ANNALI ITALIANI DI CHIRURGIA
Edizione Digitale
ISSN 2239-253X
Direttore Nicola Picardi

Relapsed metachronous pancreatic metastasis from renal cell carcinoma (RCC)

Report of a case and review of literature

Ann. Ital. Chir.
Published online (EP) 7 October 2014
pii: S2239253X1402283X
www.annitalchir.com

Antonio Macrì*, Francesco Fleres*, Antonella Putortì*, Maria Lentini**, Giorgio Ascenti***, Claudio Mastrojeni****

University of Messina, Messina, Italy
**General Surgery Unit, Department of Human Pathology*
***Pathological Anatomy, Department of Human Pathology*
****Diagnostic Radiology, Department of Biomedical Sciences and Morphological and Functional Images*
*****Vascular Surgery Unit, Department of Cardio-Thoracic and Vascular Surgery*

Relapsed metachronous pancreatic metastasis from renal cell carcinoma (RCC). Report of case and review of literature

AIM: *The pancreas is a preferred site of metastasis from renal cell carcinoma (RCC), that may occur even after many years from a radical nephrectomy. Surgical R0 resection remains the only potentially curative treatment for solitary tumor. The possibility of a multifocality of the lesions (20-45%) must be considered.*
MATERIAL OF STUDY: *We report a case of metachronous pancreatic metastasis from RCC that occurred twice. After five years from a right polar inferior nephrectomy for a RCC, two nodular lesions were identified in the body-tail of the pancreas and were treated with distal pancreatectomy and splenectomy. After six months the CT imaging revealed a nodular lesion of few millimeters in the residual pancreatic body; we followed the slow growth and in October 2012, when the size reached 2 cm, the patient was operated to remove the residual portion of pancreatic body. After 16 months of follow-up the patient is well and there isn't relapse of disease.*
DISCUSSION: *Patients with metachronous pancreatic lesions represent a particular group with a more indolent course of RCC, the appearance of metastases after a prolonged interval from nephrectomy is related to a more favorable prognosis. Radical lymph-node dissection is not necessary for the uncommon involvement of peripancreatic nodes, condition that explains the positive outcomes achieved with surgery.*
CONCLUSION: *Patients with resected metastasis present an 88% survival rate at 5 years versus 47% observed in non-operated patients; studies provide encouraging results in survival and quality of life of surgically treated patients.*

KEY WORDS: Metachronous metastasis, Pancreatic metastases, Renal cell carcinoma

Introduction

The vast majority of pancreatic tumors are primary; pancreatic metastases from any type of primary cancer are rare and only sporadic data exist on therapeutic options.

The optimal management of pancreatic metastases has not been clearly defined. The incidence of pancreatic metastases in patients with RCC has been reported to be 3% of the cases [1]; in particular the rate of solitary pancreatic metastases ranges from 1 to 3% [2] and rises to 20%-45% in case of multifocal metastases [3,4]. Among patients with renal cell carcinoma (RCC) 20-30% have metastasis at presentation and up to 40-50% will develop wide-spread metastatic disease after nephrectomy [5] with a 5-years survival rate of less than 10% -15% [6]. The pancreas is a preferred site of metastasis from RCC; this peculiarity has been reported by numerous studies [7]. Metastases from RCC frequently affect the pancreas as the only sec-

Pervenuto in Redazione Marzo 2014. Accettato per la pubblicazione Maggio 2014
Correspondence to: Francesco Fleres, MD, Department of Human Pathology, General Surgery Unit, University of Messina, Via Consolare Valeria, 98125 Messina, Sicily, Italy (e-mail: franz.fleres@gmail.com)

ondary site and typically occur after a long interval of years from nephrectomy. When there is a solitary lesion it is equally distributed to all portions of the pancreas [5]. Currently there is limited experience on surgical resection of isolated pancreatic metastasis and the role of surgery has not been clearly defined; for many years metastatic disease to the pancreas was considered a terminal-stage condition. In the past few years, the progress made in terms of morbidity and mortality after surgical resection of metastatic lesions of the pancreas has made it possible to treat patients with a radical surgical approach. In this report we describe an interesting and peculiar case where a metachronous pancreatic metastasis from RCC in the body and tail of pancreas occurred twice, after five years from the polar nephrectomy and after six months from the distal pancreatectomy.

