CASE REPORT

Renal neuroendocrine tumour and synchronous pancreas metastasis: histopathological diagnosis using prostatic acid phosphatase

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SUMMARY

A woman aged 56 years developed 2 synchronous tumours: one, 1.2 cm in diameter at the head of the pancreas; and the other, 4.0 cm in diameter, at the left side of her horseshoe kidney. Preoperative differential diagnosis of these hypovascular lesions included pancreatic ductal carcinoma (PDC) with renal metastasis, PDC with renal angiomyolipoma, renal cell carcinoma with pancreatic metastasis or PDC and renal cell carcinoma. Following pancreaticoduodenectomy and left nephrectomy, both specimens were diagnosed as grade 2 neuroendocrine tumours (NETs). Immunohistochemistry revealed that both were positive for prostatic acid phosphatase (PAP), which is specific to hindgut-derived NET, including renal NET. Accordingly, the renal tumour was diagnosed as the primary lesion, and the pancreatic tumour as a metastasis. To the best of our knowledge, this is the first report of a renal NET with a synchronous pancreas metastasis. Immunohistochemical staining for PAP was a useful diagnostic marker for synchronous NETs in the kidney and pancreas.

BACKGROUND

The diagnoses of two concurrent tumours in the kidney and the pancreas can include primary pancreatic cancer with renal metastasis, double cancer of the kidney and pancreas and combinations of benign and/or malignant neoplasms in the two organs. Types of pancreatic tumours include ductal adenocarcinoma, neuroendocrine tumour (NET), intraductal papillary mucinous neoplasm and acinar cell carcinoma; whereas types of renal tumours include renal cell carcinoma, renal squamous cell carcinoma and renal angiomyolipoma.

Pancreatic NET is a rare disorder, with annual incidence in the USA estimated at 2.2 cases per 1 000 000 individuals.¹ Renal NET is even rarer, with only 97 cases reported worldwide to date,² with many of these patients showing metastases to the lymph nodes, liver, lungs and/or bones.³ To the best of our knowledge, however, renal NET metastasis to the pancreas has not been previously documented. Here, we describe a patient with renal NET and pancreatic metastasis, diagnosed by immunohistochemical staining.

CASE PRESENTATION

An asymptomatic, woman aged 56 years who presented with two tumours, one at head of the pancreas and the other on the left side of her horseshoe kidney, was admitted for surgery.

Enhanced CT scan showed that these tumours were 1.2 and 4.0 cm in diameter, respectively. Both tumours were slightly enhanced in arterial phase (30 s after injection of contrast material), and iso-dense in equivalent phase (90 s after injection; figure 1A–C), and both were hypoechoic on endoscopic ultrasonography (figure 1D). No distant metastases were identified by preoperative modalities, including positron emission tomography (figure 1E).

DIFFERENTIAL DIAGNOSIS

Differential diagnosis of these hypovascular tumours included (1) pancreatic ductal carcinoma (PDC) with renal metastasis, (2) PDC and renal angiomyolipoma, (3) renal cell carcinoma with pancreatic metastasis and (4) PDC and renal cell carcinoma.

TREATMENT

The patient underwent pancreaticoduodenectomy and left nephrectomy because of the potential for pancreatic and renal malignancy. Her postoperative course was uneventful and she was discharged from the hospital after 14 days.

OUTCOME AND FOLLOW-UP

Macroscopically, the resected renal and pancreatic tumours were 45 and 18 mm in diameter, respectively (figure 2). The renal tumour was capsulised and lobulated, and contained haemorrhage and calcification. The pancreatic tumour was irregular in shape. Both tumours were histopathologically diagnosed as grade 2 NET using the WHO classification, which is based on positive staining for chromogranin A, synaptophysin and CD56. The renal and pancreatic tumours had a high number of mitoses (2–20 and 10, respectively, per high-power field) and high Ki-67 indices (13.8% and 17.9%, respectively). Both tumours were positive for prostatic acid phosphatase (PAP), which is specific to renal NET (figure 2). Based on these findings, the renal tumour was diagnosed as the primary lesion, and the pancreatic tumour as a synchronous metastasis.

