

## PANCREATIC METASTASIS FROM RENAL CELL CARCINOMA: A CASE REPORT

*Ljiljana Jeremić-Savić<sup>1</sup>, Milan Radojković<sup>1,2</sup>, Milica Nestorović<sup>1</sup>, Marko Gmijović<sup>1</sup>*

Metastatic pancreatic cancer is rare and makes 2% to 5% of all malignant tumors of this gland. Predominantly it is a metastatic renal cell carcinoma (RCC - renal cell carcinoma), which shows expressed affinity to the pancreas, which is often the only place of its expansion, typically several years to several decades after nephrectomy. The average time of detection of metastases is 7 years (described is the case after 32.7 years). As multifocal lesions they occur in 20-45% of cases when their treatment will depend on the resectability of changes, which is possible in about 60% of patients. We present a case of 69-year-old female patient, in whom solitary changes in the body of the pancreas were detected 3.5 years after nephrectomy for RCC. At the time of examination, the patient had no symptoms, a change was detected by control computed tomography (CT) of the abdomen. After distal splenopancreatectomy metastasis kidney cancer was confirmed. Extensive and regular follow up of the patient after nephrectomy for RCC was necessary and imposed by the unpredictable nature of this tumor. Despite the existing radio-biological therapy, surgery occupies an important place in the treatment of these metastases, the radical surgical approach in the case of resectable metastases offers the chance for years of survival.

*Acta Medica Mediana 2018;57(3):55-59.*

**Key words:** *pancreatic metastasis, renal carcinoma, pancreatic resection*

<sup>1</sup>General Surgery Clinic, Clinical Center Niš, Serbia  
<sup>2</sup>University of Niš, Faculty of Medicine, Niš, Serbia

Contact: Ljiljana Jeremić-Savić  
Bvd. Dr Zoran Djindjić 48, 18000 Niš, Serbia  
E-mail: jeremic.ni@gmail.com

cal nephrectomy for RCC, proven histopathology, the presence of typical well-differentiated clear cells without regional lymphadenopathy or distant metastases. Regular follow-up of patient for 3 years does not indicate a recurrence of the disease. After 3.5 years of nephrectomy abdominal ultrasonography, then computed tomography (CT), revealed hypervascular tumor in the body of the pancreas (Figure 1).

### Introduction

Metastatic pancreatic cancer is rare and makes 2% to 5% of all malignity tumors of this gland (1-19). The most common pancreatic metastases are RCC, lung carcinoma, lobular carcinoma of the breast, adenocarcinomas of the colon, melanoma, leiomyosarcoma (2-7, 13-19). However, pancreas is from renal cell carcinoma elective and frequently only site for metastases, a few years to several decades after nephrectomy (20-22, 26). Expressed affinity of malignancy cells to pancreatic parenchyma is probably effect of the character of the tumor, while the dissemination mechanism is not yet fully understood (23).

### Case report

We report a case of 69-year-old female patient, who had 3.5 years previously undergone a radi-

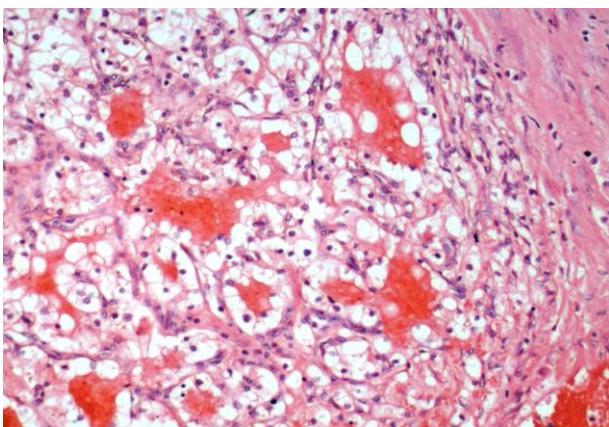


**Figure 1.** Computerized tomography of the abdomen with marked metastatic tumor of the pancreas

At the time of medical examination the patient had no symptoms, laboratory findings were with normal limits, CA 19-9 were regular. Distal pancreatectomy with splenectomy was performed (Figure 2). Histopathology confirmed metastatic RCC (Figure 3).



**Figure 2.** Metastatic tumor, macroscopically, after distal spleno-pancreatectomy



**Figure 3.** Histology of a renal carcinoma metastasis: clear cell type

The postoperative course was normal; the patient was discharged on 9<sup>th</sup> postoperative day. Twelve months after the second surgery, the patient was well, with no signs of disease recurrence.

