.

Key words: *Nonfunctioning endocrine tumor; Acute pancreatitis, Main pancreatic duct obstruction*

Nonfunctioning endocrine tumors of the pancreas are relatively rare. They are usually difficult to detect until they are large enough to cause symptoms such as abdominal pain, jaundice, and abdominal mass. Recent advances in diagnostic imaging modalities have contributed to the diagnosis of pancreatic disorders. Stenosis and complete main pancreatic obstruction are occasionally observed, both of which are generally suggestive of pancreatic malignancy. These findings are often demonstrated in invasive ductal carcinoma of the pancreas; however, they are not common in endocrine tumors of pancreas. We herein report

a patient demonstrating a main pancreatic duct obstruction due to a small nonfunctioning endocrine tumor.

CASE REPORT

A 65-year-old Japanese male was referred to our hospital for evaluation of a main pancreatic duct obstruction, which his primary physician had detected on computed tomography (CT). Two months earlier, the patient had had an episode of acute pancreatitis that had resolved with conservative treatment. Routine blood tests on admis-

sion, including amylase and liver function tests, were normal. Tumor marker assay showed CEA 2.7 ng/ml (normal range < 4.0 ng/ml) and CA19-9 13 U/ml (normal range < 36.0 U/ml). Plasma hormone concentrations of gastrin, insulin, glucagon, vasoactive intestinal polypeptide (VIP), and somatostatin were normal.

Dynamic contrast-enhanced study by multidetector row computed tomography revealed a well-enhanced 5 × 5 mm mass in the head of the pancreas with dilatation of the main pancreatic duct in the body and tail (Fig. 1). Magnetic resonance cholangiopancreatography (MRCP) showed stricture of the main pancreatic duct in the head of the pancreas and dilatation of the distal duct

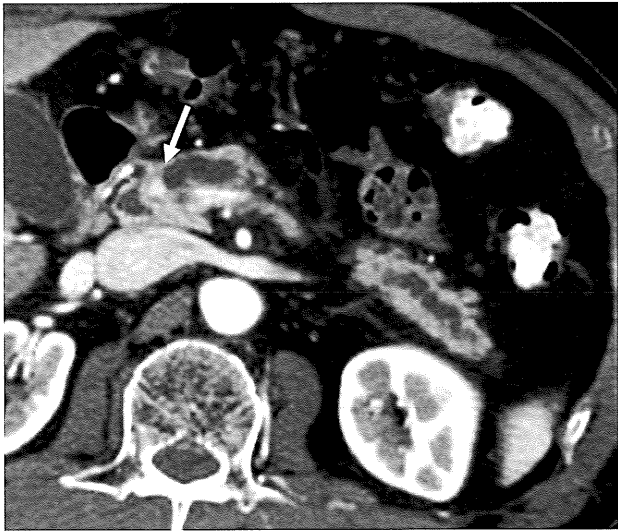


Fig. 1. Dynamic contrast-enhanced study by multidetector row computed tomography (CT) revealed a well-enhanced mass (white arrow) 5 × 5 mm in size in the head of the pancreas with dilatation of the main pancreatic duct in the body and tail of the pancreas.



Fig. 2. Magnetic resonance cholangiopancreatography (MRCP) showed stricture of the main pancreatic duct (white arrow) in the head of the pancreas and dilatation of the distal duct.

(Fig. 2). On endoscopic retrograde pancreatography (ERP), obstruction of the main pancreatic duct in the head of the pancreas was noted. There were no abnormalities or changes consistent with chronic pancreatitis in the head of the pancreas. Pancreatic juice cytological examination of brushings from the area of obstruction was non-diagnostic. Endoscopic ultrasonography (EUS) demonstrated a well-defined hypoechoic mass approximately 5 mm in size with distal main pancreatic duct dilatation (7 mm).

Although the index of suspicion was high for an endocrine tumor, neither pancreatic ductal carcinoma, nor chronic pancreatitis could be completely ruled out. The patient made an informed decision to have surgical management and subsequently underwent elective pylorus-preserving pancreaticoduodenectomy with lymphadenectomy.

Pathological examination revealed a well-differentiated endocrine tumor of the pancreas, 5.5 × 5.0 × 5.0 mm in size. The tumor was confined to the pancreas. The malignant nature of the tumor was suspected from the presence of perineural invasion and 3% of Ki-67 positive cells; however, the tumor had no angioinvasion, less than two mitosis per 10 High Power Field (HPF). The tumor obstructed the main pancreatic duct; however, it did not invade into the main pancreatic duct epithelium (Fig. 3). No extrapancreatic invasion or metastases to the regional lymph nodes or liver were observed. Immunohistochemically, the tumor was diffusely positive for chromogranin A and synaptophysin, which indicated neuroendocrine differentiation. Focally, the tumor was positive for insulin, glucagon, and CA19-9; it was negative for gastrin. The final diagnosis was main pancreatic

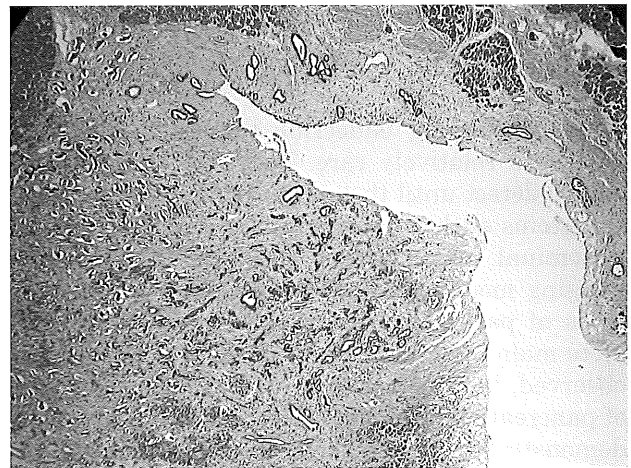


Fig. 3. Well-differentiated endocrine tumor of uncertain behavior.

