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A nonfunctioning islet cell carcinoma with tumor thrombus in both the portal and splenic veins — a case report of successful resection

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Abstract: A rare case of nonfunctioning islet cell carcinoma associated with tumor thrombi in both the portal and splenic veins is reported. The patient, a 49-year-old male, had a 2-year history of occasional abdominal pain. Computed tomography (CT) disclosed a huge mass in the body of the pancreas, and celiac arteriogram showed a tumor stain in the body and tail of the pancreas. Percutaneous transhepatic portography (PTP) demonstrated an irregular filling defect, indicating intraportal tumor growth. Curative surgery, which included total pancreatectomy with combined resection (50 mm in length) and reconstruction of the portal vein, distal gastrectomy, and partial resection of the transverse colon, was performed. Histological examination of the surgical specimen led to a diagnosis of nonfunctioning islet cell carcinoma with a negative immunohistochemical stain for insulin, glucagon, somatostatin, and adrenocorticotropic hormone. The patient has been well for 38 months to date without any sign of tumor recurrence. Our experience with this case has introduced a radical resection for islet cell tumor of the pancreas, even if the tumor has extended into the portal vein.

Key words: nonfunctioning islet cell carcinoma, tumor thrombus in the portal vein, portal vein resection

Introduction

Diagnosis of malignant islet cell tumors of the pancreas is often delayed, since this is a rare disease, with an estimated prevalence below 1 per 100 000 population.[1] Although most pancreatic islet cell tumors are associated with clinically evident hormone hypersecretion, there is a subtype, termed "nonfunctioning," that shows no clinical evidence of hormone secretion. These nonfunctioning tumors are usually detected in the advanced stage and are more likely to have metastasized and invaded to the surrounding tissues than functioning tumors. We present a successfully resected case of clinically silent islet cell carcinoma of the pancreas that presented with remarkable intraportal tumor growth. We also discuss the unusual extension pattern of tumor thrombus into the portal vein.

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Case report

The patient was a 49-year-old male whose major complaint was abdominal pain. He had a 2-year history of occasional abdominal pain prior to admission. Gastroscopy at a local clinic in June 1991 demonstrated extragastric compression. Computed tomography (CT) and endoscopic retrograde cholangiopancreatography (ERCP) at his local hospital revealed an advanced pancreatic tumor. He was referred to our hospital for further examination and possible surgery on July 29, 1991.

On physical examination, there was no jaundice or anemia. The abdomen was soft and nontender, without any palpable masses.

Results of all laboratory investigations on admission, including values for serum carcinoembryonic antigen (CEA) and carbohydrate antigen (CA19-9), were within normal limits. Serum levels of various hormones, insulin, glucagon, gastrin, and somatostatin, were within normal limits.

Abdominal CT scan with contrast enhancement (Fig. 1) demonstrated a huge mass arising from the body of the pancreas. Neither the intrapancreatic portal vein nor dilatation of the pancreatic duct was visualized. ERCP showed an abrupt obstruction and an irregular stenosis of the main pancreatic duct in the head of the pancreas (Fig. 2). Celiac arteriography

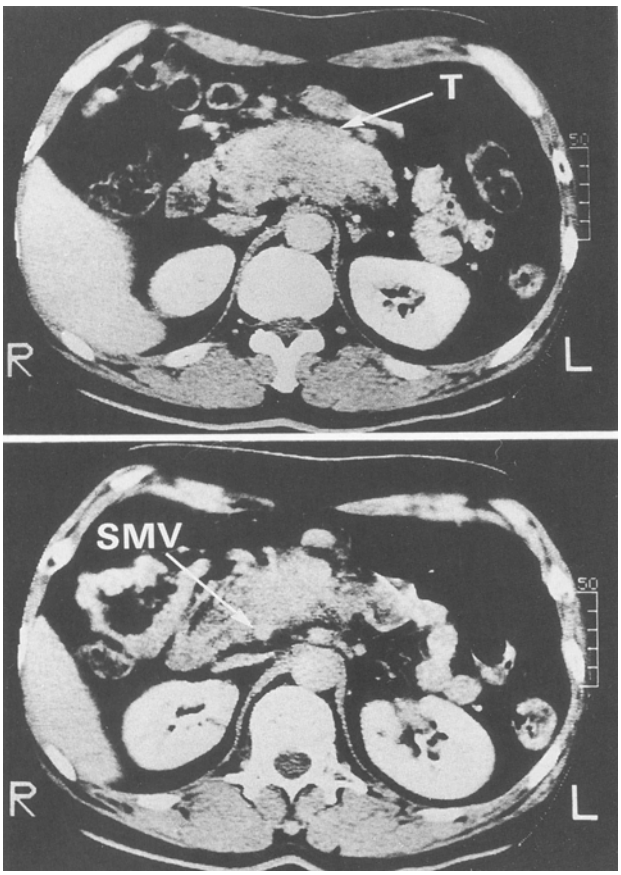

Fig. 1. Abdominal computed tomography with contrast enhancement demonstrated a huge mass (*T*) in the body of the pancreas, without visualization of the portal vein. *SMV*, Superior mesenteric vein

