

## Isolated pancreatic metastasis of hepatocellular carcinoma after curative resection

Sang Myung Woo, Joong-Won Park, Sung-Sik Han, Joon-Il Choi, Woo Jin Lee, Sang Jae Park, Eun Kyung Hong, Chang-Min Kim

Sang Myung Woo, Joong-Won Park, Sung-Sik Han, Joon-Il Choi, Woo Jin Lee, Sang Jae Park, Eun Kyung Hong, Chang-Min Kim, Center for Liver Cancer, National Cancer Center, 809 Madu 1-dong, Ilsandong-gu, Goyang, Gyeonggi 411-769, South Korea

**Author contributions:** Park JW designed the study; Woo SM and Park JW wrote the paper; Han SS and Park SJ were the surgeons responsible for the patient; Hong EK was responsible for the patient; Choi JI, Lee WJ, and Kim CM were involved in critical revision of the article regarding important intellectual content.

Supported by National Cancer Center Korea, No. 0810260  
Correspondence to: Joong-Won Park, MD, PhD, Center for Liver Cancer, National Cancer Center, 809 Madu 1-dong, Ilsan-gu, Goyang, Gyeonggi 411-769, South Korea. [jwpark@ncc.re.kr](mailto:jwpark@ncc.re.kr)  
Telephone: +82-31-9201605 Fax: +82-31-9202798  
Received: October 20, 2009 Revised: January 26, 2010  
Accepted: February 2, 2010  
Published online: April 15, 2010

### Abstract

Hepatocellular carcinoma (HCC) is a highly malignant tumor and extrahepatic metastasis is not rare. The most common organ of HCC metastasis is lung, followed by bone and adrenal gland. To the best of our knowledge, isolated pancreatic metastasis of HCC that developed after curative resection has not been described previously. We report a case of solitary pancreatic metastasis of HCC, which was found 28 mo after left hemihepatectomy for HCC. The lesion was successfully resected with the pancreas, and no other metastatic lesions have been found in follow-up.

© 2010 Baishideng. All rights reserved.

**Key words:** Hepatocellular carcinoma; Pancreas; Metastasis

**Peer reviewer:** Kjetil Søreide, Associate Professor, MD PhD, Department of Surgery, Stavanger University Hospital, POB

8100, Armauer Hansensvei 20, N-4068 Stavanger, Norway

Woo SM, Park JW, Han SS, Choi JI, Lee WJ, Park SJ, Hong EK, Kim CM. Isolated pancreatic metastasis of hepatocellular carcinoma after curative resection. *World J Gastrointest Oncol* 2010; 2(4): 209-212 Available from: URL: <http://www.wjgnet.com/1948-5204/full/v2/i4/209.htm> DOI: <http://dx.doi.org/10.4251/wjgo.v2.i4.209>

### INTRODUCTION

Hepatocellular carcinoma (HCC) is a highly malignant, generally fatal neoplasm arising from hepatocytes. HCC accounts for over 80% of all primary liver cancers, which rank fourth among the organ-specific causes of cancer-related deaths worldwide<sup>[1]</sup>. Extrahepatic metastases are not rare at diagnosis of HCC<sup>[2]</sup> and the most frequent sites of extrahepatic metastases are lung, abdominal lymph node and bone<sup>[3,4]</sup>. A review of the literature involving the surgical pathology of 355 solitary metastases to the pancreas identified 5 isolated pancreatic metastases from HCC<sup>[5]</sup>. Of these, 2 cases showed synchronous metastases and 3 cases were found at autopsy<sup>[6]</sup>. To the best of our knowledge, solitary pancreatic metastasis of HCC, which developed after curative resection, has never been described previously.

A variety of malignant tumors have been shown to metastasize to the pancreas<sup>[7-9]</sup>. At autopsy, pancreatic metastases are common and the primary carcinoma is usually located in the lung or in the gastrointestinal tract. In contrast, isolated pancreatic metastases at the time of diagnosis are rare and only account for only 2% to 3% of solid tumors of the pancreas<sup>[10]</sup>. Most do not present before the end stage of various primary neoplasms. At least 40% of these isolated metastases are derived from renal cell carcinomas while common primary sites for the remainder include lung cancer, breast cancer, colon cancer, melanoma and sarcomas<sup>[8,10,11]</sup>.