Case report

A 78 years-old asymptomatic woman was admitted to our department for evaluation of a nodular lesion developed in the body of the pancreas. Medical history revealed that in March of 2002 she had had a right polar nephrectomy due to an exophytic and encapsulated RCC of the size of 3 cm (histological exam: T2N0M0 grade 1 sec. Fuhrman and Robson stage 1). After 5 years the patient presented a lesion in the body of the pancreas, located on the left of the mesenteric artery and vein, discovered during the follow-up through imaging exams. A contrast-enhanced CT study showed the result of a "neoplasm-sparing" surgical approach to the inferior right polar kidney and highlighted a nodular lesion of the size of 2.5 cm in the body of the pancreas appearing as hypervascular in the arterial phase with a rapid wash-out. The dynamic MR imaging confirmed the nodular lesion in the body of the pancreas (27 mm) and suggested the presence of another, more defined, lesion (1 cm of size) near the posterior pancreatic margin (Fig. 1). The findings on imaging exam are typical of pancreatic metastasis from RCC. On January 2007 she had been submitted to distal pancreatectomy with splenectomy. Histopathological exam showed two yellow solid lesions, measuring respectively 2x1,5 cm and 1,2x1 cm of diameter and diagnosis was metastasis from renal cell carcinoma with clear surgical margins. The post-operative course was regular and the patient was discharged after eight days. The CT, after six months of follow-up, revealed the presence of a nodular lesion of few millimeters in the distal portion of the residual body of the pancreas, hypervascular with intense and homogeneous contrast enhancement in the arterial phase and isodense in the delayed post-contrast phases (Fig. 2). In September 2007 the patient performed a FDG-PET exam that highlighted a small accumulation of tracer, with no significant oncological feature, near the metallic clips of the previous operation. The lesion was of minimal size and did not seem related to the small lesion reported in the previous CT. In the imaging follow-up no modification was recorded until October 2012 when CT showed the growth of the lesion to 2 cm of size and the absence of secondary metastases in other organs (Fig. 3).

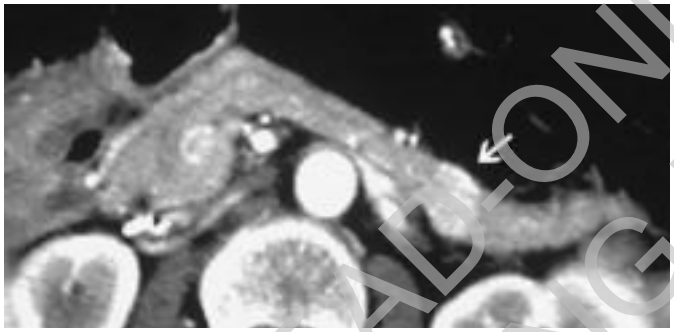

Fig. 1: MRI: metachronous metastatic lesion in the body-tail of the pancreas after 5 years from nephrectomy.

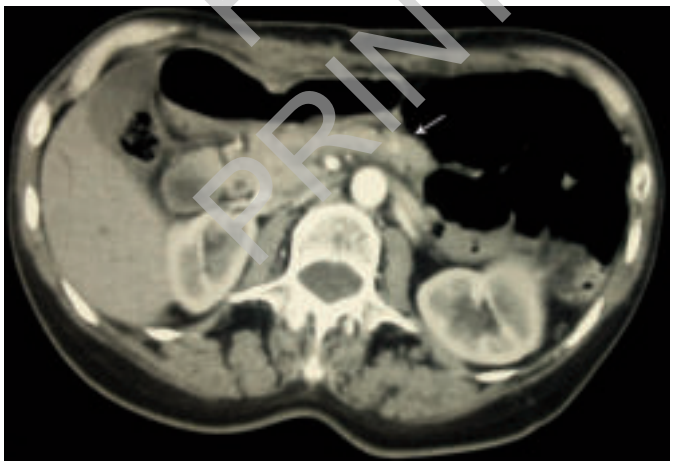

Fig. 2: CT: relapsed nodular lesion of few millimetres in the residual body of the pancreas after six months from distal pancreatectomy and splenectomy.

