

CASE REPORT

**RENAL CELL CARCINOMA METASTASIZING TO PANCREATIC
NEUROENDOCRINE NEOPLASM – THE SECOND CASE DESCRIBED
IN THE WORLD LITERATURE**KATARZYNA BEDNAREK-RAJEWSKA¹, PRZEMYSŁAW ZALEWSKI², DANUTA BRĘBOROWICZ³, ALDONA WOŹNIAK¹¹Department of Clinical Pathomorphology, Poznan University of Medical Sciences, Poznan, Poland²Department of Pharmaceutical Chemistry, Poznan University of Medical Sciences, Poznan, Poland³Department of Cancer Pathology, Greater Poland Center of Oncology, Poznan, Poland

Tumor-to-tumor metastases are very rare events. We report a case of a 64-year-old man who presented with a tumor of the pancreas. The patient underwent partial pancreatectomy. Frozen section diagnosis of the tumor was an endocrine neoplasm. Paraffin block slide examination revealed a tumor consisting of two components: pancreatic endocrine neoplasm at the periphery of the tumor and the central part composed of clear cells with delicate vessels. The results of immunohistochemical stains revealed renal cell carcinoma surrounded by pancreatic endocrine neoplasm, therefore representing an unusual case of renal cell carcinoma metastasizing to a pancreatic endocrine neoplasm.

Key words: tumor-to-tumor metastasis, renal cell carcinoma metastasizing to pancreatic endocrine neoplasm.

Introduction

The coexistence of multiple primary malignancies in the same patient has been frequently described in the literature, but cases of a malignant tumor metastasizing to a histologically distinct tumor, known as “tumor-to-tumor metastasis” (TTM), are extremely rare [1, 2]. Both benign and malignant neoplasms could be the recipient tumor. According to Petraki *et al.*, by 2003 only about 150 cases of TTM had been reported [3, 4].

Renal cell carcinoma is not only the most common recipient (pulmonary carcinoma is the most common donor) in tumor-to-tumor metastasis, but also the most common primary tumor metastasizing to the pancreas [5, 6].

Case report**Patient**

We report here a case of a renal cell carcinoma metastasizing to a neuroendocrine pancreatic neoplasm

in a 64-year-old Caucasian man with a past history of right nephrectomy (12 years ago).

Medical interview

The patient was admitted to the hospital for diagnosis and treatment of an asymptomatic pancreatic tumor which was discovered during routine computed tomography scan of the abdomen. Endosonography (EUS) revealed a hypoechoic lesion measuring 16 × 13 mm, localized in the pancreatic head with a vasculature characteristic for gastroenteropancreatic neuroendocrine tumors (GEP-NET), suspicious for insulinoma and a hypoechoic lesion of the left adrenal measuring 13 mm in the greatest dimension consistent with an adrenal cortical adenoma. Single-photon emission computed tomography (SPECT) using ^{99m}Tc-HYNIC-TOC revealed three foci absorbing the marker: one in the pancreatic head and the other two in the left and right adrenal glands. This suggested the neuroendocrine nature of

the pancreatic tumor, although it did not confirm the diagnosis of insulinoma (the somatostatin receptors are present in about 30-40% of insulinomas only) and adenoma of the adrenal glands.

In view of these findings the patient underwent laparotomy with the diagnosis of pancreatic nonfunctioning neuroendocrine tumor. The patient claimed that the previously removed tumor was a benign lesion, but he was not able to present any previous medical documentation or histological diagnosis. The surgeons did not consider a metastasis of the renal cell carcinoma, nor did they inform the pathology department about the previous nephrectomy.

At the time of surgery a small, firm nodule was palpable in the head of the pancreas. Partial pancreatectomy of the pancreatic head with dissection of the regional lymph nodes was performed.

Macroscopic findings

Grossly the head of the pancreas showed a well circumscribed red and yellow tumor measuring 19 mm, appearing on a background of unremarkable pancreatic parenchyma.