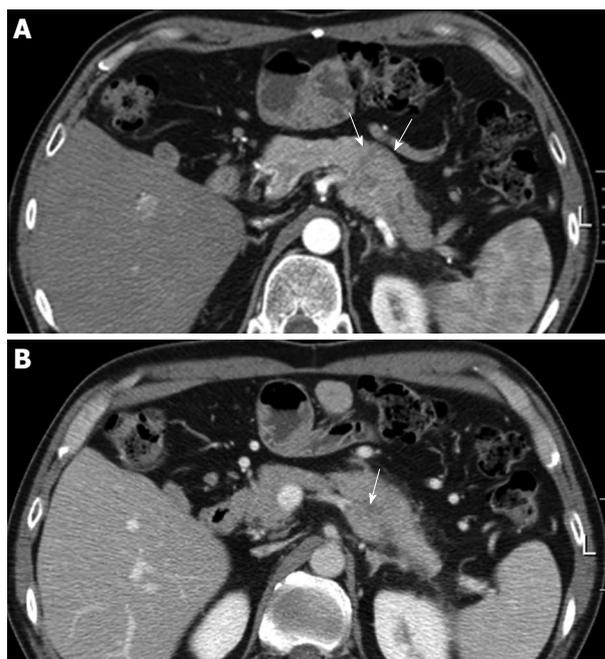
A minority of these metastases are identified by imaging at the time of diagnosis of the primary tumor, while the majority are diagnosed at follow-up, either because of routine imaging or because of the development of symptoms<sup>[8]</sup>. In renal cell carcinoma, the mean interval between nephrectomy and the diagnosis of an isolated pancreatic metastasis is approximately 9 years. Unfortunately, pancreatic metastases are difficult to differentiate from primary pancreatic neoplasms. In particular, there are similar clinical presentations and similar features on radiological imaging. In this article, we report a case of isolated metastasis of an HCC to the pancreas 28 mo after curative resection of HCC.

### CASE REPORT

A 46-year-old man with a history of surgical resection of hepatitis B associated HCC presented with a pancreatic mass that was identified with contrast enhanced dynamic computed tomography (CT) at follow-up. Two years and 4 mo previous to follow up, he was treated with an extended left hemihepatectomy for a 16.5 cm × 9 cm-sized solitary HCC compressing the intrahepatic duct. The pathology report disclosed a grade III HCC with portal vein invasion, but the resection margin was free of tumor. No obvious bile duct invasion or intrahepatic micrometastasis was noted. The patient was diagnosed as T3N0M0 stage IIIA disease by AJCC and modified UICC stage. The patient recovered well and subsequently had a 3 mo follow-up examination including liver dynamic CT and a serum  $\alpha$ -fetoprotein test. Although series examinations revealed no definite intrahepatic recurrence, liver dynamic CT showed an irregular mass in the tail of the pancreas that was associated with dilatation of the distal pancreatic duct (Figure 1A). With a contrast-enhanced scan, the mass projected into the splenic vein (arrow, Figure 1B). Liver dynamic CT and 18F-FDG-positron emission tomography (PET) showed no recurrence of the primary HCC in the remnant. On FDG-PET, there was hypermetabolic activity in the pancreatic mass. Endosonography (EUS) revealed a rounded, well-defined mass (5 cm in diameter) in the tail of the pancreas (Figure 2). EUS-guided fine needle aspirations revealed a poorly differentiated carcinoma with histological features consistent with his previous HCC (Figure 3). The lesion was successfully resected, and no other metastatic lesions have been found in follow-up. Gross specimen study showed a mass in the tail of the pancreas, invading the splenic vein (Figure 4A). Microscopic examination revealed metastatic HCC in the pancreas (Figure 4B).

### DISCUSSION

Differential diagnosis between a solitary pancreatic metastasis from a primary cancer and a double primary pancreatic cancer is difficult in almost all cases. The symptoms of metastases confined to the pancreas at the time of diagnosis are unspecific diagnostically, and imaging also rarely



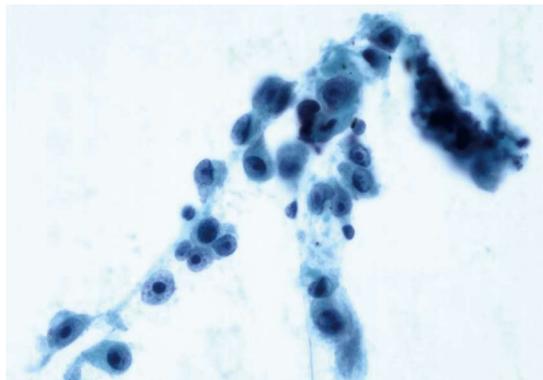
**Figure 1 Abdominal computed tomography finding.** A: Computed tomography showed an irregular mass in the tail of the pancreas that was associated with dilatation of the distal pancreatic duct (arrow); B: With a contrast-enhanced scan, the mass projected into the splenic vein (arrow).