## Discussion

The pancreas represents elective place metastasis of RCC, which described numerous studies (1-11). It typically occurs several years after nephrectomy in the seventh decade of life. The average time of detection of metastases is 7 years, but the case is described after 32.7 years (3, 4, 9, 11), usually during a routine examination of asymptomatic patients, as is the case in 50% of patients (5, 6, 12, 13). In other cases the symptoms are described as

pain, weight loss, gastrointestinal bleeding, icterus (5, 6, 12-14).

The mechanism of spread of the disease and the connection between RCC and pancreatic cancer are still not fully understood, and the affinity of metastatic RCC to the parenchyma of pancreas explains the nature of the tumor, but not their anatomical proximity. The usual routes of malignant processes cannot explain certain described cases of metachronous metastases on previously resected pancreas because of the same disease, or secondary multifocal lesions in the pancreas, along with their absence in other organs (3, 15).

Multifocal lesions of pancreatic metastasis have been reported to be in the range 20% to 45% which should be considered when selecting therapy (4, 15, 16-18).

The diagnosis usually relies on computed tomography (CT) or magnetic resonance (MR), when it is difficult to make the distinction of metastases from primary carcinoma of the pancreas. The differential diagnosis of metastases should be differentiated from primary pancreatic neoplastic process, focal infiltration of lymphoma and pancreatitis. On ultrasound the metastases were present as hypoechoic, whereas CT presentations usually showed appropriately limited hypervascularized lesions without infiltration of the retropancreatic space and adipose tissue which is commonly seen with primary pancreatic cancer and lymphoma.

In addition to those listed, PET scan and echo endoscopy may also be considered useful procedures. In nephrectomized patients the diagnosis is easily established due to RCC. In some unclear situations percutaneous biopsy of lesion controled by CT may be performed (3, 13, 19, 20).

Resection of the pancreas (a cephalic duodenopancreatectomy sec. Whipple or distal pancreatectomy), if possible, is the most effective treatment of solitary metastatic of RCC. Total pancreatectomy with the multiple lesions is indicated by some authors (21-23). Radical lymphadenectomy is unnecessary (11). A number of studies (with 5 or more patients) indicate good results of surgical treatment: the 5-year survival was present, depending on the series, in 30% to over 80% of patients (2-6, 15, 17, 24-34). Reddy et al. (2008) reported that metastatic size greater than 4 cm and perineural infiltration were related with a significantly lower percentage of survival (25), while Motzer et al. (2004) reported that the factors of poor prognosis after resection therapy was interval between nephrectomy and metastases < 12 months, previous radiotherapy, ≥ 2 metastases (35).

In the treatment of primary RCC and its metastases, chemotherapy has proved to be ineffective. There are a number of proposed protocols that include biological (molecular) therapy such as sunitinib, sorafenib, bevacizumab, everolimus, temsirolimus. Highly toxic interferon alpha and interleukin-2 is used as second-line therapy (36-39).

Radiation therapy is an alternative treatment of inoperable lesions, as well as in high-risk patients, alone or in combination with any of the above-mentioned biological therapy or surgery. In the literature there is only one study which publishes the results of

RT applied in 4 patients with multiple metastatic RCC in the pancreas.

Interferon alpha was administered combined with RT, where the stabilization of the disease was achieved in 3 patients (average 34 months), while in one patient partial response was achieved to the combined therapy (40).

Some authors suggest the possibility of treatment of multiple metastatic RCC in pancreas with radiofrequency ablation (RFA). Associated with a high percentage of significant complications such as necrotizing pancreatitis, bleeding, perforation of the duodenum, this type of therapy is reserved for individual cases in highly specialized centers (41-43).

## Conclusion

Extensive and regular follow up of the patients after nephrectomy for RCC is necessary and imposed by the unpredictable nature of this tumor for early detection of pancreatic metastases, often in asymptomatic patients.

The radical surgical approach in case of resectable changes offers the chance for years of survival. The best results are achieved in patients with good general condition, with long disease-free period after nephrectomy, when pancreatic resection is performed in high-volume centers due to solitary metastasis up to 4 cm.