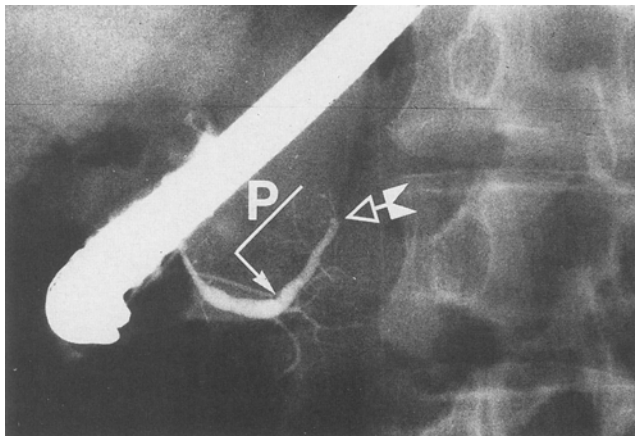

Fig. 2. Endoscopic retrograde cholangiopancreatography showed an abrupt obstruction (*arrow*) and an irregular stenosis (*P*) of the main pancreatic duct in the head of the pancreas

demonstrated dilatation of the anterior anastomosing branch and dorsal pancreatic artery with no tumor encasement in the pancreatic arcade arteries. It also showed a dense tumor blush in the body and tail of the pancreas associated with smooth encasement of the splenic artery (Fig. 3a). Superior mesenteric arteriography similarly disclosed a tumor stain with a linear border on the right side in the neck of the pancreas, probably compatible with a tumor thrombus in the portal vein (Fig. 3b). A portal venous phase of the superior mesenteric arteriogram showed occlusion of the superior mesenteric vein with venous collaterals.

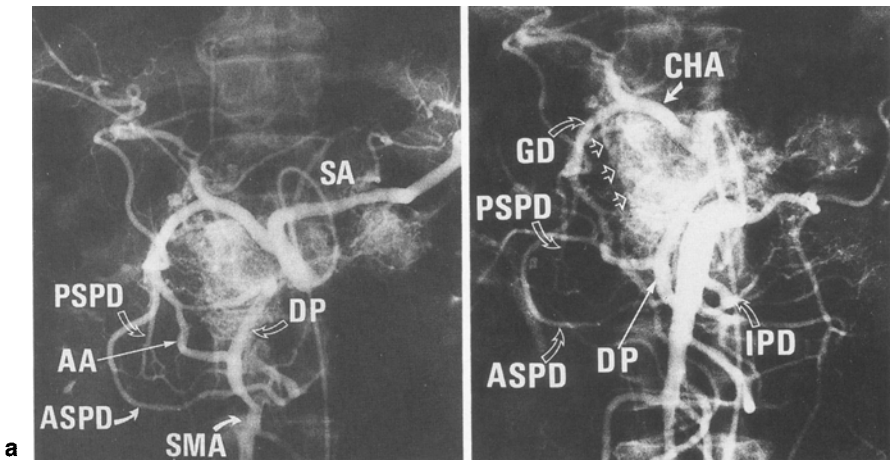

Fig. 3. a Celiac arteriogram showed a dense tumor blush in the body and tail of the pancreas, with a smooth encasement of the splenic artery (*SA*). **b** Superior mesenteric arteriogram showed a tumor stain with a linear border on the right side in the neck of the pancreas (*arrowheads*), compatible with a tumor thrombus in the portal vein. *DP*, Dorsal pancreatic artery; *ASPD*, anterior superior pancreatoduodenal artery; *PSPD*, posterior superior pancreatoduodenal artery; *AA*, anterior anastomosing branch; *CHA*, common hepatic artery; *GD*, gastroduodenal artery