**Figure 2 Linear endosonography (EUS) image revealing fine needle aspiration of a rounded, well-defined mass (5 cm in diameter) in tail of pancreas.**

shows abnormalities seen only in primary neoplasms. This, together with the generally rare occurrence of solitary pancreatic metastases, explains why solitary pancreatic metastases are sometimes mistaken for primary tumors, particularly if there is a long interval from the resection of the underlying primary neoplasm. For differential diagnosis, solitary pancreatic metastases should be distinguished from primary neoplasms of the pancreas. Therefore, the diagnostic workup for tumors in the pancreas requires meticulous elaboration of the medical history.

The typical features of metastases from renal cell cancer detected by imaging studies (e.g. ultrasonography, CT, magnetic resonance imaging, and endoscopic ultrasonography) have been described repeatedly<sup>[12-15]</sup>. However, because these features are not confined to metastases from renal cell carcinoma, differentiation from other neo-

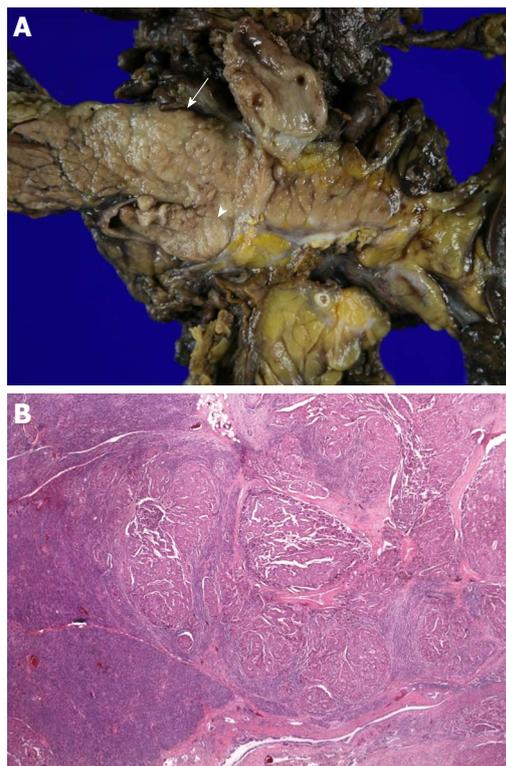


**Figure 3** Photomicrograph of cytologic specimen obtained by EUS-guided showing a poorly differentiated carcinoma with histological features consistent with a metastasis from his previous hepatocellular carcinoma (Papanicolaou stain,  $\times 200$ ).

plasms of the pancreas is problematic in individual cases. Tissue diagnosis can be established before surgery with fine-needle aspiration biopsy, ultrasonography guided<sup>[16]</sup>, CT guided<sup>[17]</sup>, or endoscopic ultrasonography guided<sup>[18,19]</sup>. These techniques allow definitive tissue diagnosis, as well as an assessment of resectability. In the case of a pancreatic mass, rare causes, such as pancreatic metastasis, should also be taken into consideration besides the most common diagnosis, adenocarcinoma pancreas with its dismal prognosis. In particular, in cases where a patient is not undergoing surgical resection, a biopsy is mandatory to determine a definite diagnosis.

Surgical treatment of solitary pancreatic metastases from neoplasms other than renal cell cancer carries a poor prognosis, because they often signal the onset of disseminated metastatic disease<sup>[7,20]</sup>. Although resectable pancreatic metastasis is uncommon<sup>[7]</sup>, metastatic pancreatic tumor from renal cell carcinoma is one of the favorable indications for radical surgery because it may offer a better prognosis for the patient<sup>[8,21,22]</sup>. Results of surgical extirpation of isolated metastases to the pancreas, not only from renal cell carcinoma but also from various primary tumors, provide improvement in long-term survival, revealing a clearly better prognosis than for primary pancreatic cancer<sup>[23,24]</sup>. This positive outcome suggests that solitary pancreatic metastases must not be regarded as accidental initial manifestations of impending diffuse metastatic disease and that a point must be made to correctly diagnose solitary pancreatic metastases and subject them to radical resection.