## References

- Ascenti G, Visalli C, Genitori A, Certo A, Pitrone A, Maziotti S. Multiple hypervascular pancreatic metastases from renal cell carcinoma: dynamic MR and spiral CT in three cases. Clin Imaging 2004; 28(5): 349-52. [\[CrossRef\]](#) [\[PubMed\]](#)
- 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): 1536-42. [\[CrossRef\]](#) [\[PubMed\]](#)
- 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):211-5. [\[CrossRef\]](#) [\[PubMed\]](#)
- 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):1161-8. [\[CrossRef\]](#) [\[PubMed\]](#)
- Hiotis SP, Klimstra DS, Conlon KC, Brennan MF. Results after pancreatic resection for metastatic lesions. Ann Surg Oncol 2002; 9(7):675-9. [\[CrossRef\]](#) [\[PubMed\]](#)
- Le Borgne J, Partensky C, Glemain P, Dupas B, de Kerviller B. Pancreaticoduodenectomy for metastatic ampullary and pancreatic tumors. Hepatogastroenterology 2000; 47(32):540-4. [\[PubMed\]](#)
- Medina-Franco H, Halpern NB, Aldrete JS. Pancreaticoduodenectomy for metastatic tumors to the periamphullary region. J Gastrointest Surg 1999; 3(2):119-22. [\[CrossRef\]](#) [\[PubMed\]](#)
- Roland CF, van Heerden JA. Nonpancreatic primary tumors with metastasis to the pancreas. Surg Gynecol Obstet 1989; 168(4):345-7. [\[PubMed\]](#)
- 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):161-6; discussion 166. [\[CrossRef\]](#) [\[PubMed\]](#)
- Bassi C, Butturini G, Falconi M, Sargentini M, Mantovani W, Pederzoli P. High recurrence rate after atypical resection for pancreatic metastases from renal cell carcinoma. Br J Surg 2003; 90(5):555-9. [\[CrossRef\]](#) [\[PubMed\]](#)
- 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. [\[CrossRef\]](#) [\[PubMed\]](#)
- Thompson LD, Heffess CS. Renal cell carcinoma to the pancreas in surgical pathology material. Cancer 2000; 89(5):1076-88. [\[CrossRef\]](#) [\[PubMed\]](#)
- Kornprat P, Bacher H, Hauser H, Cerwenka H, El-Shabrawi, Lackner C, et al. Renal cell carcinoma with metastasis to the pancreas. Eur Surg 2004; 36(6): 381-4. [\[CrossRef\]](#)

