



HOKKAIDO UNIVERSITY

Title	Pancreatic metastasis from renal cell carcinoma with intraportal tumor thrombus.
Author(s)	Kawakami, Hiroshi; Kuwatani, Masaki; Yamato, Hiroaki et al.
Citation	Internal medicine, 47(22), 1967-1970 https://doi.org/10.2169/internalmedicine.47.1418
Issue Date	2008
Doc URL	https://hdl.handle.net/2115/47169
Type	journal article
File Information	IM47-22_1967-1970.pdf



Pancreatic metastasis from renal cell carcinoma with intraportal tumor thrombus

Hiroshi Kawakami MD, PhD^{*}, Masaki Kuwatani MD, PhD^{*}, Hiroaki Yamato MD^{*},
Keisuke Shinada MD^{*}, Satoshi Hirano MD, PhD[†], Satoshi Kondo MD, PhD[†], Atsuya
Yonemori MD[‡], Yoshihiro Matsuno MD, PhD[‡] and Masahiro Asaka MD, PhD^{*}

^{*}Department of Gastroenterology, Hokkaido University Graduate School of Medicine,
Sapporo, Japan

[†]Department of Surgical Oncology, Hokkaido University Graduate School of Medicine,
Sapporo, Japan

[‡]Department of Surgical Pathology, Hokkaido University Hospital, Sapporo, Japan

Address correspondence to: Dr. Hiroshi Kawakami,

Department of Gastroenterology, Hokkaido University Graduate School of Medicine,
North 15, West 7, Kita-ku, Sapporo 060-8638, Japan

TEL: 81-11-716-1161 (Ext 5920), FAX: 81-11-706-7867

E-mail: hiropon@med.hokudai.ac.jp (H.Kawakami)

Running head: Tumor thrombus associated with pancreatic metastasis of RCC

Abstract

A 68-year-old woman with a history of renal cell carcinoma (RCC) resected curatively 12 years previously was admitted to our department for scrutiny of pancreatic tumors. Various imaging studies demonstrated heterogeneously well-enhanced masses in the head and tail of the pancreas. The well-enhanced mass in the head of the pancreas was connected with the tumor thrombus in the portal vein. To differentially diagnose the multiple pancreatic lesions, we performed endoscopic ultrasound-guided fine-needle aspiration biopsy (EUS-FNAB). Histopathologic findings of the EUS-FNAB specimens were similar to those of the renal clear cell carcinoma previously resected. The patient underwent a surgical operation with segmental resection of the portal vein with the preoperative diagnosis of RCC metastasis to the pancreas with intraportal growth. Histopathological examination of the resected specimen revealed that the masses in the pancreas were multiple pancreatic metastases with intraportal tumor thrombus of RCC. The pancreas is a rare target for metastasis. This is a rare case of pancreatic metastasis from RCC with intraportal extension, and is the first preoperatively definitely diagnosed case using EUS-FNAB.

Key words: Renal cell carcinoma, Pancreatic metastasis, Portal venous tumor thrombus, Intraportal growth, Endoscopic ultrasound-guided fine-needle aspiration biopsy

Introduction

Tumor metastases to the pancreas are rare, accounting for less than 5% of all pancreatic malignancies (1). The majority of the metastases originate from primary tumors of the kidney, lung, breast and colon (2). Among them, renal cell carcinoma (RCC) shows a particularly high tendency to metastasize to the pancreas, a rare site of metastasis, in addition to metastasizing to the lymph nodes, lung, liver, thyroid glands and bones (1,3). Herein, we present a rare metastasis of RCC, resected 12 years previously, to the pancreas with intraportal tumor thrombus, which we definitely diagnosed preoperatively by endoscopic ultrasound-guided fine-needle aspiration biopsy (EUS-FNAB).

