Journal of Gastrointestinal Cancer (2019) 50:1055–1058
https://doi.org/10.1007/s12029-019-00209-w

CASE REPORT

Unexpected Prolonged Survival After Extended and Emergent Resection of Pancreatic Metastases from Renal Cell Carcinoma

Stefania Brozzetti[1] · Antonio V. Sterpetti[1]

Published online: 15 February 2019

The pancreas is a rare site for metastases, and renal cell carcinoma is the most common origin for solitary pancreatic metastases [1, 2]. The significant reduction of the operative risk for pancreatic resection in dedicated centres has represented the basis for an aggressive surgical approach to patients with solitary pancreatic metastases from renal cell carcinoma. Pancreatic resection in this clinical setting has given satisfactory results [3–5].

Controversies exist about the indication to pancreatic resection in patients with synchronous pancreatic and extrapancreatic metastases from renal cell carcinoma in the era of tyrosine kinase inhibitors [6–8], and the best therapeutic approach to patients with symptomatic pancreatic metastases from renal cell carcinoma invading the major veins or causing bleeding.

Here, we report 1 patient who had surgery for pancreatic metastases from renal cell carcinoma with thrombus extending up to the portal vein and liver involvement, and 1 patient who had emergent pancreatectomy for major intestinal bleeding. The first patient died 8 years after surgery, enjoying a good quality of life. The second patient is alive and in good general condition 11 years after surgery. A systematic literature search was performed.

Patient 1 In October 2005, a 70-year-old man was admitted to our hospital for evaluation of a lesion in the body of the pancreas discovered at ultrasound. Eleven years before, he underwent left radical nephrectomy, followed by radio- and chemotherapy, for a renal carcinoma staged pT3b N1 M0, Fuhrman IV. The patient was in good general condition without major symptoms. He complained only of sporadic midgastric, postprandial pain. Laboratory tests were within normal range. Tumour markers were normal.

CT scan showed a lesion, well vascularised, in the body of the pancreas, 4 × 3 cm in size. The mass infiltrated the splenic vein, with a thrombus extending from the splenic vein into the portal vein (Fig. 1). There was a lesion in the segment IVb of the liver, with a maximum diameter of 2.5 cm. Fine needle biopsy of the lesion showed a solid tumour, composed of clear oval cells, with severe nuclear atypia. A diagnosis of neuroendocrine pancreatic tumour with liver metastasis was suspected.

An extended left-sided subtotal pancreatectomy was performed, with splenectomy and thrombectomy of the splenic and portal veins. The liver nodule was removed with a wedge resection.

The postoperative course was uneventful and the patient was discharged on the 12th postoperative day.

Histological examination showed that all lesions, including the thrombus, were metastases from a renal cell carcinoma. The pancreatic lesion was composed of cells arranged in trabecular and alveolar structures, with clear or eosinophilic granular cytoplasm. The tumour cells were immunoreactive for vimentin, anti-CK18 and anti-CK19, and negative for CK18.

Two years after surgery, the patient, in good general condition, had a control CT scan which showed two lesions in the liver, which were ablated by radiofrequency. Five years from surgery, a new CT scan showed multiple liver lesions, and chemo- and immunotherapy was started. The patient had a good general condition at this time. He died 8 years from surgery with diffuse liver metastases.

Patient 2 In April 2005, a 75-year-old woman was admitted to our hospital for diffuse abdominal pain and asthenia. Thirteen years earlier, she underwent right radical nephrectomy for clear cell renal cell carcinoma (pT3a N0 M0; G1) with radiotherapy. She referred a significant weight loss and she noted jaundice in the

