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Case Report

An Unusual Presentation of Tumor-to-Tumor Metastases from Renal Cell Carcinoma to Pancreatic Neuroendocrine Tumor: A Case Report and Review of the Literature

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Abstract

Tumor-to-tumor metastases are rare, and very few cases have been reported in the literature. We present an unusual case of renal cell carcinoma metastasizing to a well-differentiated pancreatic neuroendocrine tumor. A male patient in his early seventies presented with vague, generalized abdominal pain and diarrhea for 3 months. Four years earlier, the patient was diagnosed with a pancreatic neuroendocrine tumor (PanNet) and was treated conservatively. At the time of the current presentation, contrast-enhanced computed tomography revealed that the size of the PanNet had increased, and most importantly, presence of a heterogeneously enhancing irregular mass in the upper pole of the right kidney. Histopathology of pancreatic mass biopsies revealed metastatic clear cell RCC and a well differentiated grade 2 neuroendocrine tumor. Due to his general fragility, and clinical worsening, the patient could not receive RCC management and was sent to palliative care. Our case exemplifies the difficulties in diagnosing and managing TTM including hyper vascular tumors such as PanNet and RCC.

Keywords: *Multiple Tumors; Renal Cell Carcinoma; Pancreatic Neuroendocrine Tumor; Tumor-to-Tumor Metastases*

Abbreviations

CT: Computed Tomography; EUS: Endoscopic Ultrasound; PanNet: Pancreatic Neuroendocrine Tumor; RCC: Renal Cell Carcinoma; TTM: Tumor-to-Tumor Metastases

Introduction

Tumor-to-tumor metastases (TTM), in which primary tumor cells metastasize to other tumors, is a rare condition that presents significant diagnostic and management challenges. To qualify as a TTM, both host and guest tumors must be the primary, the host tumor must not be the result of a collision or embolization, the recipient tumor must be a true neoplasm, and the donor tumor (metastatic) must display growth in the guest [1,2].

Accurate diagnosis of TTM is complicated because identifying all four TTM criteria requires extensive histopathologic analysis and imaging investigations are often ambiguous. In most cases, TTM is recognized using excision specimens and a previous history. Lung cancer is the most frequent donor tumor, whereas renal cell carcinoma (RCC) is the most common receiver tumor [3], suggesting the role of organ specific metastases in TTM.

PanNets represent a rare type of pancreatic malignancy, accounting for about 1% of all cases of pancreatic cancer [4]. PanNets are often diagnosed late and present with various complexities [5]. The key rationale for a conservative approach is the inherent mortality risk in surgical treatments, such as pancreatico-duodenectomy and late diagnosis when resection is not feasible. On the other hand, RCC is a malignant tumor that arises from renal epithelial cells that account for most kidney malignancies and is treated by nephrectomy when possible. Compared to metastases to the liver, lung, adrenal gland, bone or brain, RCC metastases to the pancreas are rare and account for 2% to 5% of all malignant pancreatic tumors [6]. TTM has been described in approximately 150 cases, however, TTM involving PanNet (host) and RCC (guest) is exceedingly rare, with only three published cases. In the context of TTM, the differential diagnosis of hyper vascular pancreatic lesions is complex and encompasses pancreatic exocrine and endocrine tumors, masses or mass like lesions emerging in the pancreas.

We present an exceptionally unusual case of TTM in which RCC metastasized to a preexisting PanNet. In particular, unlike previous reports on TTM, including PanNet (host) and RCC (guest), in our case, only PanNet was found in the initial presentation. In this case report, we will discuss notable imaging findings, pertinent differential diagnosis and literature is reviewed.

Case Report

A male patient in his early seventies presented to our gastroenterology department with generalized abdominal pain and diarrhea for 3 months. He had history of type 2 diabetes mellitus, osteomyelitis of the spine and cirrhosis. He was a non-smoker and denied regular use of alcohol. His family history was unremarkable.