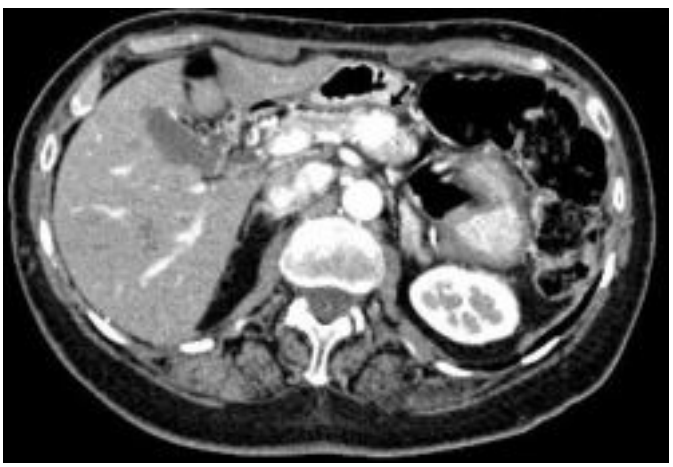

Fig. 3: CT: growth of the lesion (diameter of 2 cm) after five years of imaging follow-up.

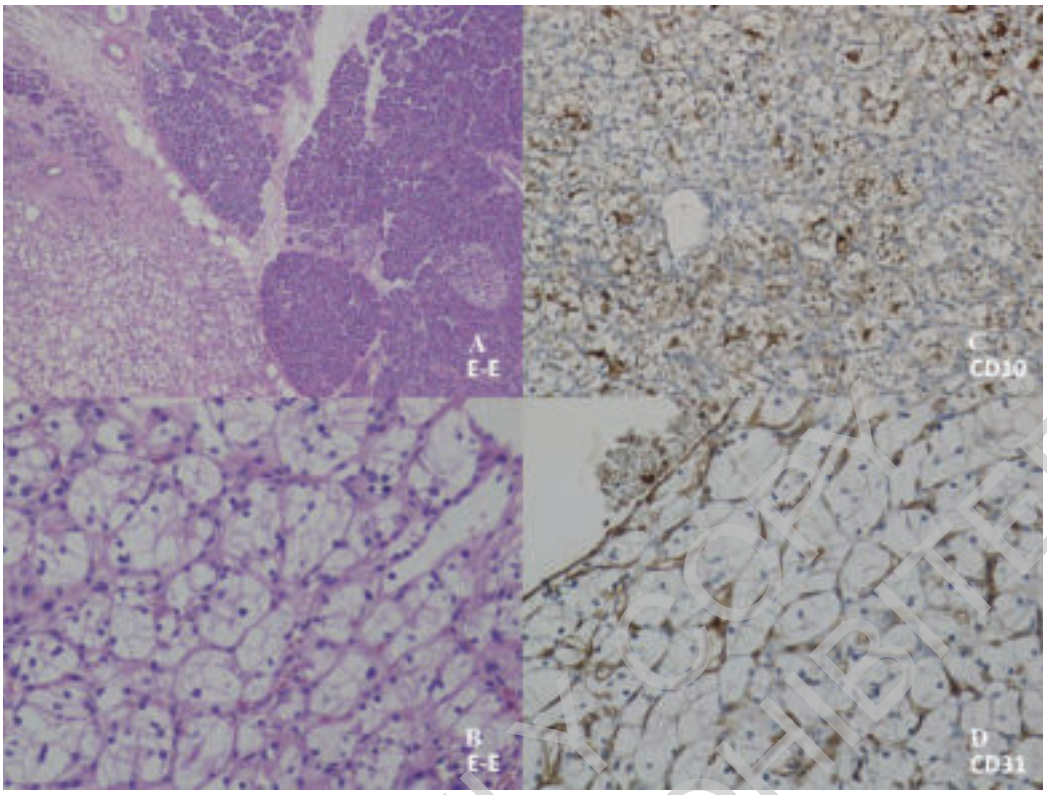

Fig. 4: **A**) In the left bottom the area of neoplastic infiltration of pancreatic tissue is clearly distinguishable for the cytoplasmic pallor.(E-E, 10x); **B**) At high magnification cytological details of neoplastic cells: small central nucleus surrounded by a large clear cytoplasm with solid architecture/alveolar, interspersed with a clear vascular network. (E-E, 40x): **C**):Immunohistochemical positivity for CD 10 marker highly sensitive for the diagnosis of renal cell carcinoma with clear cells.(antibody CD10, nuclear contrast E-E, 20x); **D**) Immunocoloration with CD31, endothelial marker, highlights the rich vascular network that develops between the neoplastic cells. (antibody CD31, nuclear contrast CD31, 40x).