Microscopic findings

A frozen section evaluation of the tumor confirmed pancreatic neuroendocrine neoplasm and unremarkable lymph nodes. Slides obtained from paraffin blocks revealed tumor tissue which was very unusual and puzzling. There was a heterogenic tumor composed of two different areas. There were trabeculae, acini

and rounded solid nests formed by cells with scant cytoplasm and “salt and pepper” nuclei confirming the presence of pancreatic endocrine neoplasm which was evident at the periphery of the lesion. Tumor cells were uniform with little pleomorphism and no mitotic activity. The central part was composed of lobules and solid nests of cells with abundant clear cytoplasm and central round nuclei with prominent nucleoli. The cells were surrounded by delicate branching “chicken wire vasculature” (Fig. 1). As we were not informed about the prior clinical history of the patient at the first differential diagnosis we considered a focal clear change within pancreatic neuroendocrine neoplasm, clear cell neuroendocrine tumor of the pancreas – a rare tumor which is mostly associated with von Hippel-Lindau syndrome – and as the third possibility clear cell renal cell carcinoma. To our surprise, immunoperoxidase stains showed two distinct areas within the tumor. The peripheral part of the tumor was strongly and diffusely positive for chromogranin, synaptophysin and CD56. The Ki67 proliferative index was less than 2%. The tumor cells in the central part were negative for those markers (Fig. 2). At this point we excluded clear cell change or clear cell neuroendocrine tumor and we started considering an unusual case of renal cell carcinoma metastasizing to a neuroendocrine pancreatic neoplasm. We contacted the surgeon, asking about the full clinical data of the patient, and only then were we told about the patient’s nephrectomy. However, the surgeon strongly suggested that the renal tumor resected 12 years ago was an angiomyolipoma. Being aware about this fact,

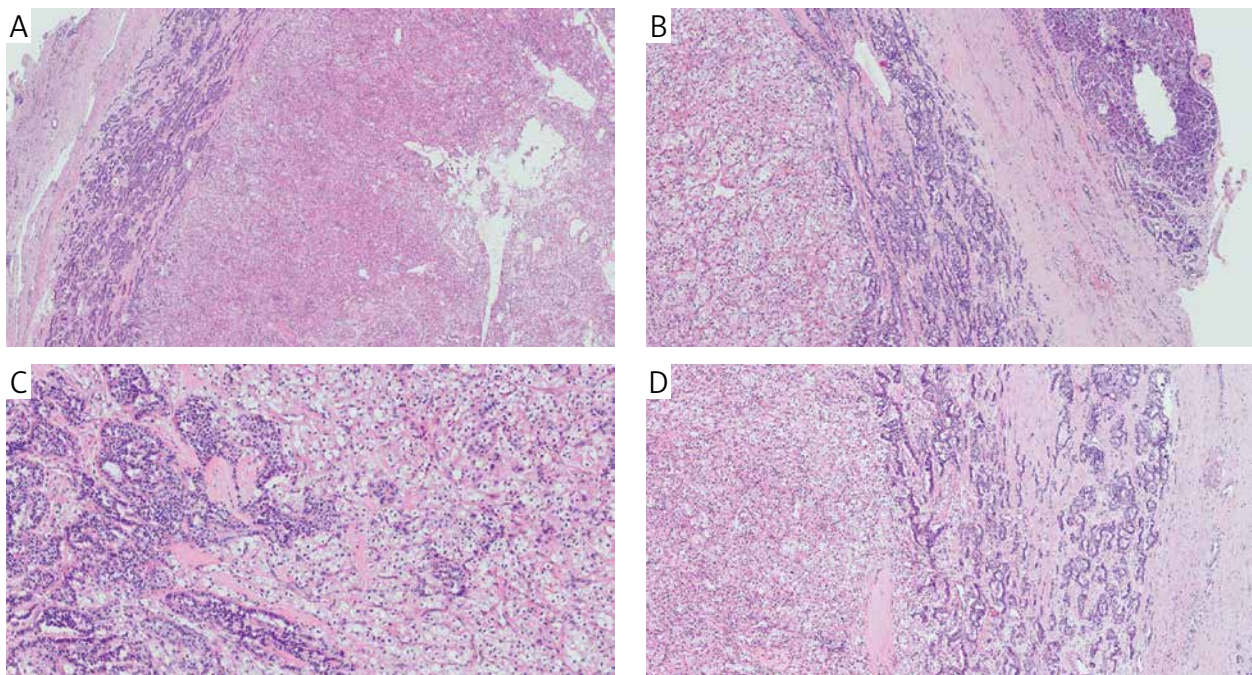


Fig. 1.