Approximately 4 years earlier, the patient presented with vague abdominal discomfort and at the time, EUS showed a 52 x 40 mm irregular hypoechoic, heterogeneous, and mixed solid and cystic mass in the pancreatic neck (Figure 1a), which was found to be a grade 1 PanNet (Figure 1b). The work-up for metastases at the time was negative, including diagnostic laparoscopy, which ruled out carcinomatosis. Consequently, no surgical resection was performed. A contrast-enhanced CT scan of the abdomen at the current admission revealed a 77 mm x 60 mm pancreatic neck mass that appeared significantly enlarged from 4 years back. CT also showed a 52 x 49 mm heterogeneously enhancing mass in the upper pole of the kidney, which was not reported in the initial presentation four years ago (Figure 2). Per imaging studies, the enlargement in the pancreatic mass could be due to metastases vs due to a functional primary PanNet that has increased in size.

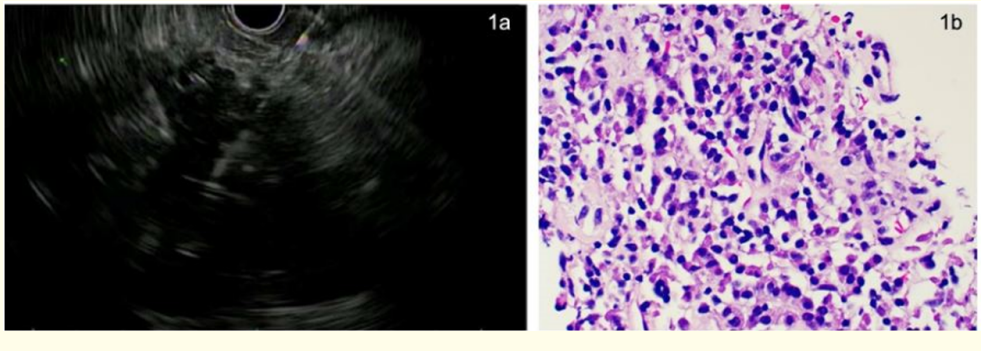

Figure 1: *Endoscopic ultrasound showing pancreatic mass (1a) which was grade 1 PNET on biopsy (1b).*

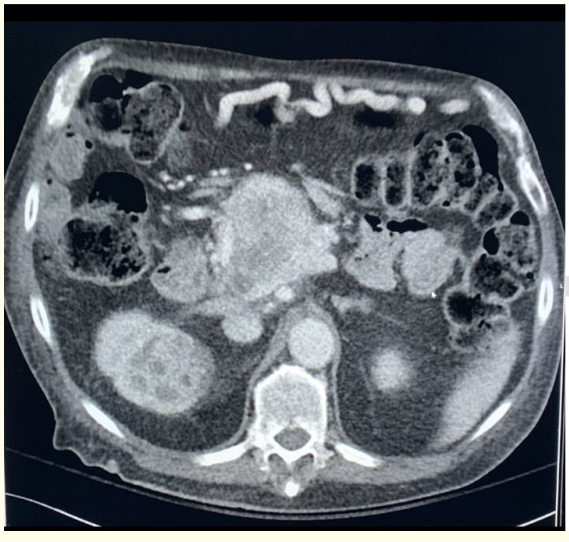

Figure 2

An EUS aspiration-biopsy was performed on the pancreatic mass and the specimen was sent to histopathology department. On histologic evaluation, two distinctly different tumor types were observed, one with clear cell features and the other with traditional neuroendocrine morphology (Figure 3). Immunohistochemical stains have been obtained, and the tumor cells in the RCC component were positive with antibodies against PAX8, CD10 while negative with CK7, Synaptophysin and Chromogranin. The tumor cells in the PanNet were positive with antibodies against CK7, Synaptophysin and Chromogranin while negative with renal cell markers including PAX-8 and CD10 confirming morphologic impression of metastatic clear cell RCC to a well differentiated primary pancreatic neuroendocrine tumor.

