Pancreatic Carcinoma Associated with Portal Vein Tumor Thrombus: Three Case Reports

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Abstract

Pancreatic carcinoma associated with portal vein tumor thrombus (PVTT) is rare. Here, we report three cases of resected pancreatic carcinoma associated with PVTT. In all three cases, preoperative images obtained using computed tomography and endoscopic ultrasonography revealed a tumor thrombus in the portal vein, which was connected to an irregular mass in the pancreas. All cases underwent surgical resection of the primary lesion and the PVTT. The pathological diagnoses of the tumors were two cases of tubular adenocarcinoma and one case of nonfunctioning endocrine carcinoma. We also retrospectively examined other patients who underwent surgical excision with portal vein resection.

Key words: portal vein, tumor thrombus, intraportal growth, pancreatic tumor, pancreatic carcinoma

(Inter Med 48: 143-150, 2009)
(DOI: 10.2169/internalmedicine.48.1049)

Introduction

Portal vein tumor thrombus (PVTT) frequently occurs in advanced hepatocellular carcinoma (1). Moreover, some recent reports have indicated an association between PVTT and gastric adenocarcinoma or colorectal adenocarcinoma (2). An obstruction of the portal vein secondary to malignant disease can result from direct invasion, compression, or tumor thrombus (3). It has been reported that the incidences of PVTT in various types of tumors are approximately 32% in hepatocellular carcinoma (1), 5% in metastatic liver tumor (1), 1.2% in gastric cancer (2), and 0.6% in colorectal carcinoma (2). Although pancreatic carcinoma often invades the portal vein, few studies have described cases of pancreatic carcinoma extending into the portal vein. We previously reported a case of pancreatic endocrine carcinoma associated with PVTT (4). Here, we describe three resected cases of pancreatic carcinoma associated with PVTT and review the relevant literature.

Case Reports

Case 1

A 60-year-old woman presented with back pain and icterus accompanied by general fatigue. A physical examination performed in May 2006 showed a mass in her epigastrium. Percutaneous biliary drainage was performed to address her jaundice and she was referred to our hospital. Her laboratory test results were as follows: serum bilirubin, 1.8 mg/dL (normal range, 0.2-1.2 mg/dL); aspartate aminotransferase, 82 IU/L (5-40 IU/L); alanine aminotransferase, 167 IU/L (4-45 IU/L); gamma-glutamyl transferase (γ-GTP), 351 IU/L (5-30 IU/L); and carbohydrate-associated antigen 19-9 (CA19-9), 158.2 U/mL (<37 U/mL). Contrast-enhanced computed tomography (CT) showed a heterogeneously enhanced mass (24×15 mm) in the head of the pancreas in the arterial phase and filling defects in the main portal vein and the superior mesenteric vein in the portal phase (Figs. 1A, 1B). Endoscopic ultrasonography (EUS) showed a heterogeneously hypoechoic mass (28×19 mm) in the head of the pancreas and in the main portal and superior mesen-

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Received for publication February 26, 2008; Accepted for publication August 31, 2008
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Figure 1.  (A, B) CT imaging of the portal phase showed filling defects in the main portal vein and the superior mesenteric vein (arrows). (C) EUS showed a heterogeneous hypoechoic mass and a hypoechoic mass in the main portal vein and in the superior mesenteric vein (arrow). (D) A photograph showed a grayish-white mass (arrows) arising from the head of the pancreas and protruding into the portal vein (dashed arrows). (E) A photomicrograph of the resected specimen showed that the tumor consisted of small irregular glands and that the neoplastic cells with enlarged nuclei were polymorphic with an elevated mitotic index (Hematoxylin and Eosin staining, original magnification ×200). (F, G) A photomicrograph of the resected specimen showed that the tumor had grown into the lumen of the portal vein (arrows), including thrombosis (F, Hematoxylin and Eosin staining, original magnification ×12.5; G, Elastica-Masson, original magnification ×12.5). (H) A photomicrograph of the resected specimen showed that the tumor had grown into the lumen of the portal vein (arrows), with fibrovascular stroma (Elastica-Masson, original magnification ×100).
Case 2

