Pancreatic Hepatoid Carcinoma Mimicking a Solid Pseudopapillary Neoplasm: A Challenging Case on Endoscopic Ultrasound-guided Fine-needle Aspiration

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Abstract

A 59-year-old man was admitted to our hospital for treatment of a 45 mm pancreatic mass found during a medical examination. Endoscopic ultrasound-guided fine-needle aspiration cytology showed polygonal cells with pseudopapillary structures. The tumor cells were positive for nuclear/cytoplasmic β-catenin and CD10, and negative for chromogranin A. After a tentative diagnosis of a solid pseudopapillary neoplasm, middle pancreatectomy was performed. Histologically, polygonal cells with abundant eosinophilic cytoplasm formed in the trabeculae and were immunohistochemically positive for HepPar1 and protein induced by vitamin K absence or antagonist-II. The tumor was finally diagnosed to be pancreatic hepatoid carcinoma. No recurrence occurred for 12 months, even without adjuvant chemotherapy.

Key words: hepatoid carcinoma, pancreatic tumor, EUS-FNA, β-catenin, solid-pseudopapillary neoplasm

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Introduction

Pancreatic hepatoid carcinoma (PHC) is an extremely rare malignant pancreatic tumor, which is characterized by morphological similarity to hepatocellular carcinoma (HCC) (1). Kuo et al. summarized 23 reported cases of PHC in the medical English-language literature and reported that the overall 5-year survival rate was 40.4% (2). Conversely, a solid pseudopapillary neoplasm (SPN) is a rare, low-grade, malignant tumor composed of poorly cohesive monomorphic epithelioid cells forming solid pseudopapillary structures. The overall 5-year survival rate of SPN is approximately 95% (3). Patients with SPN can be treated with an adapted minimized resection due to its excellent prognosis (4). Therefore, the discrimination between SPN and PHC is crucial for determining the operative method. Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) has been a well-established modality in the preoperative evaluation of pancreatic solid tumors (5). We herein present a case of pure form PHC mimicking a SPN on EUS-FNA and review the pertinent literature regarding pure form PHC.

Case Report

A 59-year-old man was admitted to our hospital for the treatment of a pancreatic mass found during a medical examination. He had no symptoms, no significant medical history, and a physical examination revealed no abnormality. The serum level of alpha-fetoprotein (AFP) (3.4 ng/mL; normal <7 ng/mL) was normal. The serum level of protein induced by vitamin K absence or antagonist-II (PIVKA-II) (87

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mAU/mL; normal <40 mAU/mL) was elevated. Other tumor markers were normal. Hepatitis B and C serology was negative. Abdominal ultrasonography revealed a round 45 mm hypoechoic mass protruding from the pancreatic body without pancreatic duct dilation (Fig. 1A). The tumor was enhanced to the same extent as the pancreatic parenchyma on a contrast-enhanced computed tomography (CT) scan (Fig. 1B-D). Low density spots were found in the tumor on arterial phase (Fig. 1B, arrows). We could not detect any lymphadenopathy or distant metastasis on CT. Magnetic resonance imaging (MRI) showed a well-defined mass with a homogeneous low signal intensity on the T1-weighted images (Fig. 2A) and iso intensity on the T2-weighted images (Fig. 2B). On diffusion-weighted imaging, the lesion had a high signal intensity (Fig. 2C) and low apparent diffusion coefficient (ADC) value (Fig. 2D). Contrast-enhanced endoscopic ultrasonography showed a hypervascular tumor with an anechoic spot (Fig. 3). According to these findings, a neuroendocrine tumor (NET) or SPN was initially suspected. EUS-FNA with a 25-gauge needle was performed for the definitive diagnosis. FNA cytology showed tumor cells with small, round nuclei of various sizes loosely adherent to branching vessels (Fig. 4A). Conversely, histology showed that polygonal tumor cells were arranged in a sheet-like pattern without pseudopapillary architecture (Fig. 4B). Immunohistochemically, the tumor cells were positive for CD10 and nuclear/cytoplasmic β-catenin (Fig. 4C and D), and negative for chromogranin A and synaptophysin (Fig. 4E and F). According to these findings, we preoperatively diagnosed the mass as a SPN, and middle pancreatectomy was performed. Macroscopically, a well-circumscribed solid mass with petechiae, measuring 50 mm and 35 mm at the greatest dimension, was located in the body of the pancreas (Fig. 5). These petechiae were consistent with the anechoic spot on the contrast-EUS image (Fig. 3, arrow) and low density spots on the contrast-CT image (Fig. 1, arrows). The cut surface was brownish-yellow. Histologically, polygonal tumor cells with round nuclei and abundant eosinophilic cytoplasm formed thick trabeculae (Fig. 6A), as visualized with reticulin silver staining (Fig. 6B). The tumor cells also showed fatty change with Mallory-Denk bodies (Fig. 6C) and partial bile production (Fig. 6D). Immunohistochemically, the tumor cells were positive for AE1/AE3 (Fig. 7A), HepPar1 (Fig. 7B), PIVKA-II (Fig. 7C), CD10 (Fig. 7D), nuclear/cytoplasmic β-catenin (Fig. 7E), and focally positive for AFP (Fig. 7F). According to these findings, we made the diagnosis of PHC. We followed up without adjuvant chemotherapy and found no recurrence 12 months after the surgery. The latest serum levels of AFP (3.0 ng/mL) and PIVKA-II (18 mAU/mL) were normal.

