CASE REPORT

Primary renal carcinoid tumour with lung metastasis misdiagnosed as renal cell carcinoma

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Accepted 26 November 2015

SUMMARY

A 58-year-old man with a history of metastatic renal cell carcinoma (RCC) diagnosed 10 years prior, status post right nephrectomy, presented for evaluation of pulmonary nodules. A year after the nephrectomy, he had undergone cutaneous metastasectomy in the right flank area, and a further 2 years later he had had his second cutaneous metastasectomy in the right chest wall. Both cutaneous pathologies had, at the time, shown metastatic neoplasm with histological features compatible with those of the previous renal tumour. He was treated with sorafenib. 3 years later he developed asymptomatic pulmonary nodules, which gradually doubled in size over the next 2.5 years. He underwent bronchoscopy and left lower lobe biopsy. Pathology revealed a metastatic renal carcinoid/neuroendocrine tumour. Second review of the previous renal neoplasm and the cutaneous metastatic pathology showed trabecular architecture, consistent with carcinoid, but mimicking the long parallel arrays that have been described in some cases of papillary RCC.

BACKGROUND

Carcinoid tumours are slow growing malignant tumours that most commonly arise in the lungs and gastrointestinal system. Primary renal carcinoid tumour (RCT) is extremely rare, with only 100 cases reported in the literature. These tumours may have morphological features that mimic those of a much more common primary renal tumour—papillary renal cell carcinoma (RCC). Once considered, the diagnosis of renal carcinoid is readily confirmed by immunohistochemical studies. Greater awareness of this entity among clinicians and pathologists would improve recognition and accurate diagnosis. We present a case of metastatic RCT that was initially diagnosed as RCC.

CASE PRESENTATION

A 58-year-old man was referred to us for a second opinion regarding management of metastatic RCC.

The patient had presented with vague epigastric discomfort 10 years earlier. Abdominal CT at the time showed a large renal mass. He underwent right nephrectomy and was diagnosed with RCC, mixed papillary and granular cell type, with focal sarcomatoid features, Fuhrman nuclear grade 4, 4.5 cm in greatest dimension, extending to the perinephric fatty tissue, with angiolymphatic invasion. One year later, he underwent cutaneous metastasectomy in the right flank, for local recurrence. The pathology of the subcutaneous nodule showed histological features compatible with those of the

previous renal tumour, and the patient was treated with sorafenib for 7 months. Two years later, he underwent another cutaneous metastasectomy in the right chest wall. The pathology again showed metastatic neoplasm with similar features, involving a lymph node in the subcutaneous tissue. He was restarted on sorafenib for another 8 months.

Three years later he developed asymptomatic pulmonary nodules in the right lower lobe (7 mm) and left infrahilar regions of the lung (12 mm), which gradually doubled in size over the next 2.5 years. He underwent bronchoscopy and left lower lobe biopsy. Pathology revealed a metastatic renal carcinoid/neuroendocrine tumour with low-grade histology, without mitotic activity (figure 1A). Immunohistochemistry was positive for CAM5.2, synaptophysin and chromogranin, and negative for cytokeratin 7, PAX-2 and PAX-8 (figure 1B). On review, the renal neoplasm in most areas showed a trabecular architecture, consistent with carcinoid, but mimicking the long parallel arrays that have been described in some cases of papillary RCC¹ (figure 1C). Focally tightly packed trabeculae arced around the vessels and stroma mimicking the fibrovascular cores of a papillary neoplasm (figure 1D). Morphology and immunohistochemistry, retrospectively performed on the previous renal tumour, and metastatic lesion of right chest wall (figure 1E) was concordant with that in the pulmonary metastasis. Serum chromogranin A was 4 (reference range 0–5). An expert pathologist consultation yielded the same diagnosis.

