VIA MEDICA

CASE REPORT

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# Do solitary pancreatic metastases of renal-cell carcinoma indicate an indolent disease with a strong indication for aggressive local treatment? A case report with literature review

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## ABSTRACT

Renal-cell carcinoma (RCC) most often metastasizes to the lungs, liver, and brain. Metastases of RCC to the pancreas are very rare. In the last decade, only a few cases of metachronous metastasis of kidney cancer to the pancreas have been reported in the literature. This article presents a case report of a 75-year-old female patient with a 16-year history of treatment of clear-cell carcinoma of the kidney, in whom pancreatic metastases were detected twice. Renal-cell carcinoma may have an indolent course with late relapse or may show dissemination. It is important to establish new recommendations for long-term follow-up in patients after radical treatment.
**Key words**: kidney cancer, metastasis, metastasectomy, pancreas

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## Introduction

Renal-cell cancer of clear-cell phenotype (RCC), in the majority of patients (98%), accounts for 3.8% and 2.3% of malignant neoplasms in males and females, respectively. Over the last two decades, there has been a 2% yearly increase in the incidence of RCC [1]. Before the advent of antiangiogenic targeted therapies, median survival of metastatic RCC (mRCC) patients was approximately 10 months. Due to the availability of new generations of antiangiogenic agents and immune checkpoint inhibitors, median overall survival (OS) approaches 47 months [2]. According to the current guidelines, not all RCC patients diagnosed with distant metastases require immediate initiation of systemic treatment and may undergo long-term active surveillance. Additionally, in the case of asymptomatic, oligometastatic disease, local therapeutic approaches (metastasectomy or stereotactic radiotherapy) represent the treatment of choice [3, 4]. Some authors emphasize that complete resection of metastases in mRCC patients in combination with targeted therapy is correlated with longer OS compared to targeted therapy alone [5].

The most common sites of RCC's distant metastases (lungs, bones, liver, and brain) [6] are typical for the majority of other solid tumors. However, one of the unique metastatic sites of RCC is the pancreas. Pancreatic metastases are rare and can be detected in approximately 5% of mRCC patients at the time of systemic treatment initiation [7]. Compared to secondary deposits located in the liver or lungs that are amenable to local treatment, pancreatic metastases represent a significant

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clinical challenge for surgeons and radiation oncologists. Therefore, data on the clinical outcome of local treatment of pancreatic oligometastases in RCC patients is relatively scarce, with a few retrospective reports but without prospective studies.

Renal cancer recurrences after radical treatment may be late. The same is true for pancreatic metastases. Antonelli et al. reported on metachronous metastases to the pancreas that occurred 8–73 months after radical nephrectomy [8]. It should be emphasized that pancreatic metastases of renal cancer are most often oligometastatic. Therefore, aggressive surgery seems to be the best option to maximize the chance of a cure. The time of follow-up in RCC patients after initial surgery of primary tumor is a subject of controversy. According to some researchers, follow-up for over 5 years is ineffective, but on the other hand, the risk of late relapse of RCC may justify long-term follow-up. Therefore, in RCC patients, the benefits of long-term follow-up must be carefully balanced against the financial costs, exposure to radiation and contrast agents, and the psychological stress associated with awaiting results of follow-up tests.