A 72-year-old woman with upper abdominal pain for five months was referred from a primary physician to our hospital for a workup in June 2006. The patient had a history of hyperthyroidism. Her abdomen was soft; no mass was palpable. Results of her laboratory tests were as follows: serum fasting plasma glucose, 125 mg/dL (normal range, 88-112 mg/dL); CA19-9, 6,495 U/mL (0-37 U/mL); DUPAN-2, 646 U/mL (<150 U/mL); and Span-1, 542.0 U/mL (<30 U/mL).

Contrast-enhanced CT of the arterial phase showed a heterogeneously enhanced mass with solid and cystic components, which was present in the pancreas from the head to the tail (Fig. 2A); contrast-enhanced CT of the portal phase showed a filling defect in the inferior mesenteric vein (Fig. 2B). EUS showed a heterogeneously hypoechoic mass with anechoic components occupying the pancreas from the head to the tail and disturbing the splenic vein (Fig. 2C). ERP indicated an interruption of the MFD. Distal pancreatectomy with segmental resection of the portal vein was performed in July 2006 based on the preoperative diagnosis of pancreatic acinar cell carcinoma with PVTT. Macroscopic examination showed that the resected specimen was an irregular, grayish-white mass with a cystic lesion (35x35 mm) occupying the pancreas from the head to the tail and protruding into the splenic vein (Fig. 2D). Morphological examination showed broad-based PVTT with a volume of 4x5x35 mm. Microscopically, the tumor consisted of irregular tubular glands embedded in desmoplastic stroma; the neoplastic cells showed moderate polymorphism of the nuclei with a moderate mitotic index (6-10 divisions per 10 high-power fields) (Figs. 2E, 2F, 2G, 2H). The intratumor cystic components were the extended ductal carcinoma lined with neoplastic epithelium (Fig. 2D). According to the WHO classification system (5), the definitive diagnosis was moderately differentiated tubular adenocarcinoma of the pancreas (TNM classification: T4N1bM0, Stage IVA). The postoperative course was uneventful. Systemic adjuvant chemotherapy with gemcitabine was performed. Ten months after the operation, however, hematological toxicity developed, and second-line chemotherapy with oral fluoropyrimidine S-1 was performed. Fourteen months after surgery, tumor recurrence was detected around the superior mesenteric vein. Third-line chemotherapy with low-dose gemcitabine was performed, and the patient is alive 19 months after surgery.

