Letter to the Editor

Extended pancreatoduodenectomy with portal vein and inferior vena cava resection and reconstruction combined with sorafenib for hepatoid carcinoma of the pancreas: a strategy of superextended surgery combined with targeted therapy

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Hepatoid carcinoma of the pancreas (HCP) is an extremely rare pancreatic cancer resembling hepatocellular carcinoma, a type of liver cancer (1). Most reports have shown that it has an aggressive behavior and is associated with early metastasis. There is no standardized treatment for HCP due to its rarity, and the limited number of cases reported in the literature (2,3). However, treatment options for this type of rare cancer include surgery, chemotherapy, and radiation therapy, depending on the stage of the cancer. Nevertheless, the prognosis of HCP is poor.

Herein, we firstly report about the use of extended pancreatoduodenectomy combined with portal vein (PV) and inferior vena cava (IVC) resection and reconstruction and sorafenib for HCP. This is a strategy for superextended surgery combined with targeted therapy of HCP.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

A 48-year-old Chinese man presented to our hospital with a mass in the pancreatic head. Physical examination did not reveal any abnormalities. Serum alpha fetoprotein (AFP) was 61,887.16 ng/mL. Hepatitis B surface antigen was positive. The quantification of hepatitis B virus DNA was 1.60×10^6. Abdominal computed tomography (CT) and magnetic resonance imaging (MRI) scan showed a mass with an irregular soft tissue density in the pancreatic head, approximately 7.5 cm × 7.0 cm × 3.7 cm (*Figure 1A*). The tumor boundaries near the liver side was clear, however, the tumor boundaries near the PV and IVC side was blurred, and mild heterogeneous enhancement was observed. The lymph node next to the pancreatic head was enlarged (approximately 2.2 cm × 1.3 cm) (*Figure 1A*).

Then, the patient underwent extended pancreatoduodenectomy combined with PV and IVC resection and reconstruction. During the operation, No. 8 lymph nodes indicated metastatic adenocarcinoma (*Figure 1B*) and PV and IVC were tumor involved. The anterior wall of the IVC was partly resected and direct repair were performed. The tumor was found invaded the PV, measuring approximately 2 cm in length and growing into the PV cavity to approximately 1/2 the diameter of the PV. After removing the tumor, measurements revealed that the actual length missing from the PV was approximately 4 cm, therefore, we performed direct end-to-end anastomosis of the vessel