## Case report

A 59-year-old female patient with hypertension and mixed hyperlipidemia underwent a right nephrectomy in June 2006. The pathological report indicated Fuhrman II clear-cell RCC at stage T1aNxM0 [according to the 2002 Tumor, Node, Metastasis (TNM) classification]. Seven years later (August 2013), a CT scan showed a suspicious pancreatic lesion. A subsequent PET-CT scan confirmed the presence of a potentially metastatic lesion (20 × 18 mm) located in a distant part of the pancreas. Pancreatic tail resection with splenectomy was performed and histopathological examination revealed RCC metastasis. The patient was left in follow-up without any additional treatment. After another seven years (March 2020), a follow-up CT revealed a new solitary lesion (22 mm) located within the head of the pancreas, which again raised suspicion of RCC metastasis. The lesion was assumed resectable, and in April 2020, the patient underwent pancreatoduodenectomy. Histopathological examination confirmed radical resection of an RCC metastatic lesion (PAX8+ and CaIX+) not presenting signs of vascular invasion or lymph node metastases. The patient recovered quickly but required initiation of insulin therapy due to iatrogenic diabetes. One year later (August 2021), a follow-up CT revealed a solitary, ambiguous 3 mm lesion in segment 3 of the right lung and a subsequent CT (February 2022) detected three additional, ambiguous, small (3 mm) lesions in segments 3 and 9 of the right lung. All pulmonary lesions were considered too small for PET/CT verification. Due to the asymptomatic nature of the lesions, and slow dynamics, the patient was qualified for continuous active observation. Two months later (April 2022), the patient underwent an emergency appendectomy due to intestinal obstruction. The pathological report indicated adenocarcinoma G2 of the appendix (CK7+; CK20+; CDX2+; CL19+; AMACR+ pT4a L1V1 PnI1 R1). Genomic analysis of tumor samples revealed no *KRAS*, *NRAS*, *BRAF* mutations, or microsatellite instable (MSI). Subsequent colonoscopy revealed only a hyperplastic polyp but no other signs of active cancer. On a follow-up CT scan (June 2022), lung lesions remained stable, and no other signs indicating dissemination were detected. In July 2022, the patient underwent a planned right hemicolectomy that revealed lymph node metastases of colon adenocarcinoma (3 out of 12 nodes involved). The patient underwent adjuvant chemotherapy in the form of XELOX regimen (6 months). Follow-up PET/CT performed after chemotherapy (April 2023) confirmed no evidence of dissemination. The patient (ECOG = 0) remains in follow-up, has recovered from surgery and chemotherapy sequelae, and is asymptomatic except for iatrogenic diabetes requiring insulin treatment.

## Discussion and conclusions

The course of renal-cell carcinoma is generally unpredictable. Although 85% of recurrences occur within 3 years after resection [9, 10], the disease may sometimes recur even decades after primary treatment [8, 11]. In the case of our patient, distant relapse in the form of pancreatic metastasis occurred 7 years after primary surgical treatment.

The late occurrence of RCC metastases is a well-known and favorable prognostic factor [9, 12]. The pancreas generally represents a rare location of neoplastic dissemination, but up to 5% of pancreatic tumors turn out to be metastatic. The majority of metastatic lesions within the pancreas originate from RCC [9, 10, 13]. In approximately 30% of patients with pancreatic RCC metastases, dissemination is multifocal; however, it is resectable in 80% of cases [13]. The high affinity of RCC cells to the pancreatic parenchyma is confirmed by reports of late metastases, which reappeared only in the residual pancreas [10, 14].

In our patient, the first metastatic lesion in the tail of the pancreas appeared 7 years after radical nephrectomy. Partial pancreatic resection was performed to minimize the adverse effects of pancreatomy, such as secondary diabetes and other metabolic or digestive disorders. The decision to perform pancreatic conserving

surgery benefited the patient since she remained in remission for the next 7 years, with good quality of life and no treatment sequelae.

Studies suggest that in the case of isolated pancreatic metastases, the most appropriate approach is local treatment (partial resection or complete pancreatoduodenectomy), which offers a chance for long-term overall survival or even a cure with 5-year OS ranging from 29 to 35% [7, 9, 14]. Although no randomized studies have been conducted to support the role of metastasectomy in treating oligometastatic RCC, observational studies strongly support this approach. The prognosis of patients after resection of isolated pancreatic RCC metastases is relatively good with the 5-year survival rates ranging from 43% to 75%, while in non-resected patients the 3- and 5-year survival rates are 21% and 0%, respectively [14]. The most important prognostic factor in the case of our patient was the radical resection of the oligometastatic disease because it significantly deferred the need for initiation of systemic treatment which up to now (17 years after primary surgery) has not been started yet. Current Polish guidelines on the treatment of RCC strongly recommend consideration of local treatment in oligometastatic patients and active surveillance in non-resectable mRCC patients not requiring immediate initiation of systemic treatment.

Optimal local treatment of our patient with pancreatic RCC metastases and withholding systemic palliative therapy have not impacted negatively her survival or quality of life. Moreover, a wise therapeutic decision allowed the patient to remain treatment-free and to undergo radical therapy for colon cancer, which required two surgical approaches and adjuvant chemotherapy. Such a complex therapy for another primary cancer would be impossible if the patient were treated simultaneously with palliative systemic treatment for RCC.

## Article Information and Declarations

### Ethics statement

Article have been conducted according to the principles stated in the Declaration of Helsinki.

### Author contributions

J.D.: conception/design, collection and/or assembly of data, data analysis and interpretation, manuscript writing, final approval of manuscript.
P.P.: collection and/or assembly of data, data analysis and interpretation, manuscript writing, final approval of manuscript.
P.J.W.: data analysis and interpretation, manuscript writing, supervision, final approval of manuscript.

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### Conflict of interest

The authors declare no conflict of interest.

### Supplementary material

None.

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