Therefore the patient was submitted to a distal pancreatectomy in order to remove the remaining part of the pancreatic body. The histopathological exam described an oval yellow lesion of 2x1,4 cm which margins were free from neoplastic invasion and the diagnosis was metastasis from RCC with clear cells (Fig. 4).
The immunohistochemistry revealed: CK 7-, CK20-, CK19-/+, CD 10+, racemase- and chromogranin-; the growth fraction, evaluated with MIB-1, was about 5%. The postoperative course was regular and the patient was discharged after seven days. After 15 months of clinical and imaging follow-up the patient is well and there isn't relapse of disease in any organ.

Discussion

Isolated solid organ metastases to the pancreas rarely occur in the absence of a widely disseminated disease; the vast majority of pancreatic tumors are primary and metastatic tumors are rare. The tumors that metastasize to the pancreas, in order of frequency, are clear cell renal carcinoma (RCC), lung cancer (adenocarcinoma and non-small cell carcinoma), lobular breast carcinoma, colorectal carcinoma, malignant melanoma and soft-tissue sarcoma [8-11]. The incidence of metastatic tumors in autoptic series has been reported to be from 3% to 11% [12,13], while in clinical series it ranges from 2% to 5% of all pancreatic malignant tumors [4,14-16]. The secondary spread to the pancreas from RCC occurs in less than 1% of patients [8,17]. The optimal management of pancreatic metastases has not been clearly defined, over the past few years, improvements in morbidity and mortality rate after surgical resection of the pancreas have enabled patients with metastatic disease to be treated with radical intent [10,11]. Radical nephrectomy has been the treatment of choice for patients with unilateral renal cell carcinoma and a functional contralateral kidney. However 20-30% of patients with limited disease will have a local or systemic recurrence after R0 nephrectomy. The median interval of relapse is 15-18 months and in 85% of the cases occurs within 3 years [18]. Late metastases may occur 10-15 years after nephrectomy [19-22]; the interval of occurrence might even exceed 25 years [8,21,23]. Therefore patients with a history of RCC should be monitored for more than 10 years after nephrectomy in order to detect recurrence.

The increasing use of imaging techniques, particularly of CT, in the follow-up of oncological patients allows an earlier detection of small pancreatic metastases. Imaging may be crucial in identifying a metastatic disease in the pancreas because patients may have few or no symptoms referable to the pancreas [21,24-26]. There isn't difficulty in identifying large lesions within the pancreas using a standard CT technique because they typically deform the margins of the pancreas; in lesions larger than 1,5 cm a rim enhancement with hypodense central areas of necrosis can be observed, while small lesions might easily be missed. Identifying the presence of multiple lesions is also important in planning total rather than regional, surgical pancreatectomy. The medical history of the patient and a correct planning of the follow-up are essential in making a proper diagnosis and an early detection of a pancreatic metastasis. The appearance of metastatic disease many years after nephrectomy is a peculiar feature of RCC. The most common sites of metastasis from RCC include the lungs (50-60%), bones (30-40%), liver (30-40%) and brain (5%) [16]; RCC has also a tendency to metastasize to rare sites such as the pancreas, thyroid, skeletal muscle, skin or soft tissue [16, 27]. Surgical treatment of isolated pancreatic metastases, from neoplasms other than RCC, carries a poor prognosis; metastases typically indicate a disseminated metastatic disease [22]. Approximately 2-6% of patients with metastatic RCC present with isolated metastatic lesions amenable to surgical resection [5]. Three types of metastatic involvement of the pancreas are described in literature: the most common, particularly in metastases from RCC, is a solitary and well-defined mass (50-73%); the second pattern of growth consists of multiple pancreatic lesions (5-10%) and the third is a diffuse metastatic infiltration causing an enlargement of the organ (15-44%) [7]. The probable spread, by abnormal lymphatic or venous communications between RCC and pancreas, does not explain the lack of relationship between the site of the pancreatic isolated metastasis and the affected part of the kidney tumor [16,22,28]. The hematic way does not explain the discrepancy between the relative frequency of multiple lesions and the absence of metastases in other organs. The preference of RCC to give metastases to the pancreas can be explained by the peculiar biology of the tumor; the neoplastic cells have a high affinity for the pancreatic parenchyma, where they find the ideal environment to mature and develop metastases. The biochemical mechanisms allowing the metastatic growth in the pancreas are still unknown.