The patient was followed-up at an outpatient clinic, without adjuvant chemotherapy. Twenty-seven months after surgery, she experienced a recurrence in the remnant pancreas, and two metastases in the left lateral section of the liver. The remnant pancreas was resected, and the liver metastases removed by two wedge resections. Both

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Figure 1 Imaging modalities, showing synchronous double tumours of the pancreas and at the left side of a horseshoe kidney. (A) Axial enhanced CT scan, showing a homogeneous tumour in the pancreatic head (arrowhead), which was slightly enhanced in the arterial (left) and portal (middle) phases 30 and 45 s, respectively, after injection of contrast material, and isodense in the equivalent phase (right), 90 s after injection. (B) Axial enhanced CT, showing a second tumour on the left side of the horseshoe kidney, with enhancement pattern similar to that of the pancreatic head tumour. (C) CT scan showing a horseshoe kidney. (D) Endoscopic ultrasonography, showing hypoechoic lesions in the pancreas head and on the left side of the horseshoe kidney. (E) F18-fluorodeoxyglucose-positron emission tomography (FDG-PET), showing uptake of F18-FDG by the renal tumour (maximum standardized uptake value, 2.8), but not by the pancreatic tumour.

of the liver lesions were histopathologically diagnosed as metastases of renal NET by positivity for PAP. A CT scan 3 months after the second surgery showed no evidence of tumour recurrence.

DISCUSSION

Synchronous double tumours were identified in this patient, one on the pancreas and the other on the left side of a horseshoe kidney. Both were histopathologically diagnosed as renal NET, with the synchronous pancreatic metastasis confirmed by immunohistochemical staining of chromogranin A, synaptophysin, CD56 and PAP. PAP positivity was useful to show that the primary site was the kidney, not the pancreas. To the best of our knowledge, this is the first report of a patient with renal NET and a synchronous pancreas metastasis.

NETs are hypervascular tumours with a rich capillary network that usually appear highly enhanced in the arterial and venous phases of CT.⁴ Renal NETs have been reported on a background of other renal abnormalities, including horseshoe kidney (18%), renal teratoma (14%) and polycystic kidney disease (2%). Renal NETs often contain components of small cell carcinoma, urothelial carcinoma, squamous cell carcinoma and adenocarcinoma.^{2 5 6} Although the renal NET in this patient developed in a horseshoe kidney, the lesion was not pre-operatively diagnosed as renal NET because of its atypical CT images. The kidney and pancreatic tumours were immunohistochemically diagnosed as NETs, with both being strongly and diffusely positive for chromogranin A and synaptophysin. The

renal tumour contained no other neoplastic components, a characteristic typical of renal NET. Therefore, before testing for PAP, this patient was regarded as having a pancreatic NET with a renal metastasis rather than a renal NET with a pancreatic metastasis.

Renal NETs are extremely rare, accounting for <1% of all NETs. Rather, NETs usually originate from the gastrointestinal system (74%), including the pancreas (7%), or the respiratory system (25%).^{2 7} Positive immunostaining of both tumours for PAP, along with the presence of a horseshoe kidney, confirmed our diagnosis.^{2 7} Although NETs of any origin are positive for chromogranin A and synaptophysin, hindgut-derived NETs have been reported positive, whereas foregut-derived and midgut-derived NETs have been reported negative, for PAP.^{8 9} Since the kidneys are derived from the hindgut and the pancreas from the foregut, this patient was diagnosed as having a renal NET with a synchronous pancreatic metastasis.

Surgery is the first-line treatment for resectable NET with metastasis.^{3 10} Resection of NET liver metastases has been found to improve long-term outcomes, with 5-year survival rates of 60–70%.^{3 10 11} Although adjuvant chemotherapy and hormonal therapies for renal NET have not been established, inhibitors of the mammalian target of rapamycin and of vascular endothelial growth factor have been evaluated clinically.¹² This patient did not receive adjuvant therapy, but showed recurrence 27 months after surgery. The remnant pancreatic and liver metastases were resected, based on reports supporting the resection of NET liver metastases.¹⁰

Figure 2 Macroscopic view of the specimens and positive immunostaining for prostatic acid phosphatase (PAP). (A) The renal tumour was 45 mm in diameter. (B) Microscopy images show a high nuclear/cytoplasmic ratio, low mitosis and scattered vessels, findings typical of neuroendocrine tumours. (C) The pancreatic tumour was 18 mm in diameter. (D) Pancreatic microscopy findings were similar to those of the renal tumour. (E–H) Immunohistochemistry showing that the pancreatic tumour cells were positive for chromogranin A (E), synaptophysin (F), CD56 (G) and PAP (H).

In conclusion, this is the first case, to the best of our knowledge, of a renal NET with a synchronous pancreatic metastasis to be identified. PAP was useful in determining the primary site of these two NETs.

Learning points

- ▶ This is the first reported case of a renal neuroendocrine tumour (NET) with a synchronous pancreatic metastasis.
- ▶ Hindgut-derived NETs are positive, whereas foregut-derived and midgut-derived NETs are negative, for prostatic acid phosphatase.
- ▶ Prostatic acid phosphatase is useful for the diagnosis of renal NET derived from the hindgut.

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Competing interests None declared.

Patient consent Obtained.

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