Case report

A 68-year-old woman was admitted to our department for further examination in August 2007. One month earlier, she had been diagnosed as having asymptomatic multiple pancreatic mass. She had no family history of pancreatic disease. However, her medical history contained left radical nephrectomy for renal clear cell carcinoma 12 years before. Physical examination at admission revealed an operation scar from the radical nephrectomy on the left upper abdomen. The abdomen was soft and no mass was palpable. The fasting blood glucose level was 200 mg/dL (<110 mg/dL), and hemoglobin A_{1C} was 7.4% (<5.8%). Ultrasonography (US) demonstrated a heterogeneously hypoechoic mass of 54 × 33-mm in the head of pancreas, forming a tumor thrombus in the portal vein. The mass in the pancreatic head and the thrombus in the PV, arising from the mass and measuring about 20 mm, were clearly shown in US imagings. Doppler examination demonstrated flow within the tumor thrombus as well as normal portal venous flow around it, confirming that the mass was a vascularized tumor rather than a pure thrombus. However, imaging of the tail of the pancreas by US was impossible. Early phase-enhanced computed tomography (CT) showed a heterogeneously well-enhanced mass in the head of the pancreas (Fig. 1A) which was connected with the tumor thrombus in the portal vein (Fig. 1B), but there was no finding of a collateral vein. CT revealed continuity of the mass in the head of the pancreas and the thrombus in the portal vein. Early phase-enhanced CT revealed solid contrast-enhanced masses also in the tail of pancreas (Fig. 1C). No other lesion was detected in the liver or other organs. Endoscopic ultrasonography revealed a heterogenous hypoechoic mass in the head of the pancreas, tumor thrombus in the portal

vein (Fig. 1D,E), and homogenous hypoechoic masses in the tail of the pancreas (Fig. 1F). To differentially diagnose the multiple lesions, whether they were metastasis from the renal clear cell carcinoma or a neuroendocrine tumor, we performed EUS-FNAB. Transduodenal EUS-guided FNA of the head of the pancreatic mass using a 22-gauge needle was performed. Two passes were made into the mass. No complications were encountered. The histopathologic pattern of the EUS-FNAB specimens (Fig. 2A) was similar to that of the previous specimens of RCC diagnosed 12 years previously (Fig. 2B). Total pancreatectomy with segmental resection of the portal vein was performed with the preoperative diagnosis of RCC metastasis to the pancreas with intraportal growth.

Grossly, the resected specimen presented a whitish nodular mass at the pancreatic head, measuring 50 × 30 mm at the greatest dimension, and one at the pancreatic tail, measuring 12 × 10 mm likewise, and whitish nodular mass in the portal vein (Fig. 2C). Cut surface of the tumors showed ill-defined whitish tumors with cystic change at the pancreatic head, and ill-defined whitish tumors at the pancreatic tail. In addition, tiny, ill-defined whitish tumors, measuring 1-2 mm at the greatest dimension, were detected in the pancreatic body to tail. Histologically, we made a definitive diagnosis of multiple pancreatic metastasis from RCC with intraportal tumor thrombus. The tumor thrombus protruded into the lumen of the portal vein (Fig. 2D). The postoperative course was uneventful with the use of insulin. The patient is well without tumor recurrence 12 months after surgery.

Discussion

We report a unique case of RCC metastasizing to the pancreas with intraportal growth. Tumor metastasis to the pancreas is very rare, accounting for 3 to 10.6% of all pancreatic malignancies (1). According to the autopsy series, metastasizing to the pancreas are mostly tumors of the breast, thyroid and lung (2). In patients with RCC, metastases to the pancreas are noted in 1.3% (4). Most of them are metachronous after nephrectomy, and 12% synchronous with the primary RCC. Overall 61% of the metastases are solitary, and 39% multiple. Between the solitary and multiple metastases, no differences are found in age, onset time, or interval between nephrectomy and onset of metastasis. No inclination for a specific part of the pancreas is recognized. The localization of the RCC does not have any effect on metastasis sites (5).

Recurrence with distant metastasis after a long lapse of time is not rare in patients with RCC, occurring in more than 10% of the patients over 10 years after nephrectomy (6). The mean interval from nephrectomy to manifestation of pancreatic metastasis is 7.1-10.0 years, and the longest interval is 32.7 years (5,7). As far as the pancreatic metastasis is concerned, RCC has a better prognosis than other primary tumors. This long disease-free interval indicates a biological pattern of slow tumor growing, favoring local surgical resection.

In the present case, the metastasis from RCC to the pancreas formed multiple lesions, and the interval between tumor nephrectomy and occurrence of pancreatic metastasis was 12 years. From this, we emphasize that patients with a history of RCC should undergo a long-term follow-up to detect pancreatic metastasis as well as metastases to other organs.