✉ Stefania Brozzetti
stefania.brozzetti@uniroma1.it

[1] Policlinico Umberto I, University "La Sapienza", Rome, Italy

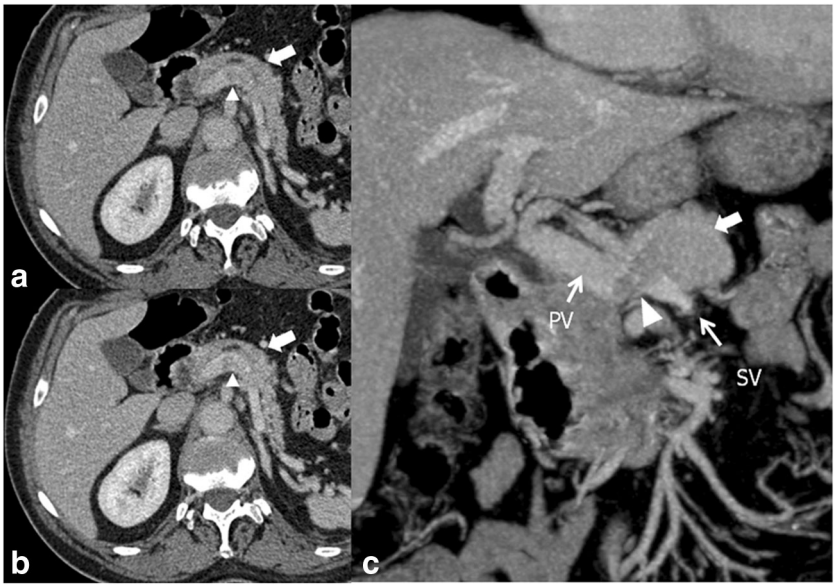

Fig. 1 Patient 1: preoperative CT scan, showing a pancreatic mass, a liver metastasis, and thrombus in the splenic vein extending into the portal vein (PV portal vein; SV splenic vein)

last 6 months. At physical examination, an abdominal mass was palpable. Blood tests confirmed increased serum bilirubin level and significant anaemia. Serum tumour markers were within normal range. CT scan showed obstruction of the intrapancreatic bile duct, dilatation of the biliary tract and of the gallbladder, and two pancreatic lesions. The two lesions of the pancreas, one in the head and one in the tail, were respectively 53 mm and 30 mm in diameter. The mass surrounding the duodenal wall, Vather ampulla, at endoscopic retrograde cholangiopancreatography (ERCP) was protruding in the duodenal lumen causing ulceration with bleeding.

The patient underwent total pancreatectomy, splenectomy, and gastroduodenal resection (Fig. 2). The patient was discharged 4 weeks after surgery in good general condition. The patient is in good general condition, free from disease recurrence 11 years after this operation.

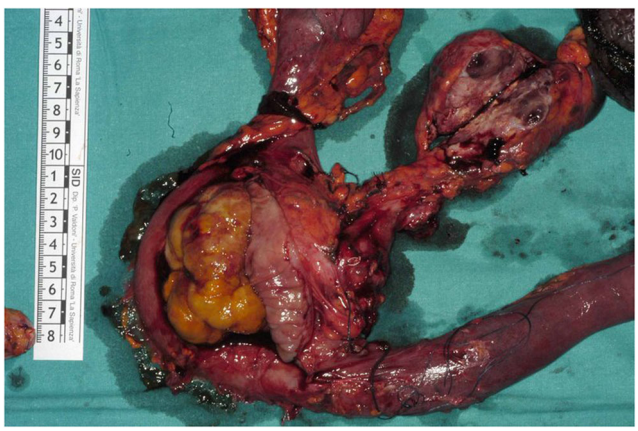

Fig. 2 Patient 2: specimen after total pancreatectomy for uncontrollable bleeding in a patient with poor general condition

Literature Search

Out of the 1080 patients who had surgery for pancreatic metastases from renal cell carcinoma, we identified 7 patients who had extended resection for pancreatic metastases from renal cell carcinoma with major vein involvement (Table 1).

Overall, 5 patients had significant survival and good quality of life (1 alive and well at 6 years, 2 alive and well at 1 year, 1 died from diffuse disease at 8 years, 1 died 48 months from surgery). One patient died 6 months from surgery. In 1 patient, information about follow-up were not available.

We found reports of 4 patients with exploratory laparotomy in whom resection was not considered advisable for involvement of the mesenteric vein. Three patients died within 8 months from the exploratory laparotomy, but 1 patient is alive and in good general condition 10 years from exploratory laparotomy [10].

The prevalence of patients with gastrointestinal haemorrhage ranged from 0 to 24%, with an overall mean of 13%, in the 1080 analysed patients. Overall, we were able to find 10 patients who had emergent or semi-emergent pancreatectomy for uncontrollable gastrointestinal bleeding. One patient died in the postoperative period from uncontrollable bleeding (Table 2). Out of the 9 survivors, 8 do not have residual disease at an average follow-up of 24 months.