The tumor obstructed the main pancreatic duct; however, it did not invade into the main pancreatic duct epithelium. Tumor cells are diffusely positive for chromogranin A, and synaptophysin, and focally positive for insulin, glucagons, and CA19-9 on immunohistochemistry.

duct obstruction due to a nonfunctioning well-differentiated endocrine tumor of the pancreas with uncertain behavior, according to the WHO classification tumours of endocrine organs.

The patient recovered uneventfully and was discharged 3 weeks after the operation. Twenty five months after surgery, he is doing well without any evidence of tumor recurrence or acute pancreatitis.

DISCUSSION

In this report, we describe a case of main pancreatic duct obstruction caused by a small nonfunctioning endocrine tumor of the pancreas.

The clinical presentation of endocrine tumors varies and depends on hormonal secretion, location, size and malignant potential. Functioning endocrine tumors present as clinical syndromes of hormone excess. Among nonfunctioning tumors, those presenting with clinical symptoms of mass effects arise more frequently in the head of the pancreas. This may be due in part to the more prominent local symptoms produced by tumors in the head of the pancreas compared to tumors in the body or tail.

The most frequent presenting signs and symptoms of nonfunctioning endocrine tumors are pain, jaundice, a palpable abdominal mass, ascites, steatorrhea, and intestinal bleeding². Nonfunctioning endocrine tumors sometimes become clinically apparent due to their large size. In a series from the Mayo clinic, the size of the nonfunctioning endocrine tumor was > 5 cm in 72% of cases⁴.

There have been several reports of endocrine tumors of the pancreas associated with obstructive pancreatitis. In an autopsy study of 75 patients with an exocrine carcinoma in the head of the pancreas, the tumor obstructed the pancreatic ducts in the majority of cases, but pancreatitis was only detected in 10 cases (13%). In contrast, 12 of 21 patients (57%) with an endocrine tumor had initially presented with an acute attack, which subsided, sometimes to recur months later⁶. Akatsu reviewed nonfunctioning endocrine tumors of the pancreas that completely obstructed the main pancreatic duct on ERP 1). Twelve of 13 patients (92%) had epigastric pain, back pain or clinical symptoms of pancreatitis. These data suggest that acute recurrent pancreatitis may be the first important sign of a nonfunctioning endocrine tumor.

It has been reported that nonfunctioning endocrine tumors of the pancreas associated with acute pancreatitis were rarely demonstrated on imaging studies⁶. Mao reported that three patients with endocrine tumors had multiple operations for pancreatitis or pseudocyst before the endocrine tumor was recognized⁶. Only two cases of pancre-

atic duct stricture by small nonfunctioning endocrine tumor (less than 10mm) have been reported so far^{3,7}. An acute attack of pancreatitis was the initial symptom in both cases. ERP revealed the strictures of the main pancreatic duct; however, the tumors were not detected by ultrasonography or CT scan. They were treated surgically by distal pancreatectomy and middle pancreatectomy. The origin of the stricture in each case was diagnosed as a nonfunctioning endocrine tumor (8mm and 10mm in size). In the present case, ERP demonstrated stenosis of the main pancreatic duct; EUS revealed a small low echoic tumor in the head of the pancreas, and dynamic contrast-enhanced study by multidetector row CT was able to show a well-enhanced 5 × 5 mm mass in the head of the pancreas. Application of such sensitive diagnostic tools might contribute to the accurate diagnosis of small nonfunctioning endocrine tumors.

According to the WHO criteria 2004, pancreatic endocrine tumors have three clinicopathological classifications: well-differentiated endocrine tumour (Benign behaviour, or uncertain behaviour), well-differentiated endocrine carcinoma, and poorly-differentiated endocrine carcinoma². Nonfunctioning tumors have a higher malignancy rate than their functioning counterparts⁴. Approximately 90-95% of non-functioning tumors are well-differentiated carcinoma and a small number of them are well-differentiated tumors showing benign or uncertain behavior². Unequivocal evidence of malignancy is either gross invasion of adjacent organs; metastases to regional lymph nodes, liver, and other distant sites². Most pancreatic endocrine tumors in patients presenting with acute pancreatitis have been reported to be diagnosed as malignant¹. In the present case, the tumor was suspected to have malignant potential because of the presence of perineural invasion and the percentage of Ki-67 index. However, this was not confirmed because the absence of angioinvasion, the small size of the tumor, and small percentage of mitosis.

In the present case, the tumor obstructed the main pancreatic duct; however, it did not invade into the main pancreatic duct epithelium. This suggests that the obstruction in our case was caused by the mass effect and that this tumor may have originated from islet cells adjacent to the main pancreatic duct epithelium. Three cases in which pancreatic nonfunctioning endocrine tumors were growing into the main pancreatic duct have been reported in the English literature^{1,5,8}. In these cases, the tumors consisted of intraductal and extraductal components. The intraductal tumors, which were connected to the extraductal lesions, grew within the lumen of the main pancreatic duct without invading the main pancreatic duct epithelium. The tumor in our case might be the early stage of one of these kinds of

nonfunctioning endocrine tumors.

The differential diagnosis of an isolated stricture of the main pancreatic duct includes: neoplasm, scarring from acute pancreatitis, focal chronic pancreatitis, trauma, pseudocyst, and pancreatic duct fibrosis³⁾. Of note, a nonfunctioning endocrine tumor of the pancreas is important in the differential diagnosis of main pancreatic duct obstruction demonstrated by radiographic examinations.

(Received October 10, 2008)

(Accepted November 18, 2008)

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