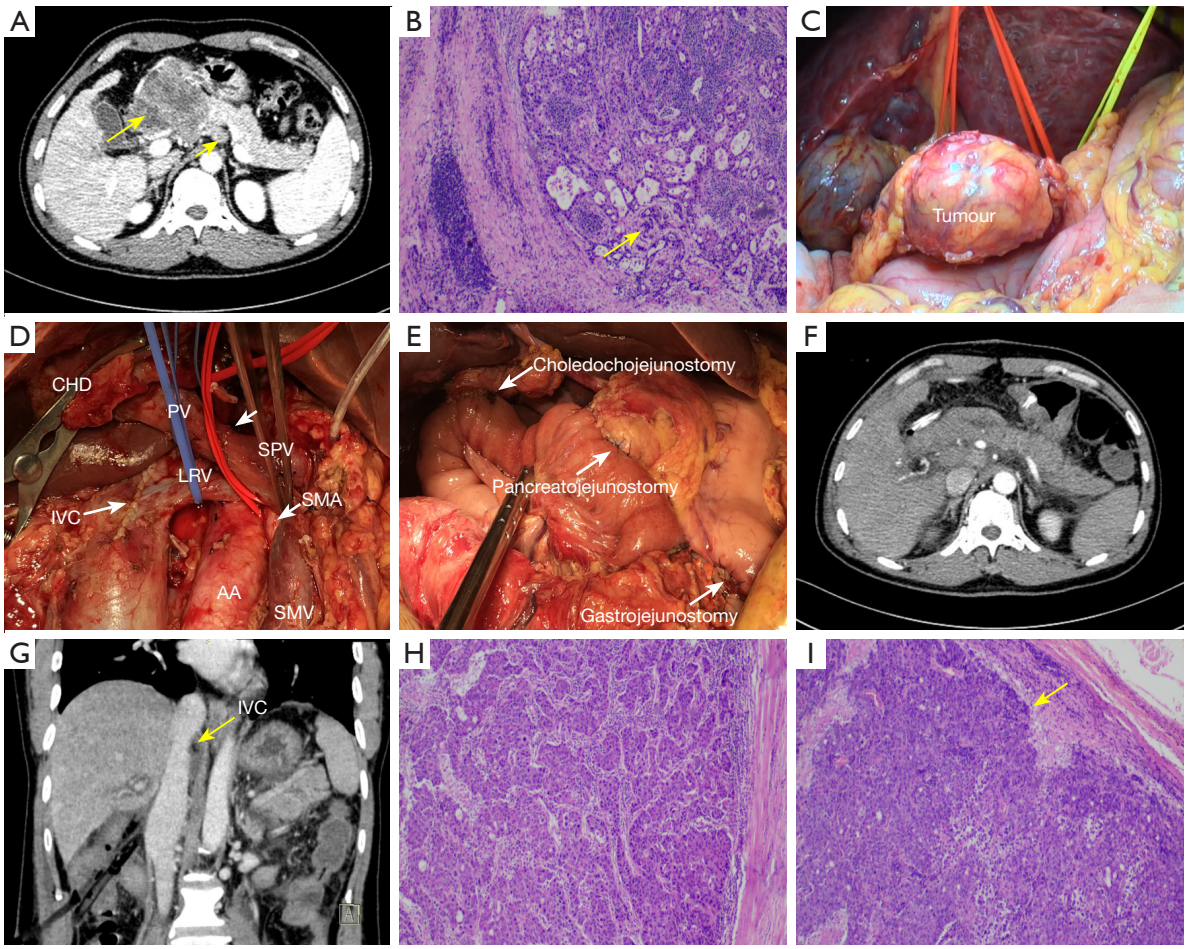

Figure 1 Imaging examination, intraoperative picture and histopathology presentation of the patient. (A) Preoperative abdominal arterial phase CT scan showed an enlarged pancreatic head with irregular soft tissue density masses. The size was approximately 7.5 cm × 7.0 cm × 3.7 cm, and the border was clear with mild heterogeneous enhancement and patchy non-enhanced hypodense areas within the tumor (long yellow arrow); the lymph node next to the pancreatic head was enlarged (approximately 2.2 cm × 1.3 cm) (short yellow arrow). (B) The pathological section image of the intraoperative frozen pathology, a large number of heterotypic cells was observed (yellow arrow) (hematoxylin-eosin staining, ×200). (C,D) Intraoperative tumor demonstration and the PV was resected and reconstructed in an end-to-end fashion (short white arrows); the IVC invaded by the tumor was resected and repaired (arrow). (E) We performed a digestive tract reconstruction (arrows). (F,G) After complete resection of the tumor, postoperative abdominal CT scan showed that the PV and IVC were not obstructed (yellow arrow). (H,I) Histopathological features of postoperative tumors. The tumor cells grow in solid sheet, nests, and trabecular patterns with few individual tumor cells, and they have abundant eosinophilic cytoplasm and prominent nucleoli (arrow). The tumor cells presented with moderate to severe atypia and mitotic activity (hematoxylin-eosin staining, ×200). CHD, common hepatic duct; PV, portal vein; SPV, splenic vein; SMA, superior mesenteric artery; LRV, left renal vein; IVC, inferior vena cava; AA, aorta abdominalis; SMV, superior mesenteric vein; CT, computed tomography.

(PV to superior mesenteric vein; SMV) (*Figure 1C,1D*). At the end, reconstruction of the digestive system was performed (*Figure 1E*). Postoperative abdominal CT scan showed that the PV and IVC were patent (*Figure 1F,1G*). On postoperative 2 months, the AFP level decreased to 1.86 ng/mL.

Pathological examination (*Figure 1H,1I*) and immunohistochemistry (*Figure 2A-2F*) (Figure S1) of specimens were conducted, and a diagnosis of HCP was confirmed. The immunohistochemical results were as follows: pancreatic head tumor arginase-1 (+), AFP (+), HepPar-1 (focally+), CK19 (+), glypican-3 (+), catenin-B