Case 3

A 33-year-old woman reported upper abdominal pain during the previous month in September 2000. She had a history of hemorrhagic duodenal ulcer. Abdominal CT showed a mass in the body of the pancreas, which was diagnosed as pancreatic cancer, as well as a liver metastasis. She was admitted to the hospital where the diagnosis was made and underwent hepatic arterial infusion chemotherapy in 2001. Although the liver metastasis disappeared after the chemotherapy, the tumor in the pancreas remained. Transcatheter arterial embolization and systemic chemotherapy were performed in 2003 and 2006 at another hospital. She then was referred to our hospital for further treatment in March 2007. Results from laboratory tests were as follows: alkaline phosphatase, 395 IU/L (normal range, 103-335 IU/L); γ-GTP, 50 IU/L (5-30 IU/L); Hb, 11.3 g/dL (11.6-15.8 g/dL); CA19-9, 65.1 U/mL (<37 U/mL); and DUPAN-2, 239 U/mL (<150 U/mL). Pancreatic hormone levels were as follows: insulin, 6.5 μU/mL (<9.9 μU/mL); glucagon, 80 pg/mL (<180 pg/mL); and gastrin, 1,570 pg/mL (<200 pg/mL). Contrast-enhanced CT of the arterial phase showed a homogeneously enhanced mass occupying the pancreas from the body to the tail, the spleen, and the left kidney (Fig. 3A). Contrast-enhanced CT of the portal phase showed a low-density mass in the portal vein (Fig. 3B) and in the left lobe of the liver (Fig. 3C). B-mode ultrasonography showed a hypoechoic mass in the portal vein (Fig. 3D), and color-doppler ultrasonography showed blood flow inside the tumor thrombus. Sonazoid-enhanced ultrasonography of the vascular phase showed a hyperechoic mass in the portal vein. EUS showed a heterogeneously hypoechoic mass 40 mm in diameter occupying the pancreas from the body to the tail and a hypoechoic mass in the splenic vein (Fig. 3E). Distal pancreatectopanelenectomy, left nephrectomy, and adrenectomy with segmental resection of the portal vein as well as partial resection of the stomach, colon, jejunum, and left lobe of the liver were performed in March 2007. Macroscopic examination of the resected specimen revealed an irregular, grayish-white mass (68x32 mm) occupying the pancreas from the body to the tail, spreading into the portal vein, and metastasizing to the stomach, colon, jejunum, and left kidney (Fig. 3F). Morphological analysis showed broad-based PVTT with a volume of 15x17x40 mm. Microscopically, the tumor consisted of a large amount of fibrovascular stroma and small and relatively uniform cuboidal cells with a low mitotic index (<10 divisions per 10 high-power fields), spreading into the portal vein (Figs. 3G, 3H, 3I). The tumor mass was immunohistochemically positive for chromogranin A and negative for anti-insulin, gastrin, glucagon, and pancreatic polypeptide antibody. According to the WHO classification system (5), the definitive diagnosis was...
Figure 2. (A) CT imaging of the early phase showed a heterogeneously enhanced mass with solid and cystic components occupying the pancreas from the head to the tail and a filling defect in the splenic vein (arrow). (B) CT imaging of the portal phase showed a filling defect in the inferior mesenteric vein (arrow). (C) EUS showed a heterogeneous hypoechoic mass occupying the pancreas from the head to the tail and a hypoechoic mass in the splenic vein (arrow). (D) A photograph of a grayish-white mass (white arrows) arising from the pancreas and protruding into the portal vein (broken arrows). The main pancreatic duct is indicated by an arrowhead, whereas the ductal carcinoma lined with neoplastic epithelium is indicated by black arrows. (E) A photomicrograph of the resected specimen showed that the tumor consisted of a mixture of irregular tubular glands of variable shapes embedded in desmoplastic stroma, and that the neoplastic cells had moderately polymorphic nuclei with a moderate mitotic index (Hematoxylin and Eosin staining, original magnification ×200). (F, G) Photomicrographs of the resected specimen showed that the tumor had grown into the lumen of the splenic vein (F, Hematoxylin and Eosin staining, original magnification ×12.5; G, Elastica-Masson, original magnification ×12.5). (H) A photomicrograph of the resected specimen showed that the tumor had grown into the lumen of the splenic vein (Elastica-Masson, original magnification ×40).
Figure 3. (A) CT imaging of the portal phase showed a homogeneously enhanced mass occupying the pancreas from the body to the tail. (B) CT imaging of the portal phase showed a low-density mass in the portal vein (arrow). (C) CT imaging of the portal phase showed a low-density mass with inner calcification occupying the left lobe of the liver. (D) B-mode ultrasonography imaging showed a hypoechoic mass in the portal vein (arrows). (E) EUS showed a heterogeneous hypoechoic mass in the pancreas from the body to the tail and a hypoechoic mass in the splenic vein (arrows). (F) A photograph showed an irregular, grayish-white mass occupying the pancreas from the body to the tail (arrows) and spreading into the portal vein (dashed arrows). (G) A photomicrograph of the resected specimen showed that the tumor consisted of a large amount of fibrovascular stroma and small uniform cuboidal cells with a low index of mild mitosis (Hematoxylin and Eosin staining, original magnification ×200). (H, I) Photomicrographs of the resected specimen showed that the tumor had grown into the lumen of the portal vein, with fibrovascular stroma (H, Elastica-Masson, original magnification ×12.5; I, Elastica-Masson, original magnification ×100).

well-differentiated endocrine carcinoma. The tumor in left lobe of the liver was similar to the pancreatic tumor. The postoperative course was uneventful. The patient is doing well nine months after surgery.
showed that the mean survival time of the two patients, in contrast with comparatively better outcomes. In fact, our results suggest that aggressive surgical resection of pancreatic carcinoma associated with PVTT potentially may result in better outcomes. PVTT (4). Therefore, the patients should be carefully monitored postoperatively.