14. Scatirige JC, Horton KM, Sheth S, Fishman EK. Pancreatic parenchymal metastases: observations on helical CT. *AJR Am J Roentgenol* 2001; 176(3):695-9. [\[CrossRef\]](#) [\[PubMed\]](#)
15. 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. [\[CrossRef\]](#) [\[PubMed\]](#)
16. Sellner F, Tykalsky N, De Santis M, Pont J, Klampfinger 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. [\[CrossRef\]](#) [\[PubMed\]](#)
17. 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(3):218-22. [\[CrossRef\]](#) [\[PubMed\]](#)
18. Sohn TA, Yeo CJ, Cameron JL, Koniaris L, Kaushal S, Abrams RA, et al. Resected adenocarcinoma of the pancreas-616 patients: results, outcomes, and prognostic indicators. *J Gastrointest Surg* 2000; 4(6):567-79. [\[CrossRef\]](#) [\[PubMed\]](#)
19. Werneck K, Peters PE, Galanski M. Pancreatic metastases: US evaluation. *Radiology* 1986; 160(2):399-402. [\[CrossRef\]](#) [\[PubMed\]](#)
20. Boudghene FP, Deslandes PM, Le Blanche AF, Bigot JMR. US and CT imaging features of intrapancreatic metastases. *J Comput Assist Tomogr* 1994; 18(6):905-10. [\[CrossRef\]](#) [\[PubMed\]](#)
21. Béchade D, Palazzo L, Desramé J, Duvic C, Hérodé M, Didelot F, et al. Pancreatic metastasis of renal cell carcinoma: report of three cases. *Rev Med Interne* 2002; 23(10):862-6. [\[CrossRef\]](#) [\[PubMed\]](#)
22. Eloubeidi MA, Jhala D, Chhieng DC, Jhala N, Eltoum I, Wilcox CM. Multiple late asymptomatic pancreatic metastases from renal cell carcinoma: diagnosis by endoscopic ultrasound-guided fine needle aspiration biopsy with immunocytochemical correlation. *Dig Dis Sci* 2002; 47(8):1839-42. [\[CrossRef\]](#) [\[PubMed\]](#)
23. Mehta N, Volpe C, Haley T, Balos L, Bradley EL, Doerr RJ. Pancreaticoduodenectomy for metastatic renal cell carcinoma: report of a case. *Surg Today* 2000; 30(1):94-7. [\[CrossRef\]](#) [\[PubMed\]](#)
24. Masetti M, Zanini N, Martuzzi F, Fabbri C, Mastrangelo L, Landolfo G, et al. 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. [\[CrossRef\]](#) [\[PubMed\]](#)
25. Reddy S, Edil BH, Cameron JL, Pawlik TM, Herman JM, Gilson MM, et al. Pancreatic resection of isolated metastases from nonpancreatic primary cancers. *Ann Surg Oncol* 2008; 15(11):3199-206. [\[CrossRef\]](#) [\[PubMed\]](#)
26. Bahra M, Jacob D, Langrehr JM, Glanemann M, Schumacher G, Lopez-Hänninen E, et al. Metastatic lesions to the pancreas. When is resection reasonable?. *Chirurg* 2008; 79(3):241-8. [\[CrossRef\]](#) [\[PubMed\]](#)
27. Butturini G, Bassi C, Falconi M, Salvia R, Caldiron E, Iannucci A, et al. Surgical treatment of pancreatic metastases from renal cell carcinomas. *Dig Surg* 1998; 15(3):241-6. [\[CrossRef\]](#) [\[PubMed\]](#)
28. Eidt S, Jergas M, Schmidt R, Siedek M. Metastasis to the pancreas-an indication for pancreatic resection? *Langenbecks Arch Surg* 2007; 392(5):539-42. [\[CrossRef\]](#) [\[PubMed\]](#)
29. Fourquier P, Regnard JF, Rea S, Levi JF, Levasseur P. Lung metastases of renal cell carcinoma: results of surgical resection. *Eur J Cardiothorac Surg* 1997; 11(1):17-21. [\[CrossRef\]](#) [\[PubMed\]](#)
30. Ghavamian R, Klein KA, Stephens DH, Welch TJ, LeRoy AJ, Richardson RL, et al. Renal cell carcinoma metastatic to the pancreas: clinical and radiological features. *Mayo Clin Proc* 2000; 75(6):581-5. [\[CrossRef\]](#) [\[PubMed\]](#)
31. Varker KA, Muscarella P, Wall K, Ellison C, Bloomston M. Pancreatectomy for non-pancreatic malignancies results in improved survival after R0 resection. *World J Surg Oncol* 2007; 5:145. [\[CrossRef\]](#) [\[PubMed\]](#)
32. Köhler K, Haroske G, Ludwig K. Management of pancreatic metastases from renal cell carcinoma report of five cases. *Zentralbl Chir* 2006; 131(5):425-8. [\[CrossRef\]](#) [\[PubMed\]](#)
33. Konstantinidis IT, Dursun A, Zheng H, Wargo JA, Thayer SP, Fernandez-del Castillo C, et al. Metastatic tumors in the pancreas in the modern era. *J Am Coll Surg* 2010; 211(6):749-53. [\[CrossRef\]](#) [\[PubMed\]](#)
34. 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. [\[CrossRef\]](#) [\[PubMed\]](#)
35. Motzer RJ, Bacik J, Schwartz LH, Reuter V, Russo P, Marion S, et al. Prognostic factors for survival in previously treated patients with metastatic renal cell carcinoma. *J Clin Oncol* 2004; 22(3):454-63. [\[CrossRef\]](#) [\[PubMed\]](#)
36. Fisher RI, Rosenberg SA, Fyfe G. Long-term survival update for high-dose recombinant interleukin-2 in patients with renal cell carcinoma. *Cancer J Sci Am* 2000; 6(Suppl 1):S55-7. [\[PubMed\]](#)
37. Yang JC, Sherry RM, Steinberg SM, Topalian SL, Schwartzentruber DJ, Hwu P, et al. Randomized study of high-dose and low-dose interleukin-2 in patients with metastatic renal cancer. *J Clin Oncol* 2003; 21(16):3127-32. [\[CrossRef\]](#) [\[PubMed\]](#)
38. Motzer RJ, Michaelson MD, Redman BG, Hudes GR, Wilding G, Figlin RA, et al. Activity of SU11248, a multitargeted inhibitor of vascular endothelial growth factor receptor and platelet-derived growth factor receptor, in patients with metastatic renal cell carcinoma. *J Clin Oncol* 2006; 24(1):16-24. [\[CrossRef\]](#) [\[PubMed\]](#)
39. Motzer RJ, Rini BI, Bukowski RM, Curti BD, George DJ, Hudes GR, et al. Sunitinib in patients with metastatic renal cell carcinoma. *JAMA* 2006; 295(21):2516-24. [\[CrossRef\]](#) [\[PubMed\]](#)
40. Saito J, Yamanaka K, Sato M, Mori N, Sekii K, Yoshioka T, et al. Four cases of advanced renal cell carcinoma with pancreatic metastasis successfully treated with radiation therapy. *Int J Clin Oncol* 2009; 14(3):258-61. [\[CrossRef\]](#) [\[PubMed\]](#)
41. Spiliotis JD, Datsis AC, Michalopoulos NV, Kekelos SP, Vaxevanidou A, Rogdakis AG, et al. Radiofrequency ablation combined with palliative surgery may prolong survival of patients with advanced cancer of the pancreas. *Langenbecks Arch Surg* 2007; 392(1):55-60. [\[CrossRef\]](#) [\[PubMed\]](#)
42. Varshney S, Sewkani A, Sharma S, Kapoor S, Naik S, Sharma A, et al. Radiofrequency ablation of unresectable pancreatic carcinoma: feasibility, efficacy and safety. *JOP* 2006; 7(1):74-8. [\[PubMed\]](#)
43. Wu Y, Tang Z, Fang H, Gao S, Chen J, Wang Y, et al. High operative risk of cool-tip radiofrequency ablation for unresectable pancreatic head cancer. *J Surg Oncol* 2006; 94(5):392-5. [\[CrossRef\]](#) [\[PubMed\]](#)