Both hepatocellular carcinoma (HCC) and RCC frequently present expansive growth; they are solid tumors, and rarely contain fibrosis. Furthermore, both are hypervascular and can form tumor thrombus in drainage vein. The frequency of intraportal thrombus in HCC is reported to be approximately 13% (8), whereas involvement of the renal venous system in RCC is seen in 4-10% (9); namely the frequencies of tumor thrombus in drainage vein seem nearly equal between HCC and RCC.

At autopsy, intraportal tumor thrombus is seen in 5% of patients with liver metastasis and it may not be a rare manifestation in advanced metastatic disease (10). However, it is particularly rare that intraportal tumor thrombus is formed by pancreatic metastasis of RCC, as in the present case. There are pancreatic hypervascular tumors, among endocrine tumors, which develop intraportal tumor thrombus (11). Therefore, it is difficult in patients with a history of RCC to differentially diagnose pancreatic hypervascular tumor with intraportal tumor thrombus from diagnostic imaging only; for the preoperative differential diagnosis, biopsy diagnosis, such as EUS-FNAB, is useful.

Recently, EUS-FNAB is noted for its accuracy and safety in cytology and biopsy of the pancreas. EUS-FNAB from the pancreatic masses is safer than percutaneous FNA from the viewpoint of accessibility and visibility (12,13). EUS-FNAB of pancreatic solid masses carries an overall complication rate of 0.5-3.3% (14-17). Neither the size of lesion nor the number of needle passes was predictive of complications (15). The complication rate after EUS-FNAB from pancreatic masses including hypervascular tumors, such as metastatic lesions from RCC and HCC appears to be acceptably low (18). In the present case, we utilized EUS-FNAB for the preoperative definite diagnosis and assessed the lesion extent. We recognize that two cases of pancreatic metastasis of

RCC with intraportal tumor thrombus have previously been reported (3,19). To our knowledge, this is the first preoperatively diagnosed case of pancreatic metastasis from RCC with intraportal extension.

Regarding the diagnostic imaging of PVTT, contrast-enhanced CT showed generally PVTT as a filling defect in the portal vein. In our case, PVTT showed a heterogeneously enhanced mass on an arterial phase of the contrast-enhanced CT. When increased attenuation is noted in the thrombus on postcontrast study, it is likely to be neoplastic; in some reported cases with a hypervascular metastatic tumor, PVTT also had a hypervascular nature and showed early enhancement during the arterial phase of dynamic CT (3,20,21). The detailed mechanism of PVTT development has not yet been elucidated. It is thought, however, that tumor thrombus formed in the portal systems by direct venous tumor invasion and via the pancreatoduodenal vein.

The treatment choice for pancreatic metastases is surgery if complete tumor excision is possible. Namely, surgical therapy results in better palliation and improved survival in patients whose metastasized pancreatic lesions are amenable to resection. It is reported that, of the total 132 patients with pancreatic metastases from RCC, 88 patients are alive with a mean follow-up of 27.1 months (range 2–127) and 44 are dead with a mean survival time of 21.3 months (range 2–120) (1). In the present case, we performed curative operation with the preoperative definite diagnosis, and expect the patient's long-term survival.

References

1. Minni F, Casadei R, Perenze B, et al. Pancreatic metastases: observations of three cases and review of the literature. *Pancreatology* **4**:509-520, 2004.
2. Mizushima T, Tanioka H, Emori Y, et al. Metastatic pancreatic malignant melanoma: tumor thrombus formed in portal venous system 15 years after initial surgery. *Pancreas* **27**:201-203, 2003.
3. Shrikhande SV, Büchler P, Esposito I, Loos M, Büchler MW, Friess H. Splenic and portal vein thrombosis in pancreatic metastasis from renal cell carcinoma. *World J Surg Oncol* **17**:25, 2006.
4. Bennington JL. Proceedings: Cancer of the kidney--etiology, epidemiology, and pathology. *Cancer* **32**:1017-1029, 1973.
5. 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* **13**:75-85, 2006.
6. Sahin M, Foulis AA, Poon FW, Imrie CW. Late focal pancreatic metastasis of renal cell carcinoma. *Dig Surg* **15**:72-74, 1998.
7. Wente MN, Kleeff J, Esposito I, et al. Renal cancer cell metastasis into the pancreas: a single-center experience and overview of the literature. *Pancreas* **30**:218-222, 2005.
8. Ikai I, Arii S, Okazaki M, et al. Report of the 17th follow-up survey of primary liver cancer in Japan. *Hepatol Res* **37**:676-91, 2007.
9. Skinner DG, Pritchett TR, Lieskovsky G, Boyd SD, Stiles QR. Vena caval involvement by renal cell carcinoma. Surgical resection provides meaningful