Regarding the diagnostic imaging of PVTT, abdominal ultrasonography revealed PVTT in eight cases (3, 6-11, our case 3), whereas B-mode ultrasonography showed PVTT as a hypoechoic mass in four cases (3, 7, 9, our case 3) and as an isoechoic mass in one case (11). Color-doppler ultrasonography revealed blood flow in the tumor thrombus in three cases (10, 11, our case 3). Contrast-enhanced CT showed PVTT as a filling defect in the portal vein in 13 cases (3, 4, 6-12, 2 cases in 13, our cases 1 and 2) and as a low-density mass in two cases of endocrine carcinoma (8, our case 3). Magnetic resonance imaging showed PVTT in four cases (3, 6, 8, 9), with two cases identified as low intensity signals on a T1-weighted image, high intensity signals on a T2-weighted image, a heterogeneously enhanced mass in the early phase on a true FISP image (6), and a homogenously enhanced mass in the portal phase on a T1-weighted enhanced image (8). F-FDG PET showed abnormal uptake.
Table 1-2. Reported Cases of Pancreatic Carcinoma Associated with Portal Vein Tumor Thrombus

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (y)</th>
<th>Gender</th>
<th>Symptoms</th>
<th>Size (cm)</th>
<th>Site</th>
<th>Histology</th>
<th>Treatment</th>
<th>Long-term outcome</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>10(1)</td>
<td>59</td>
<td>F</td>
<td>Epigastric pain</td>
<td>11.0 × 5.0</td>
<td>H</td>
<td>Solid-pseudopapillary tumor</td>
<td>PD, segmental resection of portal vein</td>
<td>5 mo</td>
<td>Alive</td>
</tr>
<tr>
<td>11(2)</td>
<td>44</td>
<td>M</td>
<td>None</td>
<td>(-)</td>
<td>B</td>
<td>Endocrine tumor</td>
<td>N.D.</td>
<td>N. D.</td>
<td>N. D.</td>
</tr>
<tr>
<td>12(3)</td>
<td>3</td>
<td>M</td>
<td>Abdominal pain</td>
<td>(-)</td>
<td>H</td>
<td>Pancreatoblastoma</td>
<td>Neoadjuvant chemotherapy, PPPD, segmental resection of portal vein, partial jejunectomy, partial colectomy, adjuvant chemotherapy</td>
<td>6 Y</td>
<td>Alive</td>
</tr>
<tr>
<td>13(4)</td>
<td>70</td>
<td>M</td>
<td>None</td>
<td>2.9 × 2.6</td>
<td>H</td>
<td>Poorly differentiated endocrine carcinoma</td>
<td>SSPPD, segmental resection of portal vein, adjuvant chemotherapy</td>
<td>7 mo</td>
<td>Dead</td>
</tr>
<tr>
<td>14(5)</td>
<td>74</td>
<td>F</td>
<td>None</td>
<td>4.0 × 4.0</td>
<td>B</td>
<td>Branch type of IPMC</td>
<td>DP</td>
<td>5 mo</td>
<td>Recurrence</td>
</tr>
<tr>
<td>15(6)</td>
<td>55</td>
<td>F</td>
<td>Epigastric pain</td>
<td>5.0 × 4.8</td>
<td>H</td>
<td>Branch type of IPMC</td>
<td>DP</td>
<td>10 mo</td>
<td>Recurrence</td>
</tr>
<tr>
<td>16 (Case 1)</td>
<td>60</td>
<td>F</td>
<td>Back pain</td>
<td>2.8 × 1.9</td>
<td>H</td>
<td>Tubular adenocarcinoma</td>
<td>SSPPD, segmental resection of portal vein, adjuvant chemotherapy</td>
<td>19 mo</td>
<td>Recurrence</td>
</tr>
<tr>
<td>17 (Case 2)</td>
<td>72</td>
<td>F</td>
<td>Abdominal pain</td>
<td>3.5 × 3.5</td>
<td>H</td>
<td>Tubular adenocarcinoma</td>
<td>DP, segmental resection of portal vein</td>
<td>4 mo</td>
<td>Dead</td>
</tr>
<tr>
<td>18 (Case 3)</td>
<td>33</td>
<td>F</td>
<td>Epigastric pain</td>
<td>6.8 × 3.2</td>
<td>B-T</td>
<td>Well differentiated endocrine carcinoma</td>
<td>Neoadjuvant chemotherapy, DP, spleenectomy, segmental resection of portal vein, Resection of left kidney and left adrenal gland, Partial jejunectomy and colectomy</td>
<td>9 mo</td>
<td>Alive</td>
</tr>
</tbody>
</table>