we managed to get a copy of the histological diagnosis and slides from the pathology department in the hospital where the first surgery took place. It turned out that the primary diagnosis was well-differentiated clear cell renal cell carcinoma (G1). From then we had no doubts about the diagnosis, which was confirmed by positive immunohistochemical stains for renal cell carcinoma (RCC) antigen (Fig. 3), vimentin and CD10 (Fig. 4). Finally an extremely unusual diagnosis of renal cell carcinoma metastatic to a pancreatic neuroendocrine tumor (NET) was made.

Further clinical evaluation

The postoperative course of the patient was complicated by internal arterial bleeding requiring re-laparoscopy. During the surgery the patient experienced myocardial ischemia with ECG changes. About a week after re-laparoscopy the patient developed a pancreatic fistula and gastrointestinal bleeding complicated by bacterial and fungal infections. Finally after nearly two months of hospitalization he was discharged and remained well for 12 months with no further metastasis or local recurrence.

Discussion

The presented case of a renal cell carcinoma metastasizing to a pancreatic neuroendocrine tumor represents an extraordinary example of tumor-to-tumor metastasis. To our knowledge this is the second case described in the literature, the first being described in 2011 by Cenkowski *et al.* [7]. In general, metas-

tases to the pancreas are rare phenomena and renal cell carcinoma is the most common primary tumor metastasizing to this organ [8, 9, 10]. According to Hung *et al.*, from a total of 329 cases of resected secondary malignancy of the pancreas, RCC was the primary site of origin in 73.9% of cases, with a median interval of 108 months (9 years) between resection of a primary tumor and metastasis. The average tumor size was 3.5 cm. The mechanism of occurrence of isolated pancreatic metastases has not been explained yet. It has been speculated that venous or lymphatic dissemination along with the proximity of those organs in the retroperitoneal space may play an important role in the pathomechanism of RCC pancreatic metastases. No relationship has been found between the location within the pancreas and the primary RCC. There are also speculations about the reasons why isolated pancreatic metastases from RCC are relatively frequent in the absence of metastases to other organs, one of them being special biology of RCC, another being some unexplained tissue features or special cytokines, tissue factors or genes that make the pancreas a good recipient of metastatic RCC [7, 11]. Having so many doubts about RCC metastasizing to the pancreas, it seems even more mysterious why this unpredictable tumor has metastasized to a preexisting pancreatic NET. We do hope that perhaps future research would answer these questions and in this way would help to prevent organ-specific metastases in patients with RCC.

The authors declare no conflict of interest.