OUTCOME AND FOLLOW-UP

Three months after the bronchoscopy, the patient presented with haemoptysis. A follow-up CT scan of the chest, abdomen and pelvis showed a left lower lobe mass as well as a pancreatic mass. Both biopsies confirmed carcinoid metastasis with histological features similar to the previous samples. The patient then underwent a left lower lobe lobectomy. Although he does not have symptoms suggestive of pancreatic or bile duct obstruction at this point, he will be scheduled for elective partial or total pancreatectomy to prevent such complications. Also, he has been started on a somatostatin analogue—lanreotide—to try to control the tumour growth.

DISCUSSION

Carcinoid tumours are rare malignant tumours that arise from neuroendocrine cells. Primary RCT is extremely rare because neuroendocrine cells are not found within normal renal parenchyma.² It was first described in 1966 by Resnick *et al.*³ Almost

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To cite: Daboul N, Monga D, Bunker M. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-213432

Figure 1 (A) Lung biopsy. Trabecular arrangement of cells with uniform round nuclei and absent mitotic activity (H&E 200×). (B) Tumour is strongly positive for chromogranin (200×). (C) Original nephrectomy with trabecular architecture similar to that of lung metastasis (200×). (D) Original nephrectomy with papillary-like pseudorosette formation (H&E 200×). (E) Chest wall metastasis with partial pseudorosette formation (H&E, 200×).

100 cases have been documented in the literature since then.⁴ RCT had a distinct entry in WHO classification in 2004.⁵ Mean age of presentation is 48 years, and there is no significant sex predominance. Both sides are affected equally.⁶ Pathogenesis is unknown. Theories include acquired/congenital abnormalities such as misplaced or entrapped neural crest or pancreatic tissue in the kidney during embryogenesis, activation of gene sequences common to neuroendocrine programmed cells in multipotent stem cells and metaplasia of pelvicalyceal urothelium induced by chronic inflammation.⁷ RCT is associated with horseshoe kidney (17.8%), teratoma (14.3%) and polycystic kidney disease (1.8%).⁸ It may present as an asymptomatic incidental finding in 25–30% of cases. Most common symptoms are abdominal pain, haematuria, constipation, urinary frequency, fever, epigastric discomfort, weight loss and abdominal mass.⁶ The clinical course is difficult to predict due to the rarity of the disease. Neuroendocrine syndromes of carcinoid, Cushing and

Verner Morrison types, are rarely (12.7%) found.⁸ Imaging work up includes ultrasound, CT scan and MRI, none of which reliably distinguishes RCT from RCC. Misdiagnosis with RCC or Wilms tumour has been reported in 15% of cases.⁹ Diagnostic work up includes somatostatin receptor scintigraphy (SRS) and chromogranin A (CgA). Both are useful tools in the evaluation of metastasis, with SRS being more sensitive, specific and accurate than CgA.¹⁰ The most common histological pattern is the trabecular pattern; although granular, solid, nested, insular and mixed patterns also occur.⁶ Though not emphasised in the previous literature, in this case, long trabecular formations mimicked parallel tubular arrays, and perivascular pseudorosettes mimicked epithelium-lined fibrovascular cores of papillary RCC. Immunohistochemical staining is useful in confirming the diagnosis, since these tumours are positive for chromogranin, synaptophysin, cytokeratins and other markers.⁶ Negative staining for PAX-2 and PAX-8 antigens distinguishes

carcinoid from RCC and suggests a non-nephrogenic origin.¹¹ Although RCT is less aggressive than RCC, 50–60% of cases had metastasis on initial evaluation.¹² Metastasis rate is related to tumour size, and metastases to lungs, breast, thyroid, orbit, lymph nodes, liver, bone¹³ and uvea have been reported. Metastasis has been reported for up to 7 years after nephrectomy, making long term follow-up important.⁸ Partial or radical nephrectomy with lymph node dissection has been recommended as treatment of choice in localised RCT. Usually, metastatic disease is resistant to chemotherapy, with response rates of 20% with single agent 5 fluorouracil or cisplatin, with no superiority of combination chemotherapy over single agents.¹⁴ Response to somatostatin analogue therapy has strong correlation to SRS positivity. Studies suggest that octreotide significantly lengthens time to tumour progression.⁶