The result of treatment for extrahepatic recurrent HCC is poor<sup>[2,25,26]</sup>. Most metastases of HCC are multiple and are not amenable to surgical resection. Solitary metastases may be encountered occasionally. If considered resectable, the patient should be examined to exclude the presence of other metastasis, especially in the liver remnant, before embarking on surgery. Resection of isolated extrahepatic recurrences of HCC has been shown to prolong survival in selected patients<sup>[27-30]</sup>. The unusually positive outcome after treatment prompted a research group to question, rightfully, whether the positive outcome was really attributable to the successful removal of the metas-



**Figure 4** Surgical specimen. A: The tumor was 4.5 cm  $\times$  3.4 cm  $\times$  2 cm in size in the tail of the pancreas (arrow) and invaded the splenic vein (arrow head); B: Microscopic examination revealed metastatic hepatocellular carcinoma in the pancreas (HE,  $\times 40$ ).

tases or whether it reflected an extremely protracted natural history of solitary pancreatic metastases.

To our knowledge, this is the first case of solitary pancreatic metastases of HCC that developed after curative resection. Our patient developed solitary pancreatic metastasis, which was documented 28 mo after resection of HCC. In patients with a pancreatic mass and history of HCC, the possibility of metastasis to the pancreas should also be taken into consideration besides the most common diagnosis, adenocarcinoma pancreas with its dismal prognosis.

## REFERENCES

- 1 **Parkin DM**, Bray F, Ferlay J, Pisani P. Estimating the world cancer burden: Globocan 2000. *Int J Cancer* 2001; **94**: 153-156
- 2 **Park KW**, Park JW, Choi JI, Kim TH, Kim SH, Park HS, Lee WJ, Park SJ, Hong EK, Kim CM. Survival analysis of 904 patients with hepatocellular carcinoma in a hepatitis B virus-endemic area. *J Gastroenterol Hepatol* 2008; **23**: 467-473
- 3 **Katyal S**, Oliver JH 3rd, Peterson MS, Ferris JV, Carr BS, Baron RL. Extrahepatic metastases of hepatocellular carcinoma. *Radiology* 2000; **216**: 698-703
- 4 **Nakashima T**, Okuda K, Kojiro M, Jimi A, Yamaguchi R, Sakamoto K, Ikari T. Pathology of hepatocellular carcinoma in Japan. 232 Consecutive cases autopsied in ten years. *Cancer* 1983; **51**: 863-877
- 5 **Showalter SL**, Hager E, Yeo CJ. Metastatic disease to the pancreas and spleen. *Semin Oncol* 2008; **35**: 160-171
- 6 **Minni F**, Casadei R, Perenze B, Greco VM, Marrano N, Margiotta A, Marrano D. Pancreatic metastases: observations of three cases and review of the literature. *Pancreatol* 2004;