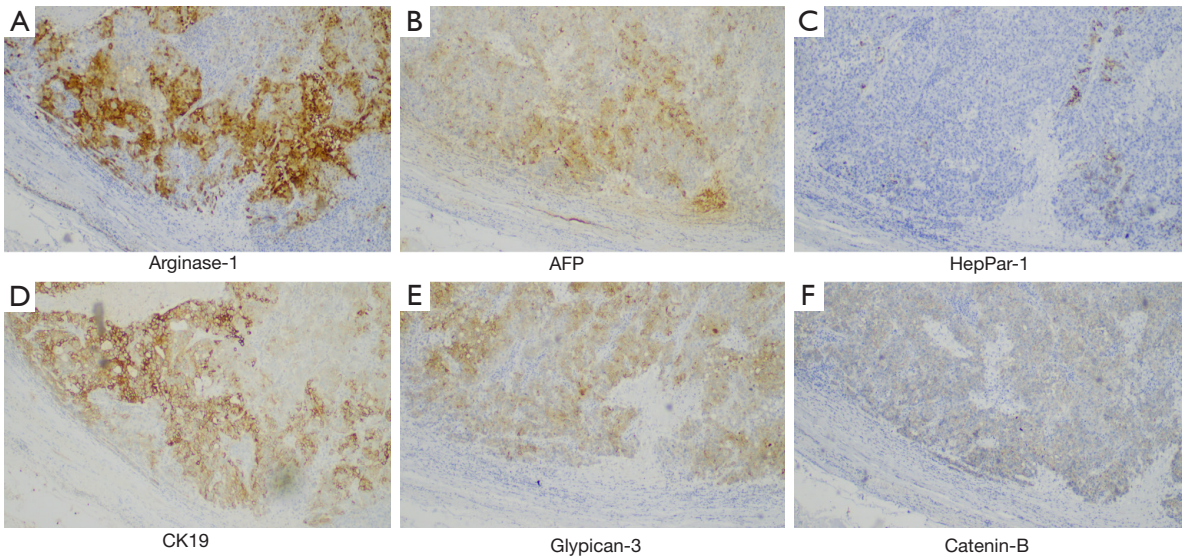

Figure 2 Histopathology and immunohistochemical characteristics of the patient. (A-F) The immunohistochemical of patient tested positive for arginase-1, AFP, HepPar-1 (focally+), CK19, glypican-3 and catenin-B (×200). AFP, alpha fetoprotein.

(+) and CD34 (+), Ki-67 (+, about 40%), P53 (+), CK20 (+), Villin (+), AAT (+), CK (+), CK818 (+), CEA (–).

The pathophysiology of HCP is not fully understood, but it is believed to be related to the aberrant expression of AFP, a fetal protein normally produced by the liver and yolk sac during embryonic development (3). In addition to AFP expression, HCP shares other histological and biological features with HCC, such as high expression of glypican-3 (GPC3), a protein that plays a role in cell growth and differentiation. The expression of GPC3 and other hepatocyte-specific markers may contribute to the aggressive behavior of HCP, such as rapid growth, invasion, and metastasis (4,5).

Surgery is the most common treatment for localized HCP, and several studies have reported a survival benefit with surgical resection. Retrospective studies reported a median overall survival of 12.5–13 months, with a 1-year survival rate 71%, and a 2-year survival rate of 40% (6,7). Due to be a rare type of pancreatic cancer, there are limited research reports and treatment guidelines specific to this disease. We have retrieved 36 English literature prior reported cases of HCP, which involve 40 cases and summarized them into a table (Tables S1,S2).

The Whipple operation, also known as a pancreaticoduodenectomy, is often performed as a treatment for pancreatic cancer, including HCP. Pancreatic cancer often invades the adjacent major vasculatures, such as PV, SMV, superior mesenteric artery, and common hepatic artery. However, direct invasion of IVC by pancreatic tumors is rare. Involvement of IVC is not contraindication of radical surgery. The long-term efficacy of pancreatic cancer combined with IVC resection and repair is unclear. To date, there is no report about the use of combined IVC and PV resection in patients with HCP.

Chemotherapy is commonly used in the treatment of advanced pancreatic cancer, including HCP. Some studies have reported improved survival with chemotherapy (5). Radiation therapy may also be used in the combination with chemotherapy to increase the effectiveness of the treatment. Immunotherapy is newer treatment option that has shown promise in the treatment of pancreatic cancer. However, there is limited data on the effectiveness of immunotherapy in HCP (8).

During the period of follow up, AFP values can provide useful information for monitoring treatment efficacy, early recurrence, and metastasis (2). In the present case, 2 months after postoperative, the AFP level decreased to the normal range. Furthermore, the patient received sorafenib treatment postoperatively. Petrelli *et al.* and Metzgeroth *et al.* also reported that sorafenib might be helpful in the treatment of HCP (9,10). The patient was followed-up for 2 years and 3 months without recurrence. The survival time of patients has been improved. To sum up, combined complex surgery and sorafenib can provide a benefit strategy for the treatment of HCP. The treatment of HCP is still changing due to its rarity and aggressive nature.

Patient with this type of cancer should be treated by a multidisciplinary team of experts in pancreatic cancer and hepatocellular carcinoma to determine the most effective treatment plan.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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