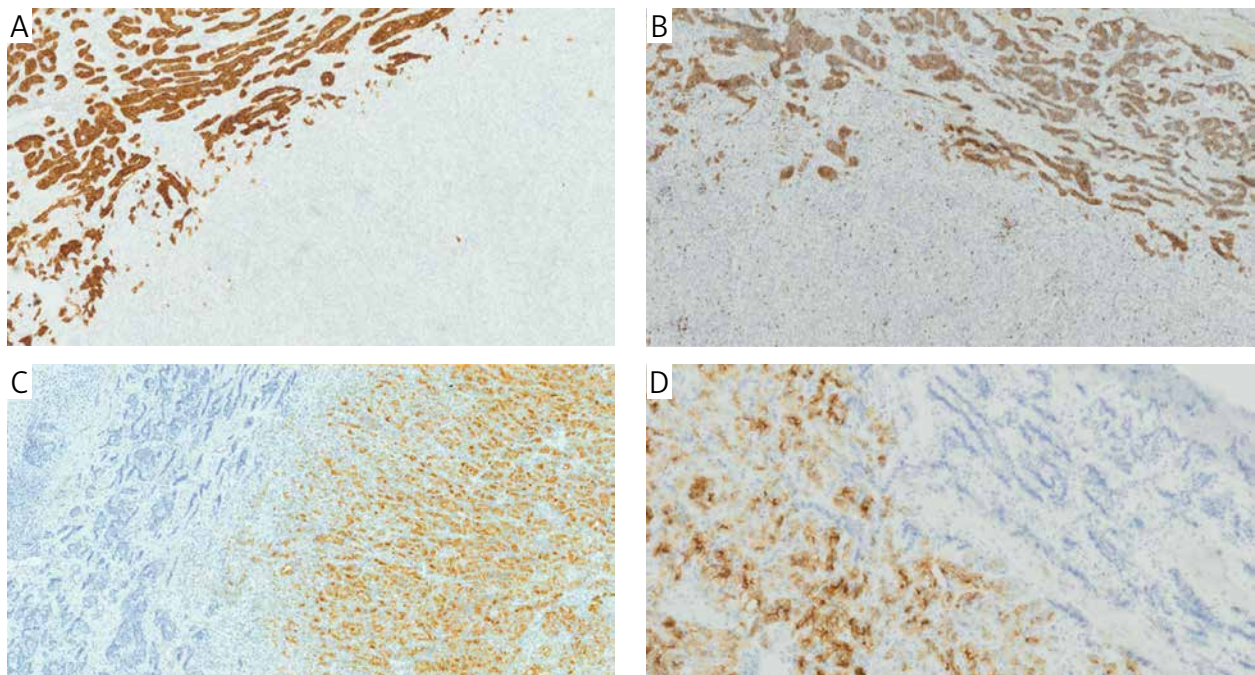


Fig. 2.

References

1. Crippa S, Angelini C, Mussi C, et al. Surgical treatment of metastatic tumor to the pancreas: A single center experience and review of the literature. *World J Surg* 2006; 30: 1536-1542.
2. Machado NO, Chopra P. Pancreatic metastasis from renal carcinoma managed by Whipple resection: A case report and literature review of metastatic pattern, surgical management and outcome. *JOP* 2009; 10: 413-418.
3. Aggarwal N, Amin R, Chung D, et al. Tumor-to-tumor metastasis: Case report of a pulmonary adenocarcinoma metastatic to a clear cell renal cell carcinoma. *Pathol Res Pract* 2012; 208: 50-52.
4. Petraki C, Vvaslamatzis M, Argyrakos T, et al. Tumor to tumor metastasis: report of two cases and review of the literature. *Int. J Surg Pathol* 2003; 11: 127-135.
5. Sella A, Ro JY. Renal cell cancer: best recipient of tumor-to-tumor metastasis. *Urology* 1987; 30: 35-38.
6. Sawada T, Takahashi H, Hasatani K, et al. Tumor-to-tumor metastasis: Report of an autopsy case of lung adenocarcinoma metastasizing to renal cell carcinoma. *Intern Med* 2009; 48: 1525-1529.
7. Cenkowski M, Gibson JW, Lategan B, et al. Tumor-to-tumor metastasis: report of a case of renal cell carcinoma metastasizing to a pancreatic endocrine neoplasm. *J Clin Oncol* 2011; 29: e303-e304.
8. Konstantinidis I, Dursun A, Zheng H, et al. Metastatic tumors in pancreas in modern era. *J Am Coll Surg* 2010; 211: 749-753.
9. Hirota T, Tomida T, Iwasa M, et al. Solitary pancreatic metastasis occurring eight years after nephrectomy for renal cell carcinoma. *Int J Pancreatol* 1996; 19: 145-153.
10. Ghavamian R, Klein KA, Stephens D, et al. Renal cell carcinoma metastatic to the pancreas: clinical and radiological features. *Mayo Clin Proc* 2000; 75: 581-585.
11. Hung JH, Wang SE, Shyr YM, et al. Resection for secondary malignancy of the pancreas. *Pancreas* 2012; 41: 121-129.

Address for correspondence

Katarzyna Bednarek-Rajewska
 Department of Clinical Pathomorphology
 Poznan University of Medical Sciences
 Przybyszewskiego 49
 Poznan, Poland
 tel. +48 61 869 14 66
 fax +48 61 869 15 09
 e-mail: patomorfolog.kbr@gmail.com