- long-term survival. *Ann Surg* **210**:387-392, 1989.
10. Sakamoto N, Monzawa S, Miyake M, et al. Portal venous tumor thrombus associated with hepatic metastasis of renal cell carcinoma: case report. *Abdom Imaging* **31**:245-8,2006.
 11. Kawakami H, Kuwatani M, Hirano S, et al. Pancreatic endocrine tumors with intraductal growth into the main pancreatic duct and tumor thrombus within the portal vein: a case report and review of the literature. *Intern Med* **46**:273-277, 2007.
 12. Di Stasi M, Lencioni R, Solmi L, et al. Ultrasound-guided fine needle biopsy of pancreatic masses: Results of a multicenter study. *Am J Gastroenterol* **93**:1329–1333, 1988.
 13. Mallery JS, Centeno BA, Hahn PF, Chang Y, Warshaw AL, Brugge WR. Pancreatic tissue sampling guided by EUS, CT/US, and surgery: A comparison of sensitivity and specificity. *Gastrointest Endosc* **56**:218–224, 2002.
 14. Gress FG, Hawes RH, Savides TJ, Ikenberry SO, Lehman GA. Endoscopic ultrasound-guided fine-needle aspiration biopsy using linear array and radial scanning endosonography. *Gastrointest Endosc* **45**:243-250, 1997.
 15. O'Toole D, Palazzo L, Arotçarena R, et al. Assessment of complications of EUS-guided fine-needle aspiration. *Gastrointest Endosc* **53**:470-474, 2001.
 16. Harewood GC, Wiersema MJ. Endosonography-guided fine needle aspiration biopsy in the evaluation of pancreatic masses. *Am J Gastroenterol* **97**:1386-1391, 2002.
 17. Al-Haddad M, Wallace MB, Woodward TA, et al. The safety of fine-needle aspiration guided by endoscopic ultrasound: a prospective study. *Endoscopy*

- 40**:204-208, 2008.
18. DeWitt J, Jowell P, Leblanc J, et al. EUS-guided FNA of pancreatic metastases: a multicenter experience. *Gastrointest Endosc* **61**:689-696, 2005.
 19. Pestana IA, David-West G, Livingstone A. Metastatic renal cell carcinoma to the pancreas with splenic portal vein tumor thrombus. *Am Surg* **74**:359-360, 2008.
 20. Tublin ME, Dodd GD 3rd, Baron RL. Benign and malignant portal vein thrombosis: differentiation by CT characteristics. *Am J Roentgenol* **168**:719-723, 1997.
 21. Lee HK, Park SJ, Yi BH, Yeon EK, Kim JH, Hong HS. Portal vein thrombosis: CT features. *Abdom Imaging* **33**:72-79, 2008.

Figure legends

Figure 1

(A) Early-phase-enhanced computed tomography (CT) image showing a heterogeneously well-enhanced mass of 55×35 -mm in the head of pancreas (arrows).

(B) Early-phase-enhanced CT image showing a homogeneously well-enhanced mass of 20×20 -mm in the portal vein (arrows).

(C) Early-phase-enhanced CT image showing a homogeneously well-enhanced mass of 15×14 -mm and 8×6 -mm in the tail of pancreas (arrows).

(D) Endoscopic ultrasonography (EUS) image showing a heterogenous hypoechoic mass in the head of the pancreas.

(E) EUS image showing a heterogenous hypoechoic mass in the portal vein.

(F) EUS image showing homogenous hypoechoic masses in the tail of the pancreas.

Figure 2

(A) Photomicrograph of the resected kidney tumor showing renal clear cell carcinoma. (H&E, original magnification, $\times 200$.)

(B) Photomicrograph of the EUS-FNAB specimen from the head of the pancreas, showing metastatic renal clear cell carcinoma. (H&E, original magnification, $\times 200$.)

(C) A gross appearance of the resected specimen showing white nodular mass in the portal vein (arrows).

(D) Photomicrograph of the resected specimen showing that tumor thrombus projects into the lumen of the portal vein. (Elastica-Masson, original magnification, $\times 20$.)