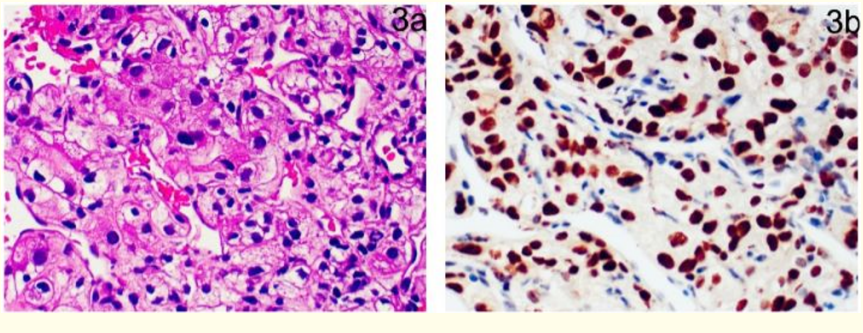

Figure 3: *EUS specimen showing RCC metastases (H&E) and PAX8 stain.*

Discussion

TTM is a rare clinical entity involving the propagation of one neoplasm (donor) to a histologically distinct primary tumor (recipient) [3]. So far, only 3 cases of PanNet as a recipient tumor for metastases from a RCC have been reported [7]. In this current study, we describe a case of TTM involving PanNet as a recipient tumor for metastases from RCC diagnosed on EUS cytology specimen (Table 1).

Reference	Age/sex	Duration in months to TTM	Intervention
Cenkowski., *et al*. 2011	53m	2	Left Nephrectomy and partial pancreatectomy
Bednarek-R., *et al*. 2017	64m	12	Nephrectomy and partial pancreatectomy
Minezaki., *et al*. 2022	72m	Unknown	Nephrectomy and subtotal Whipple procedure
Current Case	72m	4	None

Table 1: *Summary of the literature on TTM from RCC to PanNet.*

Cenkowski., *et al*. [7] reported the first case of TTM involving PanNet as a recipient tumor for RCC metastases in a man in his early 50s presenting with painless hematuria. The kidney tumor was detected first and resected by radical nephrectomy. However, two years later, PanNet was detected in this patient with well-defined nodules of metastatic RCC. In the second case, a patient in his 60s was admitted for the treatment of an asymptomatic pancreatic tumor discovered during routine medical examination. In particular, at the time of admission, no previous malignancy was reported. Immuno-peroxidase stains showed two distinct areas within the tumor with three histologic characteristics: (i) clear cell change within the PanNet, (ii) Clear cell PanNet (as commonly observed in VHL), and (iii) clear cell RCC. Thorough evaluation of patient's chart for medical history revealed that the patient had angiomyolipoma 12 years ago, which was managed by nephrectomy. However, re-evaluation of previous surgical records and biopsy specimens, the diagnosis was revised to a well differentiated clear cell RCC. These revelations prompted the authors to make diagnosis of RCC metastatic to a PanNet [8]. Minezaki, Misawa., *et al*. [9] in 2002 reported the third case of RCC metastasis to PanNet that was managed by nephrectomy and stomach preserving pancreatico-duodenectomy.

Our case, the fourth of its kind, is unique in several aspects. At first presentation, 4 years prior, only PanNet was diagnosed and treated conservatively. In the current presentation, RCC metastasis was detected in association with PanNet on biopsy material from EUS aspiration and not on surgically resected specimens which is unique to our case. It should be noted that PanNets are often discovered as tiny tumors of 2 cm or less, and preoperative imaging makes the diagnosis of TTM difficult. However, in our study, the PanNet was much larger. The diagnosis of TTM could have been missed if an extensive histopathologic examination had not been performed. Taking into account the general physical and mental health of the patient, no intervention was initiated and the patient was referred to palliative care. At the first presentation, we opted for a conservative approach due to no revelation of metastases and invasion into vasculature.

In general, metastases to the pancreas are rare, and RCC is the most common primary tumor metastasizing to this organ [10]. The mechanism of pancreatic metastases from RCC is yet unknown, however, hematogenous metastases through collateral arteries or lymphatic metastases is suspected to play a role [11]. Organ specific metastases can be understood by paying particular attention to predicted gene signatures and metastasis-specific mediators [12]. In this scenario, RCC cells were more likely to move into the PanNet than into normal pancreatic tissue, indicating the probability of hematogenous spread.

Conclusion

This study describes a rare case of TTM involving metastases to PanNet from RCC. Our case was remarkable because PanNet was diagnosed at first presentation while RCC was not observed. Our case was also unique that the diagnosis of TTM on EUS aspirated material only. Our case also highlights that, before deciding on conservative management of PanNet, it is crucial to carefully rule out other malignancies. More studies are needed to fully understand TTM involving hyper vascular organs and to allow faster diagnosis and timely treatment.

Conflict of Interest

None.

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