Discussion

Pancreas involvement by cancer is associated to diffuse intraabdominal cancer spreading [1]. Solitary metastases to the pancreas from renal cell carcinoma are rare. Reported observed 5-year survivals for patients who had pancreatic resection for metastases from renal cell

Table 1 Reported patients who had resection of pancreatic metastases from renal cell carcinoma with major vein involvement

Author	*N* pts	Age	Months from nephrectomy	Symptoms	Associated surgery	Follow-up
-Removal neoplastic thrombus from splenic and portal veins and pancreatectomy						
Shrikhande et al. (2006) [6]	1	62	12	Pain-weight loss	Resection PV	Died 5 months (diffuse disease)
Pestana et al. (2008) [7]	1	63	36	None	Resection PV	Alive 60 months (no disease)
Kawakami et al. (2008) [8]	1	68	144	None	Resection PV	Alive 12 months (no disease)
Tanis et al. (2009) [1]	1	?	?	?	Resection PV	Died 48 months (?)
Facy et al. (2013) [9]	1	?	48	?	Resection PV	?
Brozzetti et al.	1	70	132	Periodic pain	Liver resection	Died 72 months (diffuse disease)
-Resection involved the vena cava						
Tuech et al. (2008) [10]	1	70	156	None	Resection vena cava	Alive 12 months (no disease)

PV portal vein

carcinoma are around 60% [1–6]. Patients candidate for pancreatectomy are selected on the basis of good general condition, making any possible comparison with medical therapy error prone. In general, patients with solitary pancreatic metastases have a long time interval from nephrectomy from the primary tumour, representing per se a very selected group with good prognosis, for the indolent nature of the primary tumour. The mean time interval between nephrectomy from primary renal cancer and pancreatic metastases was 8 years in a review of more than 1000 patients. The Memorial Sloan Kettering Cancer Center scoring system represents a valid prognostic indicator, and the majority of the patients who had pancreatic resection had a good MSKCC score (good 78%; medium 22%). Even if time between nephrectomy and pancreatic metastasis resection was not found to be a valid prognostic factor in several reports [1–5], we should underline that almost all patients had pancreatectomy 2 years from nephrectomy. Negative risk factors for survival in patients who had resection of pancreatic metastases from renal cell carcinoma were nerve and vessel invasion by the pancreatic metastases at histology and lymph node involvement [6, 7, 10]. A comparison between surgical and medical therapies is not possible for several reasons, including the inevitable biases in selection, with patients in better conditions considered candidates for surgery. The common conclusion in this clinical scenario is that surgical therapy in selected patients can be followed by unexpected long-term survival [1–5]. Invasion to the major veins by the pancreatic metastases from renal cell carcinoma is considered a contraindication to resection [17], with the assumption that the patient has probably a very short life expectancy, and that the risk of a major operation is not acceptable.

It is logical to accept a conservative attitude in patients with no symptoms and pancreatic metastases from renal cell carcinoma with major vessel involvement, but the presence of symptoms, including recurrent haemorrhage or pain, determines a difficult situation, in which a definition of the balance between risks and benefit is error prone for the absence of clear data about the natural history of the disease.

Table 2 Emergent pancreatectomy for uncontrollable bleeding from metastases from renal cell carcinoma

Author	*N* pts	Age	Months from nephrectomy	Surgery	Follow-up
Kassabian et al. (2000) [11]	1	56	48	Total pancreatectomy	Alive no disease 7 months
Hiotis et al. (2002) [12]	1	(?)	(?)	Total pancreatectomy	Alive no disease 15 months
Hiotis et al. (2002) [12]	1	(?)	(?)	Whipple	Alive with disease 16 months
Kobayashi et al. (2004) [13]	1	53	108	Total pancreatectomy	Alive no disease 20 months
Demirjian et al. (2009) [14]	1	48	60	Total pancreatectomy	Alive no disease 4 months
	1	68	108	Total pancreatectomy	Alive no disease 4 months
	1	69	180	Whipple	Alive no disease 4 months
Fragulidis et al. (2015) [15]	1	66	324	Total pancreatectomy	Alive and well 9 months
Law et al. (2013) [16]	1	67	114	Whipple	Postoperative death
Brozzetti et al.	1	75	156	Total pancreatectomy	Alive and well 132 months

Resection of pancreatic metastases with major vein involvement can be followed by long-term survival and good quality of life.

