

Primary renal carcinoid tumour with inferior vena caval tumour thrombus

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Abstract

Carcinoid tumours, most frequently reported in the gastrointestinal and respiratory tracts, are exceedingly rare primary renal cancers. Few cases have been published to date. To our knowledge, we report the first case of a primary carcinoid tumour of the kidneys involving the inferior vena cava. We treated a 58-year-old woman with an open radical nephrectomy and cavotomy with thrombectomy. We describe the presentation, investigations and pathology results. We discuss the current experience with carcinoid tumours as a literature review relating to the diagnosis of the disease and the prognosis of patients with this neoplasm. Localized carcinoid tumours of the kidneys, including those involving the vena cava, can be successfully treated with surgical excision.

Can Urol Assoc J 2009;3(3):E7-E9

Résumé

Les carcinoïdes, principalement observés dans le tractus digestif et les voies respiratoires, sont des tumeurs rénales primitives extrêmement rares. Quelques cas seulement ont été publiés jusqu'à présent. Nous décrivons le premier cas de carcinoïde primitif du rein touchant la veine cave inférieure. Nous avons traité la patiente, âgée de 58 ans, par néphrectomie radicale ouverte et thrombectomie par cavotomie. Nous présentons ici les détails du cas au moment de la consultation, les examens effectués et les résultats des analyses de pathologie. Le niveau actuel d'expérience avec ce type de tumeur est discuté sous forme de revue de la littérature en lien avec le diagnostic et le pronostic. Les carcinoïdes localisés du rein, y compris ceux touchant la veine cave, peuvent être traités avec succès par excision chirurgicale.

Case report

A 58-year-old woman presented with an 8-month history of gross, total, painless hematuria. The patient denied having any lower urinary tract or constitutional symptoms. She also denied any symptoms of malignant carcinoid syndrome (e.g., diarrhea, facial flushing or asthmatic episodes). Our physical examination revealed a nontender mass in the right upper quadrant and mild, bilateral pitting edema. Investigations included a computed tomography (CT) scan of her

abdomen and pelvis that demonstrated a 5.5 × 5.9 × 8.2-cm lower pole mass of the right kidney with moderate hydronephrosis and absence of lymphadenopathy (Fig. 1). We subsequently obtained a magnetic resonance image (MRI) and confirmed the presence of an inferior vena cava (IVC) thrombus up to the level of the hepatic veins (Fig. 1). A metastatic workup, including blood serum chemistries, bone scan and CT scan of the thorax, was negative. The patient underwent a right radical nephrectomy, cavotomy and extraction of the IVC tumour thrombus.

Pathological examination revealed a 7-cm solid renal mass with areas of necrosis and gross invasion of the renal vein wall and hilar fat. Surgical margins were negative. Histology and immunohistochemistry supported a diagnosis of a renal neuroendocrine tumour compatible with typical carcinoid tumour. Tumour cells showed a trabecular and nested architecture with bland nuclear features consisting of finely granular "salt and pepper" chromatin (Fig. 2). Tumour cells were immunopositive for low molecular weight cytokeratin Cam 5.2 and the neuroendocrine marker synaptophysin. Neoplastic cells were immunonegative for vimentin, p63, MSA, S-100, CD10 and HMB-45. The postoperative course was uneventful. Given the advanced stage of the tumour (pT3b) and the fact that postoperative metastases have been reported in these tumours,¹ systemic chemotherapy was recommended. However, the patient refused adjuvant therapy. At the 18-month follow-up visit, she had no evidence of clinical or radiological recurrence and remains asymptomatic.

Discussion

Carcinoid tumours are rare, low-grade cancers with a neuroendocrine differentiation. Most are found in primitive gut derivatives, namely, the gastrointestinal (74%) and respiratory tracts (25%),¹ whereas otolaryngeal, breast and genitourinary carcinoids make up the remainder (1%–2%).² The kidneys are the second most common genitourinary site after the gonads, with rare cases reported in the prostate, bladder, urethra, uterus and cervix.¹

With growing use of medical imaging and more

accurate pathological diagnosis, the incidence of reported primary renal carcinoids is on the rise. A total of 88 cases of this rare cancer (based on case reports and case series) have been published,^{1,3-9} with the largest multicentre series involving 21 patients.¹⁰ To our knowledge, we present the first published case of renal carcinoid tumour presenting with an IVC thrombus.

As no neuroendocrine cells have ever been detected in the kidneys,¹¹ several theories have been proposed as to the exact pathogenesis of renal carcinoid tumours, including urothelial metaplasia,¹² metastases from undiscovered primaries, entrapped neural crest or pancreatic cells and primitive stem cell differentiation.^{1,10} Although our patient did not have any anatomical urological abnormalities, the high associations of renal carcinoid with horseshoe kidneys (17.8%) and teratomas (14.3%) suggest that the development of these tumours is related to predisposing embryological factors.

Since renal carcinoid tumours grow slowly, 28.6% are detected incidentally.¹ The most commonly reported symptom is abdominal or flank pain, followed by hematuria, constipation, fever, weight loss and testicular pain. A palpable abdominal mass, like in our patient's case, can be found in 26.8% of cases. Although about half (46%–57%) of patients with renal carcinoid tumours present with metastases and 52% have extra renal extension (perirenal or hilar fat),^{1,10} we found no published cases of renal carcinoid tumours with an associated caval thrombus. As neuroendocrine tumours, some carcinoids secrete biologically active molecules.¹ The classically described malignant carcinoid syndrome is primarily due to serotonin oversecretion and is characterized by diarrhea, facial flushing and bronchoconstriction. The syndrome occurs when serotonin bypasses liver metabolism, as in cases of gastrointestinal

carcinoids with hepatic metastases or extragastrointestinal primary tumours; it has been observed in 7% of patients with renal carcinoid tumours.¹ Diagnosis is made with urine 5-hydroxyindoleacetic acid (5-HIAA), a serotonin metabolite. There is currently no biochemical test to detect endocrinologically silent carcinoid tumours.