Learning points

- ▶ Carcinoid tumours, also known as low-grade neuroendocrine tumours, may rarely present as primary neoplasms of the kidney, with variable mortality.
- ▶ Carcinoid tumours may have morphological features that mimic those of a much more common primary renal tumour—papillary renal cell carcinoma (RCC)—a point that has not been emphasised in the previous literature. These features of carcinoid include long trabecular formations that mimic the parallel tubular arrays—and perivascular arrangements that mimic the epithelium-lined fibrovascular cores—of papillary RCC.
- ▶ Once considered, the diagnosis of renal carcinoid is readily confirmed by immunohistochemical studies. Greater awareness of this entity among clinicians and pathologists would improve recognition and accurate diagnosis.

Contributors ND wrote the case, and gathered data and references. DM reviewed and edited the case. MB reviewed and edited the case, and chose the pathology images.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Amin MB, Corless CL, Renshaw AA, *et al.* Papillary (chromophil) renal cell carcinoma: histomorphologic characteristics and evaluation of conventional pathologic prognostic parameters in 62 cases. *Am J Surg Pathol* 1997;21:621–35.
- 2 Guy L, Bégin LR, Oligny LL, *et al.* Searching for an intrinsic neuroendocrine cell in the kidney. An immunohistochemical study of the fetal, infantile and adult kidney. *Pathol Res Pract* 1999;195:25–30.
- 3 Resnick ME, Unterberger H, McLoughlin PT. Renal carcinoid producing the carcinoid syndrome. *Med Times* 1966;94:895–6.
- 4 Tanaka T, Yamamoto H, Imai A, *et al.* A case of primary renal carcinoid tumor. *Case Rep Urol* 2015;2015:736213.
- 5 Eble JN, Sauter G, Epstein JL. *World Health Organization classification of tumours. pathology and genetics of tumours of the urinary system and male genital organs.* Lyon: IARC Press; 2004:81–2.
- 6 Omiyale AO, Venyo AK. Primary carcinoid tumour of the kidney: a review of the literature. *Adv Urol* 2013;2013:579396.
- 7 Verma R, Gupta P. Atypical carcinoid presenting as dumb-bell-shaped tumour in the normal kidney. *BMJ Case Rep* 2013;2013:pii: bcr2013008624.
- 8 Romero FR, Rais-Bahrami S, Permpongkosol S, *et al.* Primary carcinoid tumors of the kidney. *J Urol* 2006;176:2359–66.
- 9 Unger PD, Russell A, Thung SN, *et al.* Primary renal carcinoid. *Arch Pathol Lab Med* 1990;114:68–71.
- 10 Namwongprom S, Wong FC, Tateishi U, *et al.* Correlation of chromogranin A levels and somatostatin receptor scintigraphy findings in the evaluation of metastases in carcinoid tumors. *Ann of Nucl Med* 2008;22: 237–43.
- 11 Jeung JA, Cao D, Selli BW, *et al.* Primary renal carcinoid tumors: clinicopathologic features of 9 cases with emphasis on novel immunohistochemical findings. *Hum Pathol* 2011;42:1554–61.
- 12 Fine SW. Neuroendocrine lesions of the genitourinary tract. *Adv Anat Pathol* 2007;14:286–96.
- 13 Hansel DE, Epstein JA, Berbesue E, *et al.* Renal carcinoid tumor: a clinicopathologic study of 21 cases. *Am J Surg Pathol* 2007;31:1539–44.
- 14 Khan MU, Coleman RE. Diagnosis and therapy of carcinoid tumors—current state of the art and future directions. *Nucl Med Biol* 2008;35:577–91.

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