Pancreatic RCC metastases may present synchronously or metachronously; most patients have widespread systemic disease at the time of diagnosis. As a matter of fact, the clinical occurrence of isolated or exclusive metastasis to the pancreas is rare. Experience with pancreatic resection for the treatment of isolated metastatic lesions is growing; for multiple isolated metastases, although still controversial, radical resections are being recommended with increasing survival rates [4,22,29].

Surgical resection of metastatic lesions to the pancreas should be approached by carefully applying of proper selection criteria, because of the substantial morbidity associated with pancreatic resection and the questionable benefit of resection for pancreatic metastasis. Reddy [30], in a systemic review of the literature, concluded that the effectiveness of pancreatic resection for metastatic tumor is related to the biology of the primary cancer. RCC was found to be associated with best outcome whereas lung cancer predicted the worst; median survival and 5-year survival rates in patients with metastatic RCC are 8.75 years and 66%. Reddy [30] suggested also some criteria for patients selection, namely the primary cancer associated with a good outcome, control at the primary cancer site, isolated metastasis, resectability of metastasis and the patient's ability to tolerate pancreatic resection. The most appropriate surgical resection of metastatic disease of the pancreas depends on the aggressiveness of the primary tumor, the extent of metastatic disease and the patient's functional status. The pancreatic metastases can be multifocal in approximately 30% of patients and are resectable in about 80% of the cases [23]. Patients with multiple metastatic lesions have a poor prognosis compared to the solitary ones [4,8,23,31]; the factors associated with worse survival were symptoms at diagnosis and a disease-free interval of less than two years in patients with metachronous lesion [32]. Patients with RCC metastases to the pancreas are usually discovered either during the initial staging workup for treatment of primary tumor or by means of a routine imaging follow-up after the primary tumor has been treated or for the initial presence of symptoms related to pancreatic lesion. In our patient the presence of a metachronous metastasis to the pancreas became evident after an interval of five years from the surgical approach to the RCC and was discovered through routine follow-up. It may often be difficult to distinguish a pancreatic RCC metastasis from a primary pancreatic ductal adenocarcinoma (PDA) or a neuroendocrine tumor (NET). Patients may be completely asymptomatic at presentation or may present subtle and aspecific signs and symptoms; they may experience epigastric abdominal pain or an acute pancreatitis secondary to pancreatic ductal obstruction from the metastatic lesion. Other potential signs and symptoms are early satiety, gastrointestinal bleeding, painless jaundice secondary to biliary obstruction. All of them may be caused by the presence of a primary pancreatic neoplasia or an isolated metastatic disease. 69% of the patients with isolated pancreatic metastases were completely asymptomatic at presentation and so was our patient [10]. Radiographic imaging techniques of cross-sectional type (abdominal MRI, MRCP, and contrast-enhanced CT) with thin cuts through the pancreas lead to peculiar findings in diagnosing RCC metastatic dis-

ease from PDA. The former lesion is hypervascular and gives contrast enhancement during the arterial phase of contrast injection while the latter lesion typically appears as hypointense in the contrast phase. Metastases to the pancreas can be multicentric and typically do not cause peripancreatic lymphadenopathy; both these findings can be used to distinguish metastasis from PDA. On the contrary, pancreatic NETs are also hypervascular and constrast-avid and distinguishing them from RCC metastases can be difficult [33]. Standard operative procedures are adopted for resectable tumors, the type of surgical resection depends on location of the tumor in the pancreas.

