



## Oncology

# Metastatic rectal neuroendocrine tumor to kidney, pancreas, and bone following renal tumor resected with robot-assisted laparoscopic partial nephrectomy

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## ABSTRACT

Neuroendocrine tumor (NET) is a rare tumor commonly found in the gastrointestinal tract and lungs and rarely originates from and metastasizes to the kidney. We report a case of a 66-year-old man with metastatic rectal NET to the kidney, pancreas and bone following the resection of renal tumor with robot-assisted partial nephrectomy (RAPN). A rectal tumor of 10mm in diameter had been endoscopically resected and diagnosed NET with positive surgical margin 9 years before RAPN. Somatostatin receptor (SSR) scintigraphy revealed the other two metastases postoperatively, therefore is an effective tool to detect primary and metastatic sites of NETs.

## 1. Introduction

Neuroendocrine tumor (NET) is a rare tumor arising from neuroendocrine cells and is commonly found in the gastrointestinal tract, pancreas, and lungs. NETs in the genitourinary tract account for less than 1% of all NETs, among them the kidney is an extremely rare site accounting for 5–19% of them.<sup>1</sup> Metastatic renal NETs from other primary organ are even rarer. We report here a case of metastatic rectal NET to kidney, pancreas, and bone following a partial resection of a renal tumor by robot-assisted laparoscopic partial nephrectomy (RAPN).

## 2. Case presentation

A 66-year-old man presented to our hospital with a 12 mm right renal tumor which was incidentally revealed at a follow-up computed tomography (CT). He had a history of rectal primary NET 9 years before and early gastric cancer 5 years before his visit to our department. He also had a history of hypertension and prescribed antihypertensive medication. He was asymptomatic, and showed no significant abnormalities in blood and urine tests. Urine cytology was class II. Abdominal ultrasound showed the tumor was highly echogenic with poor blood flow. Contrast-enhanced CT showed the mass was 12 mm in diameter with mild contrast enhancement. Magnetic Resonance Imaging (MRI)

showed a capsular structure in T2-weighted image and a high signal inside the mass in diffusion-weighted imaging (Fig. 1).

Initial diagnosis with imaging modalities was renal cell carcinoma, and RAPN was performed. The resected tumor has a diameter of 15.0 × 10.0 mm with tan-color. Pathological examination showed cells with round nuclei forming a cording structure, which was atypical for renal carcinoma. Immunostaining was added to further analyze the characteristics of the tumor. The tissue was positive of synaptophysin and CD56 with several areas positive of chromogranin A. The proliferative index of the tissue was provided by Ki-67 labeling was up to 5%. These findings introduced the diagnosis of a grade 2 NET (Fig. 2). After the diagnosis of NET, somatostatin receptor (SSR) scintigraphy using <sup>111</sup>In-octreotide was performed to detect other metastatic sites. It showed multiple concentrations in the pancreatic head and bone. There evoked a question that the primary site being the pancreas or rectum (Fig. 3). Fine needle aspiration (FNA) of the pancreatic tumor was performed at the gastroenterology department in our hospital and the pathological diagnosis was NET similar to renal tumor, except for the negative immunostaining of chromogranin A. The endoscopically treated rectal NET had been followed up for nine years because it had positive surgical margins. Based on the above findings, we concluded that renal, pancreatic, and multiple bone metastatic recurrence of rectal NET had occurred in this patient. Everolimus, an mTOR inhibitor, was started for the treatment of these metastatic NETs.

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Abbreviations	
NET	neuroendocrine tumor
CT	computed tomography
MRI	magnetic resonance imaging
RAPN	robot-assisted partial nephrectomy
SSR	somatostatin receptor
FNA	fine needle aspiration

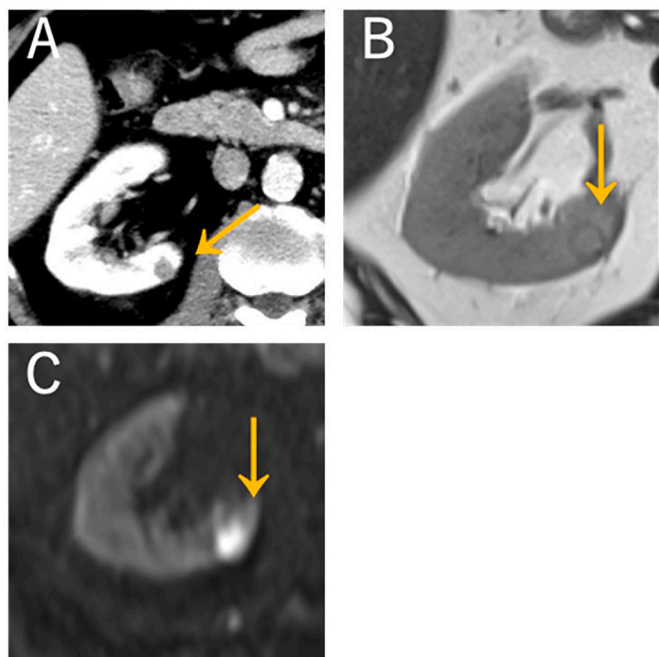


Fig. 1. Contrast-enhanced CT showed the right renal mass with mild contrast enhancement, (A) and MRI showed a capsular structure on the T2-weighted image (B) and a high signal on diffuse water imaging (C).