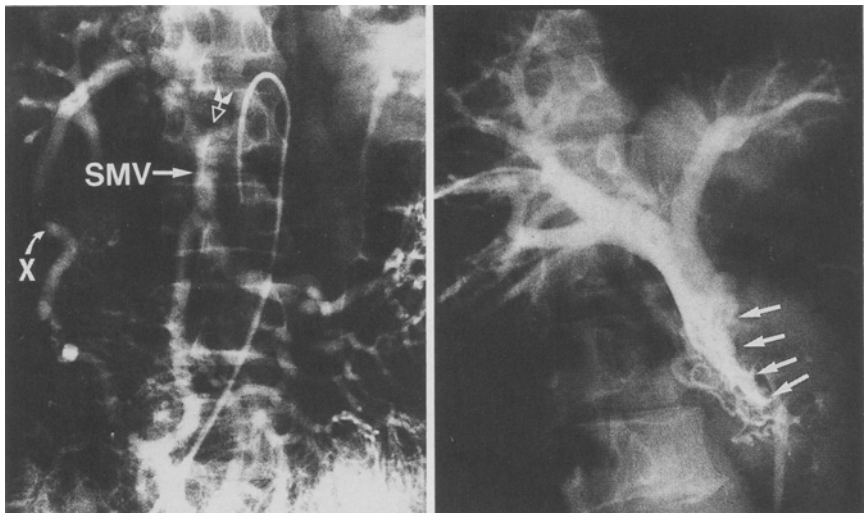

Fig. 4. a Portography via superior mesenteric arteriography demonstrated occlusion (*arrow*) of the SMV with venous collaterals (*X*). **b** Percutaneous transhepatic portography (*PTP*) showed an irregular filling defect (*arrows*) in the portal vein, indicating a tumor thrombus

Percutaneous transhepatic portography (PTP) demonstrated an irregular filling defect in the portal vein due to the tumor thrombus (Fig. 4).

Based on the above findings, a preoperative diagnosis of islet cell tumor with a tumor thrombus in the portal vein was made. Surgery was performed on August 7, 1991.

Laparotomy disclosed a firm and ill-defined mass arising from the body and tail of the pancreas, infiltrating the duodenal cap and associated with a tumor thrombus in the left branch of the middle colic vein (MCV). Neither hepatic metastases nor peritoneal dissemination was found. First, a veno-venous bypass from the ileocecal vein to the left greater saphenous vein was made with an antithrombogenic catheter[2] (Anthron; Toray Industries Inc., Tokyo, Japan) to prevent intestinal vascular congestion during surgery. Total pancreatectomy, splenectomy, distal gastrectomy, and partial resection of the transverse colon were performed. Combined portal vein resection and reconstruction (50 mm in length) was carried out, with end-to-end anastomosis between the main portal trunk and the superior mesenteric vein.

The resected specimen showed a mass measuring about 80 × 50 mm, arising in the body and tail of the pancreas. Yellow tumor thrombi were observed in the portal trunk and the splenic vein (Fig. 5). On the cut surface, a grayish-white tumor had replaced the parenchyma of the body and tail of the pancreas, with normal pancreatic tissue remaining in the head of the pancreas only. The cut surface at section 3 in Fig. 5 disclosed the tumor thrombus growing and extending