Pylorus-preserving pancreaticoduodenectomy is suitable for tumors in the head, neck and uncinate process, on the other hand middle segment or distal pancreatectomy with splenectomy is necessary for tumors located in the body or tail of the pancreas. In some cases small encapsulated and exophytic metastatic tumors to the pancreas can be treated through enucleation of the lesions thus preserving the pancreatic parenchyma. In case of multicentric pancreatic metastases a total pancreatectomy can been performed, although this treatment is fairly uncommon. Although metastasis to the pancreas is commonly associated with disseminated systemic disease, RCC typically spreads to the pancreas as an isolated lesion, often making it amenable to surgical treatment [34]. When pancreatic spread of RCC is identified as a synchronous lesion, the resection of the metastasis performed at the same time of nephrectomy offer a survival benefit over nephrectomy alone [5,35]. The goals of pancreatic metastasectomy include resection of the lesion with clear surgical margins and preservation of as much viable pancreatic tissue as possible. 5-year survival rate after surgical resection of RCC metastasis to the pancreas is 53-75%, whereas patients who reject surgical resection or have widely disseminated disease have a 5-year survival rate of 5-30% [35,36]. These findings highlight the importance of post-nephrectomy surveillance in patients with RCC. The increase of small renal tumors incidentally discovered at earlier stages has led to organ-preserving surgery which is more frequently preferred to radical nephrectomy for tumors of less than 4 cm and limited to the kidney. For smaller tumors, measuring less than 2 cm, a simple enucleation, dissecting around the pseudocapsule of the tumor, can be applied [37]. The biology of the primary tumor would be the same as if metastasis is solitary and the size is small. Therefore, metastatic RCC to the pancreas of the size of less than 2 cm in diameter that are not close to a main pancreatic duct can be a good indication for organ-preserving pancreatectomy such as enucleation. Further studies in organ-preserving pancreatectomy for small metastatic RCC are necessary.

The peculiar features that we observed in our patient were the long interval of time (5 years) from the treatment of the primary tumor (RCC), that for the size (3 cm of diameter), the position (inferior right polar kidney) and the surgical characteristics (exophytic and encapsulated) had required a conservative surgical approach in order for organ to be preserved and the appearance of a metachronous solitary pancreatic metastasis. We also observed the development of a relapsed metachronous pancreatic metastasis of a few millimeters after six months from the operation of distal pancreatectomy and splenectomy, that in the imaging follow-up was characterized by a very slow growth (it reached the size of 2 cm within a time-lapse of five years). We underline the absence of kidney relapse of malignant disease and of secondary metastases in other organs. The critical review of therapeutic approach that we have adopted in this clinical case raises the question: shall the second metastatic lesion, that appeared six months later, be considered as synchronous to the first lesion, but just too small to be identified or as a new metachronous lesion? The pathological exam demonstrated that surgical margins were clear of tumor invasion and the lesion developed near the metallic clips of previous operation. In conclusion we can underline that a solitary pancreatic metastasis from RCC is usually rare, it occurs many years after the diagnosis of primary tumor and requires a careful follow-up with the use of the modern techniques related to specific laboratory tests; it should be differentiated from PDA or NET and the usefulness of surgical resection of metastatic lesions as the only effective curative treatment needs to be acknowledged.

Patients with isolated pancreatic metastasis from RCC represent an unique group with a more indolent course of RCC. A prolonged interval from nephrectomy to the appearance of metastasis is associated with a more favorable prognosis. Radical lymph-node dissection is not necessary, as peripancreatric lymph-node involvement is uncommon; this peculiar feature may be one of the factors that explains the favorable outcomes achieved with the help of surgery.

Riassunto

Le metastasi pancreatiche, originate da qualsiasi tipo di tumore primario, sono rare. In letteratura sono riportati solo pochi dati sporadici su quale sia l'approccio terapeutico ottimale. La frequenza rilevata nella casistica clinica varia dal 2% al 5% di tutti i tumori pancreatici maligni. Il pancreas è il sito preferito delle metastasi da RCC (carcinoma a cellule renali), che può presentarsi anche dopo molti anni dalla nefrectomia parziale o radicale. In caso di tumore solitario la resezione chirurgica R0 rimane il solo trattamento potenzialmente curativo, poichè RCC ha mostrato solo una relativa o incosistente risposta alle terapie sistemiche: chemioterapia, radioterapia ed immunoterapia. Nell'approccio al trattamento dei pazienti con metastasi pancreatiche da RCC deve essere considerata la possibilità della multifocalità delle lesioni, che ricorre nel 20- 45% dei casi.