- 4: 509-520
- 7 **Roland CF**, van Heerden JA. Nonpancreatic primary tumors with metastasis to the pancreas. *Surg Gynecol Obstet* 1989; **168**: 345-347
  - 8 **Crippa S**, Angelini C, Mussi C, Bonardi C, Romano F, Sartori P, Uggeri F, Bovo G. Surgical treatment of metastatic tumors to the pancreas: a single center experience and review of the literature. *World J Surg* 2006; **30**: 1536-1542
  - 9 **Le Borgne J**, Partensky C, Glemain P, Dupas B, de Kerviller B. Pancreaticoduodenectomy for metastatic ampullary and pancreatic tumors. *Hepatogastroenterology* 2000; **47**: 540-544
  - 10 **Faure JP**, Tuech JJ, Richer JP, Pessaux P, Arnaud JP, Carretier M. Pancreatic metastasis of renal cell carcinoma: presentation, treatment and survival. *J Urol* 2001; **165**: 20-22
  - 11 **Robbins EG 2nd**, Franceschi D, Barkin JS. Solitary metastatic tumors to the pancreas: a case report and review of the literature. *Am J Gastroenterol* 1996; **91**: 2414-2417
  - 12 **Ng CS**, Loyer EM, Iyer RB, David CL, DuBrow RA, Charnsangavej C. Metastases to the pancreas from renal cell carcinoma: findings on three-phase contrast-enhanced helical CT. *AJR Am J Roentgenol* 1999; **172**: 1555-1559
  - 13 **Merkle EM**, Boaz T, Kolokythas O, Haaga JR, Lewin JS, Brambs HJ. Metastases to the pancreas. *Br J Radiol* 1998; **71**: 1208-1214
  - 14 **Palazzo L**, Borotto E, Cellier C, Roseau G, Chaussade S, Couturier D, Paolaggi JA. Endosonographic features of pancreatic metastases. *Gastrointest Endosc* 1996; **44**: 433-436
  - 15 **Biset JM**, Laurent F, de Verbizier G, Houang B, Constantes G, Drouillard J. Ultrasound and computed tomographic findings in pancreatic metastases. *Eur J Radiol* 1991; **12**: 41-44
  - 16 **Chou YH**, Chiou HJ, Hong TM, Tiu CM, Chiou SY, Su CH, Tsay SH. Solitary metastasis from renal cell carcinoma presenting as diffuse pancreatic enlargement. *J Clin Ultrasound* 2002; **30**: 499-502
  - 17 **Gupta RK**, Lallu S, Delahunt B. Fine-needle aspiration cytology of metastatic clear-cell renal carcinoma presenting as a solitary mass in the head of the pancreas. *Diagn Cytopathol* 1998; **19**: 194-197
  - 18 **Fritscher-Ravens A**, Sriram PV, Krause C, Atay Z, Jaeckle S, Thonke F, Brand B, Bohnacker S, Soehendra N. Detection of pancreatic metastases by EUS-guided fine-needle aspiration. *Gastrointest Endosc* 2001; **53**: 65-70
  - 19 **Béchade D**, Palazzo L, Fabre M, Algayres JP. EUS-guided FNA of pancreatic metastasis from renal cell carcinoma. *Gastrointest Endosc* 2003; **58**: 784-788
  - 20 **Ghavamian R**, Klein KA, Stephens DH, Welch TJ, LeRoy AJ, Richardson RL, Burch PA, Zincke H. Renal cell carcinoma metastatic to the pancreas: clinical and radiological features. *Mayo Clin Proc* 2000; **75**: 581-585
  - 21 **Sellner F**, Tykalsky N, De Santis M, Pont J, Klimpfinger M. Solitary and multiple isolated metastases of clear cell renal carcinoma to the pancreas: an indication for pancreatic surgery. *Ann Surg Oncol* 2006; **13**: 75-85
  - 22 **Stankard CE**, Karl RC. The treatment of isolated pancreatic metastases from renal cell carcinoma: a surgical review. *Am J Gastroenterol* 1992; **87**: 1658-1660
  - 23 **Sohn TA**, Yeo CJ, Cameron JL, Nakeeb A, Lillemoe KD. Renal cell carcinoma metastatic to the pancreas: results of surgical management. *J Gastrointest Surg* 2001; **5**: 346-351
  - 24 **Wente MN**, Kleeff J, Esposito I, Hartel M, Müller MW, Fröhlich BE, Büchler MW, Friess H. Renal cancer cell metastasis into the pancreas: a single-center experience and overview of the literature. *Pancreas* 2005; **30**: 218-222
  - 25 **Yang Y**, Nagano H, Ota H, Morimoto O, Nakamura M, Wada H, Noda T, Damdinsuren B, Marubashi S, Miyamoto A, Takeda Y, Dono K, Umeshita K, Nakamori S, Wakasa K, Sakon M, Monden M. Patterns and clinicopathologic features of extrahepatic recurrence of hepatocellular carcinoma after curative resection. *Surgery* 2007; **141**: 196-202
  - 26 **Tanaka K**, Shimada H, Matsuo K, Takeda K, Nagano Y, Togo S. Clinical features of hepatocellular carcinoma developing extrahepatic recurrences after curative resection. *World J Surg* 2008; **32**: 1738-1747
  - 27 **O'Suilleabhain CB**, Poon RT, Lau CW, Fan ST. Repeated resections of extrahepatic metastases after hepatic resection: an aggressive approach to hepatocellular carcinoma. *Hepatogastroenterology* 2004; **51**: 825-829
  - 28 **Tomimaru Y**, Sasaki Y, Yamada T, Eguchi H, Takami K, Ohgashi H, Higashiyama M, Ishikawa O, Kodama K, Imaoka S. The significance of surgical resection for pulmonary metastasis from hepatocellular carcinoma. *Am J Surg* 2006; **192**: 46-51
  - 29 **Lam CM**, Lo CM, Yuen WK, Liu CL, Fan ST. Prolonged survival in selected patients following surgical resection for pulmonary metastasis from hepatocellular carcinoma. *Br J Surg* 1998; **85**: 1198-1200
  - 30 **Pandey D**, Tan KC. Surgical resection of adrenal metastasis from primary liver tumors: a report of two cases. *Hepatobiliary Pancreat Dis Int* 2008; **7**: 440-442

S- Editor Li LF L- Editor Lutze M E- Editor Yang C