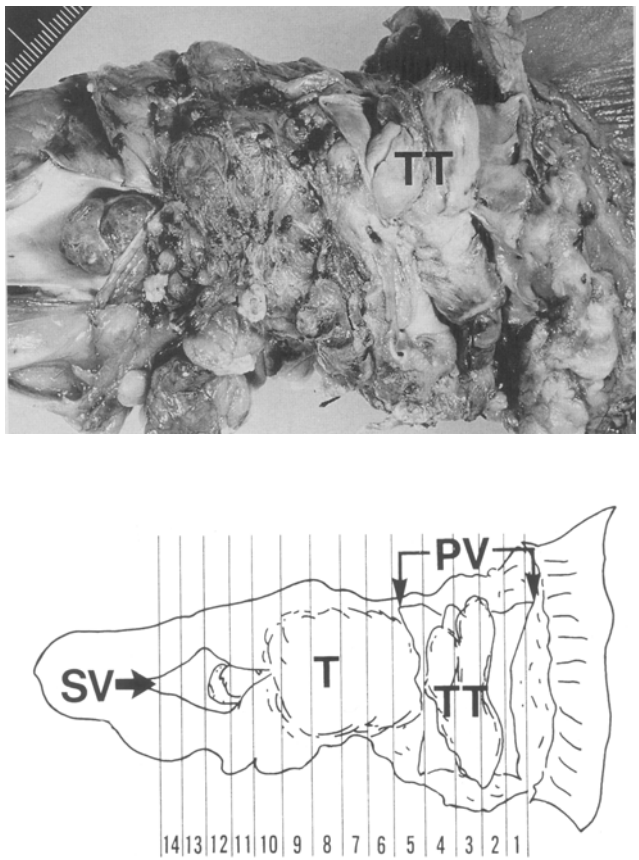

Fig. 5. a Resected specimen. A mass (*T*) measuring about 80 × 50 mm was found in the body and tail of the pancreas. A yellow tumor thrombus (*TT*) was found in the portal vein (*PV*) and splenic vein (*SV*). **b** Schema of the resected specimen

to the lumen of the portal vein from the main tumor (Fig. 6).

Histopathologically, the tumor was composed of cells with hyperchromatic and dysplastic nuclei, forming a trabecular and nest pattern (Fig. 7). Immunoperoxidase staining for insulin, glucagon, somatostatin, and adrenocorticotropic hormone (ACTH) was all negative. On electronmicroscopic studies, there were no obvious granular structures. A diagnosis of nonfunctioning islet cell carcinoma was therefore made. There was neither perineural invasion nor lymph node involvement.

Postoperative recovery was uneventful and the patient was discharged from our hospital on the 52nd postoperative day. He has since been treated with tegafur and remains well with no signs of recurrence 38 months after surgery. Diabetes remains well controlled with insulin administration.

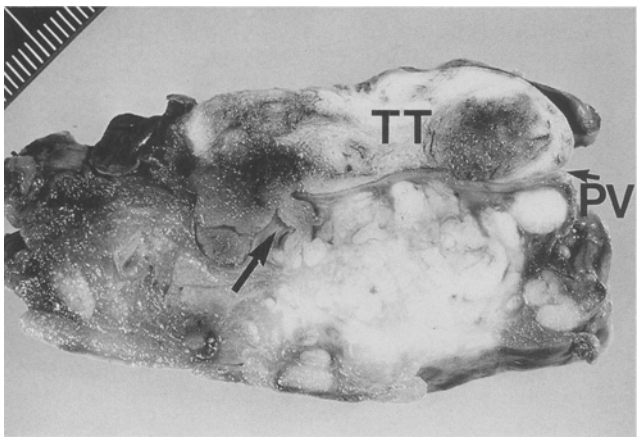

Fig. 6. Cut surface (Section 3 in Fig. 5b). Tumor thrombus (*TT*) arising from the pancreas was found in the portal vein (*PV*). *Arrow* indicates the part of the tumor extending and growing into the PV

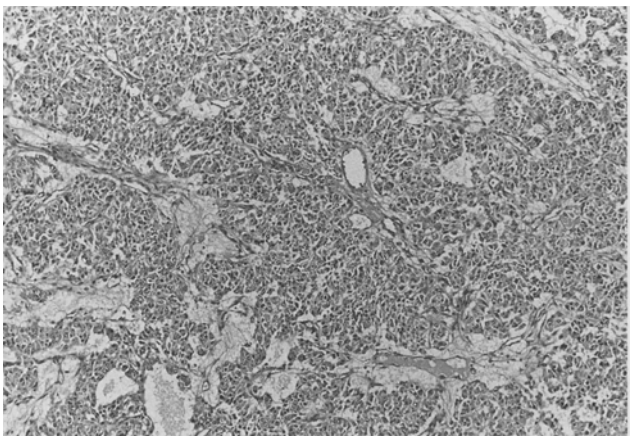

Fig. 7. Histological findings demonstrated islet cell carcinoma, consisting of cells with hyperchromatic and dysplastic nuclei, forming a trabecular and nest pattern. H&E

Discussion

The pancreatic islets, like other neuroendocrine cells, have the potential to produce a wide variety of amine and peptide hormones. With some tumors arising from the pancreatic islets patients show symptoms that are due to hormone secretion. These hormones can be identified by immunohistochemical staining methods and such tumors are termed functioning tumors. However, with other islet cell tumors, neither clinical symptoms nor elevation of gastrointestinal hormones are shown, regardless of whether positive staining was shown on immunohistochemical study;[3,4] these are termed nonfunctioning tumors. Functioning tumors are usually detected in the early stage because of the symptoms arising from the hormone production. In contrast, nonfunctioning tumors are usually detected in the advanced stage and are thus generally larger at presentation and more likely to have metastasized than their functioning counterparts. The present patient had a history of occasional abdominal pain for approximately 2 years before he was diagnosed as having an advanced pancreatic tumor with intraportal tumor thrombus.