**Discussion**

Hepatoid carcinoma is a rare extrahepatic malignant tumor sharing the cytomeorphological and immunohistochemical features of HCC. Microscopically, hepatoid carcinoma is
composed of polygonal cells with abundant eosinophilic cytoplasm arranged in a sheet-like or trabecular pattern, and occasionally with bile production or bile canaliculi formation. Although the tumor cells are primarily positive for AFP, AFP is not specific to hepatoid carcinoma. However, the hepatocyte-specific antigen is more specific for the verification of hepatocellular differentiation. Ishikura et al. reported the first case of gastric hepatoid carcinoma in 1985 (6). Among primary tumor sites, the stomach is the most common organ, and several other organs have been reported, including the ovary, esophagus, papilla of Vater, colon, gallbladder, lung, adrenal grand, kidney, urinary bladder, uterus, vagina, and testicle (6-12). The first case of PHC was reported by Hruban et al. in 1987 (1). Until now, an additional 25 cases have been reported (2, 13-35). PHCs often have components of other tumors, such as neuroendocrine tumor or ductal adenocarcinoma, and these components might affect the clinical outcome of PHC. We summarized the clinicopathological features of pure form PHC in Table. Only 15 cases of pure PHC have been reported, not including the present case (Table). The median age of the patients was 58 years (range, 32-80). Twelve (75%) patients

Figure 2. Magnetic resonance images, showing a well-defined mass with a homogeneous low signal intensity on the T1-weighted images (A) and iso intensity on the T2-weighted images (B). On diffusion-weighted imaging, the lesion had a high signal intensity (C) and low apparent diffusion coefficient value (D).

Figure 3. An endoscopic ultrasound (EUS) image (A) showing a well-demarcated hypoechoic mass in the pancreatic body (arrowheads). A contrast-EUS image (B) showing a hypervascular tumor with an anechoic spot (arrow).
were men and four (25%) were women. Most patients (69%) were symptomatic. The most common symptom was abdominal pain (25%), followed by weight loss (19%), jaundice, and nausea (13%). The predilection site was the body-tail of the pancreas (75%), followed by the head (19%). One patient had a tumor which spread throughout the pancreas. The median tumor size was 6 cm (range, 2-11 cm). In 11 of 15 cases undergoing contrast-enhanced CT, eight patients had radiographic characteristics with various vascular patterns in tumor enhancement. An elevated serum level of AFP, which is characteristic in hepatoid carcinoma, was observed in only five of 14 cases (36%). An elevated serum level of PIVKA-II was observed in two out of three cases (67%). Although seven cases had no information available about hepatitis B virus (HBV) and hepatitis C virus (HCV) infection, nine were negative for HBV or HCV infection. Immunohistochemically, only six out of 14 cases (43%) were immunoreactive for AFP, whereas all were immunoreactive for hepatocyte-specific antigen. Five cases (31%) had metastasis at the diagnosis of PHC, including liver metastasis in two cases, liver metastasis and lymphadenopathy in one case, liver and lung metastasis in one case, and wide spreading tumor in one case. Regarding antineoplastic therapy, 12 cases (75%) underwent surgical resection. Three cases (19%) underwent chemotherapy. One case underwent surgical resection and right lobectomy after chemotherapy for liver metastasis. The overall one-year survival rate was 72%.

In the present case, the CT and EUS imaging findings resembled NET or SPN, and we presumed a SPN because the tumors were immunoreactive for CD10 and nuclear/cytoplasmic β-catenin and immunonegative for chromogranin A and synaptophysin in the specimen obtained through EUS-FNA. Because PHC has non-specific CT and MRI results, it is difficult to suspect PHC from preoperative imaging. Although the prognosis of SPN is excellent, that of PHC is poor. Therefore, the preoperative diagnosis is crucial for determining the operative method, including minimal resection. Recently, EUS-FNA has been a key modality for the preoperative diagnosis. However, the specimen from EUS-FNA is often inadequate for a histological assessment. Regarding the specimen of the present case, the peculiar structure of PHC was destroyed, thus the pseudopapillary architecture along the hepatoid sinusoid mimicked SPN. Therefore, an immunohistochemical analysis plays an important role in the auxiliary diagnosis. Nearly all SPNs express vimentin, CD10, and nuclear/cytoplasmic β-catenin. In particular, β-catenin is a key marker because almost all SPNs have a somatic point mutation in exon 3 of \( CTNNB1 \), which is the gene encoding β-catenin. On the other hand, PHCs share
Figure 6. Histological findings of the resected specimen revealing polygonal tumor cells with round nuclei and abundant eosinophilic cytoplasm, which formed thick trabeculae (A), visualized with reticulin silver stain (B). The tumor cells showed fatty change with Mallory-Denk bodies (C, arrow) and partial bile production (D, arrow).

Figure 7. Immunohistochemical staining of the resected specimen. The tumor cells were positive for AE1/AE3 (A), HepPar1 (B), PIVKA-II (C), CD10 (D), nuclear/cytoplasmic β-catenin (E) and focally positive for AFP (F).

similar immunohistochemical features of HCC, which have canalicular patterns with positive immunohistochemical staining with CD10, and negative staining for chromogranin A and synaptophysin. It has been reported that approximately 26% of HCC were immunoreactive for nuclear/cytoplasmic β-catenin because of the Wnt/β-catenin signaling pathway due to a β-catenin mutation (36, 37). These data suggest that PHC can also be immunoreactive for nuclear/
cytoplasmic β-catenin. To the best of our knowledge, this is the first case of nuclear/cytoplasmic β-catenin immunopositivity among pure form PHC. Although an EUS-fine needle biopsy using a 19-gauge core needle might help to diagnose PHC (35), it is noteworthy to recognize that PHC might share the immunohistochemical features of SPN.

In summary, we described a case of PHC mimicking a SPN on EUS-FNA. In a case of suspected non-typical SPN, PHC (35), it is noteworthy to recognize that PHC might share the immunohistochemical features of SPN.

The authors state that they have no Conflict of Interest (COI).

References