Octreotide scintigraphy has been used in the diagnosis and staging of renal carcinoid tumours, as more than 85% have high affinity receptors for somatostatin.¹ An important disadvantage of using this technique to evaluate primary renal carcinoids is that a suspicious lesion may be obscured by normal renal uptake of the tracer. But it remains an important investigation during follow-up. In the case of our patient, since the diagnosis of carcinoid tumour was postoperative and she remained asymptomatic and radiologically free of disease, we did not perform octreotide scintigraphy. ¹⁸F-fluorodeoxyglucose positron emission tomography (FDG-PET) has not been shown to be helpful because FDG uptake is typically low in well-differentiated neuroendocrine tumours.¹³ Several other PET tracers are currently being investigated.

Localized disease is treated surgically. In the largest review to date, which involved 56 patients, nonmetastatic disease was associated with cure and survival rates of 86% and 96%, respectively, at 3-year follow-up.¹ Operative approaches include both open and laparoscopic radical and partial nephrectomy.⁷ Preoperatively detected nodal involvement treated with a radical nephrectomy and adenopathy excision seems to have a 47% disease-free survival after 43 months.¹

Although no standard therapy has been proposed for metastatic renal carcinoid tumours, surgery can help relieve symptoms. Survival of up to 4 years has been reported for metastatic disease treated with chemotherapy.^{1,10} When

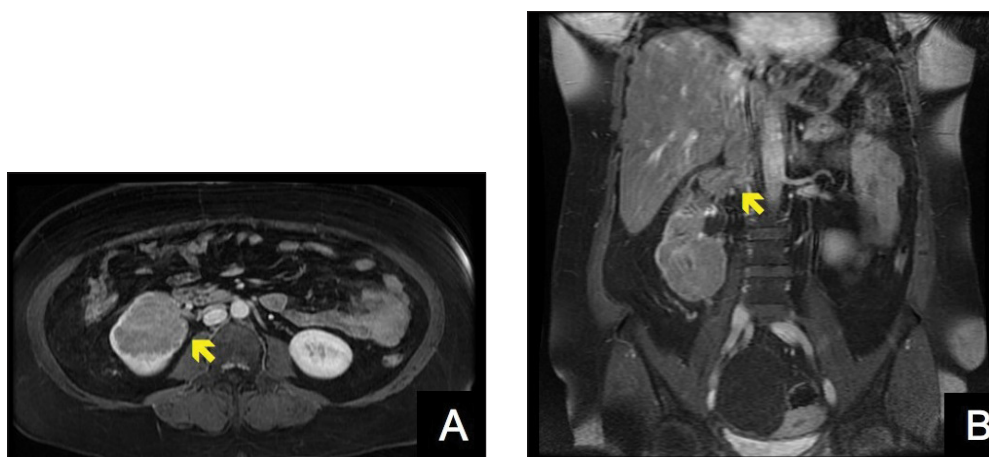


Fig. 1. Magnetic resonance image (fat saturated T_2) demonstrating the (A) right renal mass and (B) inferior vena caval tumour thrombus.

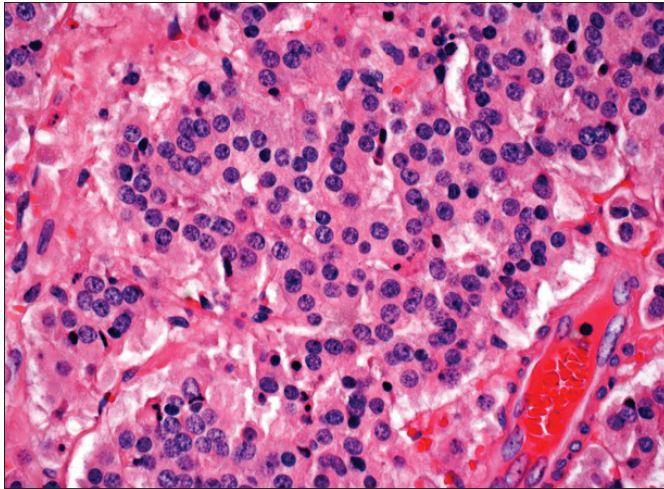


Fig. 2 Tumour histology with bland nuclear features and “salt and pepper” chromatin distribution (hematoxylin and eosin stain, original magnification $\times 40$).

managing locally advanced gastrointestinal carcinoid tumours, surgery is the mainstay therapy. The most recent guidelines for gastrointestinal carcinoids recommend that all patients should receive cytoreductive surgery at the earliest opportunity, mostly for symptom control.¹¹ There is good evidence for survival after excision of involved lymph nodes and resection of metastatic hepatic metastases, but not for debulking of unresectable primary or secondary tumours.¹²

The choice of chemotherapeutic agents remains controversial even for the more common gastrointestinal and respiratory carcinoid tumours. Response rates are low, with combination regimens of streptozocin and fluorouracil (33%) or streptozocin and cyclophosphamide (26%), as well as single agents such as fluorouracil, streptozocin, or doxorubicin (20%).¹⁴ The literature on the role of adjuvant chemotherapy is sparse and inconclusive.

Conclusion

Renal carcinoid tumours are rare, slow-growing neuroendocrine cancers. A cure is often achieved in organ-

confined disease with a variety of surgical approaches. Proper local control of the disease remains the treatment of choice, given the disappointingly low response to chemotherapy in malignant disease.

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This article has been peer reviewed.

Competing interests: None declared.

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