Riportiamo un caso di metastasi pancreatica metacrona da RCC verificatasi due volte. Dopo cinque anni dalla nefrectomia polare inferiore destra per un RCC esofitico e incapsulato delle dimensioni di 3 cm (T2N0M0), due lesioni nodulari furono identificate alla CT e alla MRI nel corpo - coda del pancreas e furono trattate con pancreasectomia distale e splenectomia. Dopo sei mesi il controllo TC rilevò la presenza di una lesione nodulare di alcuni millimetri nella parte residua del corpo pancreatico; abbiamo seguito con esami di imaging la lenta crescita della lesione secondaria e nell'ottobre 2012, quando la dimensione aveva raggiunto i 2 cm, il paziente è stato operato per rimuovere la parte residua del corpo del pancreas. Dopo 16 mesi di follow- up il paziente sta bene e non vi è stata recidiva.

I pazienti con lesioni pancreatiche metacrone rappresentano un gruppo particolare con un decorso molto più lento del RCC, la comparsa di metastasi dopo un intervallo prolungato dalla nefrectomia è connessa ad una prognosi più favorevole. La radicale dissezione linfonodale non è necessaria per il coinvolgimento raro dei linfonodi peripancreatici, condizione che spiega i risultati positivi ottenuti con la chirurgia. I pazienti con metastasi resecate presentano un tasso di sopravvivenza dell'88% a 5 anni contro il 47% osservato nei pazienti non operati; gli studi forniscono risultati incoraggianti in termini di sopravvivenza e qualità di vita dei pazienti trattati chirurgicamente.

References

1. Whittington R, Moylan DJ, Dobelbower RR, Kramer S: *Pancreatic tumours in patients with previous malignancy.* Clin Radiol, 1982; 33(3):297-99.

2. Stankard CE, Karl RC: *The treatment of isolated pancreatic metastases from renal cell carcinoma: A surgical review*. Am J Gastroenterol, 1992; 87(11):1658-60.

3. Ramia JM, Muñak K, Villar J, Mansilla A, Garrote D, Ferrón JA: *Metástasis pancreática tardía de cáncer renal.* Rev Esp Enferm Dig, 2004; 96(6):428-29.

4. Zerbi A, Ortolano E, Balzano G, Borri A, Beneduce AA, Di Carlo V: *Pancreatic metastasis from renal cell carcinoma: Which patients benefit from surgical resection?* Ann Surg Oncol, 2008; 15(4):1161-168.

5. 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(4):346-51.

6. Janzen NK, Kim HL, Figlin RA, Belldegrun AS: *Surveillance after radical or partial nephrectomy for localized renal cell carcinoma and management of recurrent disease*. Urol Clin North Am, 2003; 30(4):843-52.

7. Ballarin R, Spaggiari M, Cautero N, De Ruvo N, Montalti R, Longo C, et al.: *Pancreatic metastases from renal cell carcinoma: The state of the art.* World J Gastroenterol, 2011; 17(43): 4747-756.

8. Thompson LD, Heffess CS: *Renal cell carcinoma to the pancreas in surgical pathology material: A clinicopathologic study of 21 cases with a review of the literature*. Cancer, 2000; 89:1076-88.

9. Medina-Franco H, Halpern NB, Aldrete JS: *Pancreaticoduodenectomy for metastatic tumors to the periampullary region*. J Gastrointest Surg, 1999; 3(2):119-22.

10. Hiotis SP, Klimstra DS, Conlon KC, Brennan MF: *Results after pancreatic resection for metastatic lesions*. Ann Surg Oncol, 2002; 9(7):675-79.

11. Sperti C, Pasquali C, Liessi G, Pinciroli L, Decet G, Pedrazzoli S: *Pancreatic resection for metastatic tumors to the pancreas*. J Surg Oncol, 2003; 83(3):161-66.

12. Adsay NV, Andea A, Basturk O, Kilinc N, Nassar H, Cheng JD: *Secondary tumors of the pancreas: an analysis of a surgical and autopsy database and review of the literature*. Virchows Arch, 2004; 444(6):527-35.

13. Washington K, McDonagh D: *Secondary tumors of the gastrointestinal tract: Surgical pathologic findings and comparison with autopsy survey*. Mod Pathol, 1995; 8(4):427-33.

14. Ascenti G, Visalli C, Genitori A, Certo A, Pitrone A, Mazziotti S: *Multiple hypervascular pancreatic metastases from renal cell carcinoma: dynamic MR and spiral CT in three cases*. Clin Imaging, 2004; 28(5):349-52.

15. Crippa S, Angelini C, Mussi C, Bonardi C, Romano F, Sartori P, et al.: *Surgical treatment of metastatic tumors to the pancreas: A single center experience and review of the literature.* World J Surg, 2006; 30(8):1536-542.