Tumor thrombus in the portal vein or splenic vein in islet cell tumors is extremely rare, although intravenous tumor growth has frequently been visualized on arteriography of hepatocellular carcinoma.[7] Watase et al.[8] reported a case of nonfunctioning islet cell tumor with tumor thrombus in the splenic vein resected by subtotal pancreatectomy; the patient survived for more than 5 years without liver metastases. Bok et al.[9] reported angiographic findings of the venous involvement of islet cell tumors in 1984, showing three types of venous involvement: (1) venous occlusion; (2) venous encasement; and (3) intravenous extension. In their review, islet cell tumors with intraportal tumor growth were reported in only 3 of 76 patients, and all 3 patients had liver metastases. In our patient, the tumor was radically resected and there has been no sign of liver metastases for 38 months after surgery; why liver metastasis has not occurred remains unclear. To our knowledge, resection of intravenous tumor growth in both the portal and splenic veins has not previously been reported.

In our patient, the cut surface demonstrated the tumor thrombus in the intrapancreatic portal branch communicating with the pancreas and the portal trunk, suggesting that the growth was not by direct

invasion to the portal vein, but by tumor extension through the portal branch. This is a very interesting finding, and histological findings revealed that the tumor thrombus growing through the portal branch had not invaded the wall of the portal vein.

Case reports of total pancreatectomy with combined resection of the portal vein performed for islet cell tumors are also rare, although resection of the portal vein performed for ductal adenocarcinoma is not so rare.[10] In 1975, Pliam and ReMine[11] reported the results of 64 total pancreatectomies performed at the Mayo Clinic, including those performed in patients with islet cell tumor. However, combined resection of the portal vein was not performed in these patients. In the English literature, only a few reports were found. In 1975, Dardick et al.,[12] reported a patient with islet cell carcinoma who underwent total pancreatectomy with combined resection of the superior mesenteric artery and vein. Vascular reconstruction was accomplished by primary anastomosis of the superior mesenteric vein to the portal vein, and with the aortomesenteric interposition of a Dacron graft. The patient died of other disease 6 months after surgery. Tashiro et al.[10] reported a case of nonfunctioning islet cell carcinoma treated by total pancreatectomy with combined resection of the portal trunk (3 cm in length); the patient survived for 5 years and 9 months. Aszodi et al.[13] reported a 17-year-old girl with giant nonfunctioning islet cell tumor who underwent pancreatoduodenectomy with revascularization of the hepatic artery and portal vein and had been well for 6 months after surgery without a sign of recurrence. In our case, the patient has survived 38 months after surgery without a sign of recurrence. The prognosis of islet cell tumors with portal vein involvement seems to be relatively good, although the prognosis of ductal adenocarcinoma of the pancreas with portal vein involvement is usually poor.

The malignancy rate of nonfunctioning islet tumors was reported to be 92% by Kent et al.[3] and 82% by Dial et al.[14], but prognosis is relatively good and long survival is commonplace. Kent et al.[3] reported that the 3- and 5-year survival rates were 60% and 44%, respectively, even though most patients had metastatic disease at the time of exploration. Thompson et al.[5] reported that 3-year survival was 87% and 66% for patients who received curative surgery (n = 15) and palliative surgery (n = 43), respectively, with an overall 5-year survival rate of 42%. In our case, the patient was diagnosed as having an inoperable pancreatic carcinoma at his local hospital and was referred to our hospital for surgical treatment. The preoperative diagnosis was suspected islet cell tumor or acinal cell tumor with tumor thrombus in the portal vein and without liver metastases. We therefore took an aggressive approach and performed total pancreatectomy with combined resection of the portal vein. The patient has now been well for 38 months after surgery, without any evidence of tumor recurrence. Most nonfunctioning islet cell tumors are slow-growing and allow a long life expectancy; metastatic disease with these tumors does not preclude extended survival, although ductal carcinoma of the pancreas is usually fatal, regardless of the type of therapy employed. Some authors[15,16] have reported that chemotherapy with 5-fluorouracil and streptozotocin was beneficial for patients with islet cell carcinoma. Thus, it would seem that both treatment by surgical resection and chemotherapy contributes to improving the quality of life and prognosis of the patient.

In conclusion, an aggressive surgical approach seems to be indicated for these nonfunctioning islet cell tumors, even if adjacent organs around the pancreas, such as the portal vein, are involved.

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