IPMC: Intraductal papillary-mucinous carcinoma of the pancreas; H, Head of the pancreas; B, Body of the pancreas; T, Tail of the pancreas; DP, Distal pancreatectomy; PD, Pancreaticoduodenectomy; SSPPD, Subtotal stomach-preserving pancreaticoduodenectomy; PPPD, Pylorus-preserving pancreatoduodenectomy; N.D., Not Described.

References

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in the tumor thrombus in one case (12). EUS showed PVTT as a hypoechoic mass in each of our three cases; diagnosis of portal vein thrombus using EUS, however, was difficult. In fact, PVTT with thrombus due to decreased blood flow in the portal vein was the diagnosis in all three of our cases. Sonazoid-enhanced ultrasonography is reported to be effective for detecting small hepatic tumors (17). In one of our cases (case 3), sonazoid-enhanced ultrasonography was useful for detecting not only a metastatic liver tumor but also blood flow inside the tumor thrombus. Even when a primary tumor and PVTT are hypovascular, ultrasonographic imaging is preferable to CT imaging for evaluating blood flow in tumor microvessels; thus, this technique allows clinicians to determine whether a tumoral lesion is portal vein tumor thrombosis or tumoral embolism. Color-doppler EUS in combination with an ultrasound contrast agent is likely to enhance the detectability of PVTT.

The detailed mechanism of PVTT development has not yet been elucidated. It is thought, however, that tumor thrombus formed in the portal systems of each of 13 reported cases by direct venous tumor invasion (4, 9-11, 14, 15, 16, 18, 2 cases in 13, our case 1, 2, and 3) and via the pancreaticoduodenal vein in one case (3). Shizuma et al (19) reported that the incidence of alpha-fetoprotein (AFP)-producing gastric carcinoma among all gastric carcinomas with PVTT was approximately 67.4% (31/46). Yamauchi et al (7) also reported a case of AFP-producing acinar cell carcinoma of the pancreas with PVTT, although the relationship between the AFP and PVTT formation was not clarified. Li Q et al (20) identified three vascular-specific growth factors (vascular endothelial growth factor, angiopoietin 2, and endocrine gland-derived vascular endothelial growth factor) that are related to carcinogenesis and portal vein tumor thrombus formation in hepatocellular carcinoma. No correlation, however, was found between pancreatic carcinogenesis and any of those growth factors.

In summary, we have described three cases of pancreatic carcinoma with PVTT. Ultrasonography, contrast-enhanced CT, and EUS demonstrated all the necessary features to make a diagnosis of PVTT in each of these cases and allowed us to plan the surgery. It is likely that surgical excision of pancreatic carcinoma with the portal vein improved the prognosis of the patients, although adjuvant chemotherapy should be considered in addition to surgical treatment.


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