### 3. Discussion

Primary renal NETs are extremely rare, accounting for only 0.05–0.4% of NETs. The reason is the absence of neuroendocrine cells in normal renal pelvic tissue.<sup>1</sup> Renal metastasis of primary NETs in other

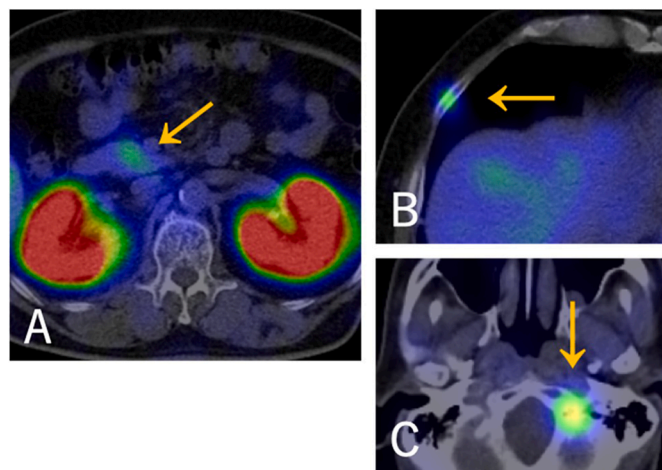


Fig. 3. SSR scintigraphy showed multiple concentrations in the pancreatic head (A), right 6th rib (B), C1 vertebrae (C).

organs is even rarer than primary renal NETs. The most common metastatic site of NET is the liver, and the exact incidence of renal metastasis is unknown.<sup>2</sup> In our hospital, 230 patients underwent RAPN between August 2016 to January 2023, and this was the only case diagnosed as a neuroendocrine tumor histopathologically.

Only three metastatic renal NET cases have been reported in the literature.<sup>2–4</sup> Two of the three cases were metastases from rectal NETs, and two cases had a history or comorbidity of liver metastases. Our case showed renal metastasis from a rectal NET, but lacked liver metastasis.

We retrospectively examined the possibility of exact preoperative diagnosis and the appropriateness of partial nephrectomy in this case. The patient was asymptomatic and preoperative contrast-enhanced CT and MRI failed to detect a pancreatic and multiple bone metastases. The NCCN guidelines of NET recommend resection of resectable metastatic lesions, so we believe that RAPN was the appropriate treatment in this case.<sup>5</sup> The former reports of metastatic renal NETs were also surgically resected and confirmed the diagnosis.

When NETs are diagnosed postoperatively, it is important to identify whether they are primary or metastatic. In NCCN guidelines, SSR-based imaging is recommended, especially SSR-Positron Emission Tomography (SSR-PET) using <sup>111</sup>In-octreotide.<sup>5</sup>

We could use only SSR scintigraphy in our hospital, however, it was effective to diagnose pancreatic and bone metastasis. SSR scintigraphy was performed only in the case reported by Tal et al. to identify the cervical tumor as metastatic NET.<sup>3</sup> Since a preoperative diagnosis of metastatic renal NET is often difficult, it is the most important to identify

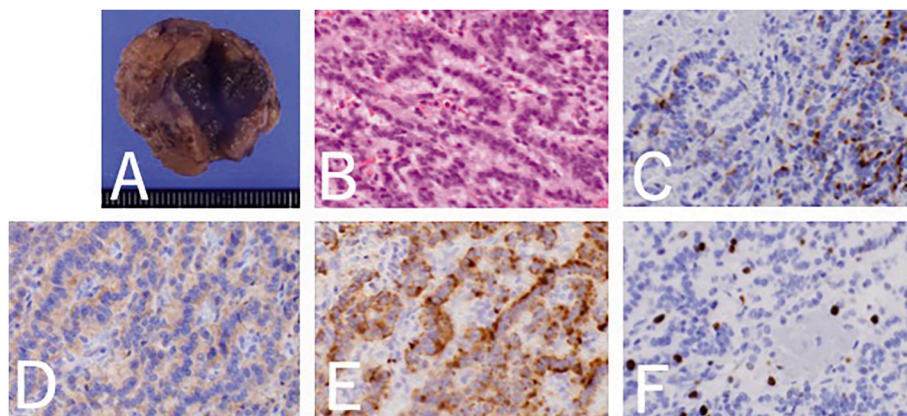


Fig. 2. (A) The gross specimen of the tumor measured 15.0 mm × 10.0 mm × 10.0mm. (B) The histological features of hematoxylin and eosin staining. Immunohistochemical staining for tumor cells positive for neuroendocrine markers including chromogranin A (C), synaptophysin (D), CD56 (E) and Ki67 (F).

primary or other metastatic sites and provide appropriate therapeutic intervention. NETs are thought of as a relatively benign character and follow an indolent course, but there is a clear risk of local and distant metastases associated with mortality. The size of the primary tumor is important, traditionally, 10mm, 10–20mm, and >20mm are used to classify neuroendocrine tumors to predict the risk of spread and for guiding the proper management. The size of the tumor being 10mm in diameter, pT stage, and lymphovascular invasion were independently associated risk of metastatic disease, however, none was applied to this case. The only meaningful information from the primary rectal NET was that it was resected endoscopically with positive surgical margin.

#### 4. Conclusion

Metastatic renal NETs are rare and difficult to diagnose preoperatively because of the absence of symptoms and its indolent clinical course. Imaging studies using SSR are effective in search of primary and metastatic sites, and useful to proceed with appropriate therapeutic interventions.

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#### Author agreement

All authors have approved the final version of the manuscript.

#### Author statement

Norifumi Sawada, the corresponding author, is responsible for ensuring that the descriptions are accurate and agreed by all authors. The roles of all the authors are listed as follows. Mayuko Kusuda: Conceptualization, Investigation, and Writing Original draft preparation, Norifumi Sawada: Writing, Reviewing, Editing, and Supervision, Junki Aikawa: Data curation and Conceptualization, Koki Sugimura: Validation and Data curation, Satoru Kira: Validation, Visualization, and Supervision, Takahiko Mitsui: Editing and Supervision.

#### Declaration of competing interest

The authors declare no conflict of interest.

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