Emergent pancreatectomy for uncontrollable gastrointestinal bleeding is justified when angiographic embolization has failed.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Tanis PJ, van der Gaag NA, Busch ORC, van Gulik TM, Gouma DJ. Systematic review of pancreatic surgery for metastatic renal cell carcinoma. Br J Surg. 2009;96:579–92.
2. Konstandinitis IT, Dursun A, Zheng H, et al. Metastatic tumours in the pancreas in the modern era. J Am Coll Surg. 2010;211:749–53.
3. Tosoian JJ, Cameron JL, Allaf ME, et al. Resection of isolated renal cell carcinoma metastases to the pancreas. Outcomes from the John Hopkins Hospital. J Gastrointest Surg. 2014;18:542–8.
4. Untch BR, Allen BR. Pancreatic metastasectomy: the memorial Sloan-Kettering experience and review of the literature. J Surg Oncol. 2014;109:28–30.
5. Brozzetti S Systematic review of surgery for pancreatic metastases from renal cell carcinoma professorship thesis University of Rome Sapienza 2017.
6. Shrikhande SV, Buchler P, Esposito I, Loos M, Buchler MV, Friess H. Splenic and portal vein thrombosis in pancreatic metastases from renal cell carcinoma. World J Surg Oncol. 2006;4:25. https://doi.org/10.1186/1477-7819-4-25.
7. Pestana IA, David-West G, Livingstone A. Metastatic renal cell carcinoma to the pancreas with splenic portal vein tumor thrombus. Am Surgeon. 2008;74:359–60.
8. Kawakami H, Kuwatani M, Yamato H, et al. Pancreatic metastasis from renal cell carcinoma with intraportal tumor thrombus. Inter Med. 2008;47:1967–70.
9. Facy O, Angot C, Guiu B, et al. Interest in intraoperative ultrasonography during pancreatectomy for metastatic renal cell carcinoma. Clin Res Hepatol Gastroenterol. 2013;37:530–4.
10. Tuech JJ, Lefebure B, Bridoux V, Albouy B, Lermite E, Le Pessot F, et al. Combined resection of the pancreas and inferior vena cava for pancreatic metastasis from renal cell carcinoma. J Gastrointest Surg. 2008;12:612–5.
11. Kassabian A, Stein J, Jabbour N, Parsa K, Skinner D, Parekh D, et al. Renal cell carcinoma metastatic to the pancreas: a single-institution series and review of the literature. Urology. 2000;56:211–5.
12. Hiotis SP, Klimstra DS, Conlon KC, Brennan MF. Results after pancreatic resection for metastatic lesions. Ann Surg Oncol. 2002;9:675–9.
13. Kobayashi A, Yamaguchi T, Ishihara T, Tadenuma H, Nakamura K, Ohshima T, et al. Spontaneous rupture of pancreatic metastasis from renal cell carcinoma. Jpn J Clin Oncol. 2004;34:696–9.
14. Demirjian AN, Vollmer CM, McDermott DF, Mullen JT, Atkins MB, Callery MP. Refining indications for contemporary surgical treatment of renal cell carcinoma metastatic to the pancreas. HPB. 2009;11:150–3.
15. Fragulidis GP, Vezakis A, Chondrogiannis K, Mellou A, Melemeni A, Plydorou A. Clinical presentation and management of gastrointestinal and pancreatic secondary metastatic tumors. JBUON. 2015;20:1009–14.
16. Law CH, Wei AC, Hanna SS, Al-Zahrani M, Taylor BR, Greig PD, et al. Pancreatic resection for metastatic renal cell carcinoma: presentation, treatment, and outcome. Ann Surg Oncol. 2003;10(8):922–6.
17. Bassi C, Butturini G, Falcomi M, et al. High recurrence rate after atypical resection for pancreatic metastases from renal cell carcinoma. Br J Surg. 2003;90:555–9.