**Prikaz bolesnika**

**UDC: 616.37-033.2:616.61-006.6  
doi:10.5633/amm.2018.0307**

## **PANKREASNE METASTAZE RENALNOG KARCINOMA: PRIKAZ SLUČAJA**

*Ljiljana Jeremić-Savić<sup>1</sup>, Milan Radojković<sup>1,2</sup>, Milica Nestorović<sup>1</sup>, Marko Gmijović<sup>1</sup>*

<sup>1</sup>Klinika za opštu hirurgiju, Klinički centar, Niš, Srbija

<sup>2</sup>Univerzitet u Nišu, Medicinski fakultet, Niš, Srbija

*Kontakt:* Ljiljana Jeremić-Savić  
Bul. dr Zorana Đindića 48, 18000 Niš, Srbija  
E-mail: jeremic.ni@gmail.com

Metastatski tumor pankreasa je redak i čini 2% do 5% svih malignih tumora ove žlezde. Predominantno se radi o metastazama renalnog karcinoma (RCC - renal cell carcinoma), koje pokazuju izraženi afinitet prema tkivu pankreasa, koji je često jedino mesto njegovog širenja, tipično nekoliko godina, do nekoliko decenija nakon nefrektomije. Prosечно vreme detekcije metastaza je period od sedam godina (opisan je i slučaj nakon 32,7 god). Kao multifokalne se javljaju u 20-45% slučajeva, kada će njihov tretman zavisiti od resekabilnosti promena, što je moguće kod 60% bolesnika. U ovom radu opisan je slučaj 69-godišnje bolesnice, kod koje je detektovana solitarna promena u telu pankreasa, 3,5 godine nakon nefrektomije zbog RCC. U momentu pregleda, bolesnica je bez ikakvih simptoma, a promena je otkrivena kontrolnom kompjuterizovanom tomografijom (CT) abdomena. Nakon distalne splenopankreatektomije, potvrđeno je da se radi o metastazi karcinoma bubrega. Dugogodišnje i redovno praćenje bolesnika nakon nefrektomije zbog RCC je obavezno i nametnuto nepredvidljivom prirodom ovog tumora. Uprkos postojećoj radio-biološkoj terapiji, hirurgija zauzima važno mesto u lečenju ovih metastaza, gde radikalni hirurški pristup u slučaju resekabilnih promena nudi šansu za višegodišnje preživljavanje.

*Acta Medica Medianae* 2018;57(3):55-59.

***Ključne reči:*** pankreasne metastaze, renalni karcinom, resekcija pankreasa