16. 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(2):211-15.

17. Z'graggen K, Fernández-del Castillo C, Rattner DW, Sigala H, Warshaw AL: *Metastases to the pancreas and their surgical extirpation*. Arch Surg, 1998; 133:413-17; discussion 418-19.

18. Sandock DS, Seffel AD and Resnick M: *A new protocol for follow up of renal cell carcinoma based on pathological stage*. J Urol, 1995; 154(1):28-31

19. Jarufe N, McMaster P, Mayer AD, Mirza DF, Buckels JA, Orug T, Tekin K and Bramhall SR: *Surgical treatment of metastases to the pancreas*. Surgeon, 2005; 3(2):79-83.

20. Taylor AS, Charles JY, Cameron JL, Nakeeb A, Lillemoe KD: *Renal cell carcinoma metastatic to the pancreas: results of surgical management.* J Gastrointest Surg, 2001; 5:346-51.

21. Hirota T, Tomida T, Iwasa M, Takahashi K, Kaneda M, Tamaki H: *Solitary pancreatic metastasis occurring eight years after nephrectomy for renal cell carcinoma. A case report and surgical review*. Int J Pancreatol, 1996; 19(2):145-53.

22. 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(1):75-85.

23. Wente MN, Kleeff J, Esposito I, Hartel M, Müller MW, Fröhlich BE, et al.: *Renal cancer cell metastasis into the pancreas: A single-center experience and overview of the literature.* Pancreas, 2005; 30:218-22.

24. Fabre JM, Rouanet P, Dagues F, Blanc F, Baumel H, Domergue

J: *Various features and surgical approach of solitary pancreatic metastasis from renal cell carcinoma*. Eur J Surg Oncol, 1995; 21:683-86.

25. Boudghène FP, Deslandes PM, LeBlanche AF, Bigot JM: *US and CT imaging features of intrapancreatic metastases*. J Comput Assist Tomogr. 1994; 18(6):905-10.

26. Rypens F, Van Gansbeke D, Lambilliotte JP, Van Regemorter G, Verhest A, Struyven J: *Pancreatic metastasis from renal cell carcinom*a. Br J Radiol, 1992; 65(774):547-48.

27. Tanis PJ, van der Gaag NA, Busch OR, van Gulik TM, Gouma DJ: *Systematic review of pancreatic surgery for metastatic renal cell carcinoma.* Br J Surg, 2009; 96(6):579-92.

28. 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(1):20-2.

29. Reddy S, Edil BH, Cameron JL, Pawlik TM, Herman JM, Gilson MM, Campbell KA, Schulick RD, Ahuja N, Wolfgang C: *Pancreatic resection of isolated metastases from nonpancreatic primary cancer*s. Ann Surg Oncol, 2008; 15(11):3199-206.

30. Reddy S, Wolfgang CL: *The role of surgery in the management of isolated metastases to the pancreas.* Lancet Oncol, 2009; 10(3):287-93.

31. David AW, Samuel R, Eapen A, Vyas F, Joseph P, Sitaram V: *Pancreatic metastasis from renal cell carcinoma 16 years after nephrectomy: A case report and review of the literature*. Trop Gastroenterol, 2006; 27(4):175-76.

32. Masetti M, Zanini N, Martuzzi F, Fabbri C, Mastrangelo L, Landolfo G, Fornelli A, Burzi M, Vezzelli E, Jovine E: *Analysis of prognostic factors in metastatic tumors of the pancreas: A single-center experience and review of the literature.* Pancreas, 2010; 39(2):135-43.

33. Lavu H, Yeo CJ: *Metastatic renal cell carcinoma to the pancreas*. Gastroenterol Hepatol (NY), 2011; 7(10):699-700.

34. 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):922-26.

35. Kavolius JP, Mastorakos DP, Pavlovich C, Russo P, Burt ME, Brady MS: *Resection of metastatic renal cell carcinoma.* J Clin Oncol, 1998; 16(6):2261-266.

36. Showalter SL, Hager E, Yeo CJ: *Metastatic disease to the pancreas and spleen*. Semin Oncol, 2008; 35:160-71.

37. Tobisu K: *Function-preserving surgery for urologic cancer.* Int J Clin Oncol, 2006; 11(5):351-56.