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Case Report

A synchronous lesion: Papillary renal cell carcinoma mistaken as an adrenal gland mass[☆]

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ABSTRACT

In this case report, we describe a diagnosis of papillary renal cell carcinoma in a 76-year-old male patient who was incidentally found to have a left adrenal mass during routine aneurysm surveillance. Computed tomography demonstrated a left adrenal mass and left renal structure which was concerning for renal cell carcinoma. He underwent left adrenalectomy and initial histopathology demonstrated papillary renal cell carcinoma. He subsequently underwent left radical nephrectomy with lymph node dissection. Histopathological analysis of the removed left renal and nodal specimens revealed papillary renal cell carcinoma with lymph node metastasis. However, re-review of the adrenal pathology slides determined the specimen as represented by primary kidney tumor and not adrenal metastasis. This report reviews the presentation and radiological findings of synchronous papillary renal cell carcinoma and differential diagnosis for indeterminate adrenal mass on computed tomography.

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Introduction

Renal Cell Carcinoma (RCC) is one of the most common malignant cancers and comprises 90% of all kidney cancers [1]. RCC is on average, the 7th most common cancer in North America, Japan, Australia, and New Zealand [2]. In the United States, incidence rates of RCC in males have increased from 8.0/100,000 in 1975 to 13.4/100,000 in 2012. The median age of diagnosis

is 64 years old and male predominance of up to 2:1 male to female ratio [1].

RCC derives from the renal epithelium and has over 10 different histological subtypes [3]. Papillary Renal Cell Carcinoma is the second most common histological subtype of Renal Cell Carcinoma following the clear cell subtype, comprising close to 15–20% of all RCC's [4]. In comparison to Clear Cell Renal Cell Carcinoma (ccRCC), Papillary tumors have a unique appearance on CT imaging, appearing as hypovascular lesions.

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Fig. 1 – Seventy-six-year-old man with metastatic papillary renal cell carcinoma. Axial computed tomography with (A) noncontrast, (B) nephrographic and (C) 15-min delayed phases demonstrate a small left renal hypoattenuating lesion (white arrows) with rim hyperenhancement. Also noted is a heterogeneous left adrenal mass (white arrowhead).

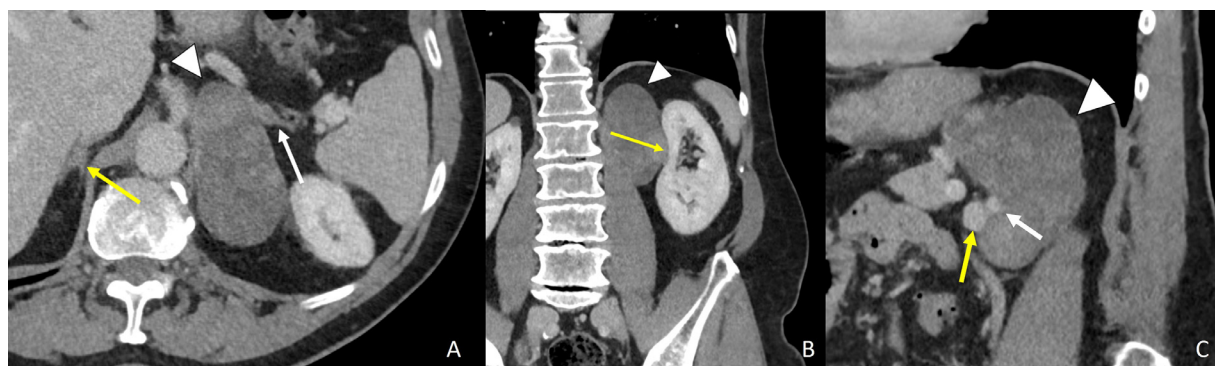


Fig. 2 – Seventy-six-year-old man with metastatic papillary renal cell carcinoma. (A) Axial computed tomography nephrographic phase shows the heterogeneously enhancing lesion arising from the medial limb of the adrenal gland (white arrowhead) with a corresponding intact lateral limb of the adrenal gland (white arrow). There is normal appearance of the right adrenal gland (yellow arrow). (B) Coronal computed tomography nephrographic phase shows the large heterogeneously enhancing left adrenal lesion (arrowhead) with indentation on the adjacent left kidney with a tiny intervening fat plane (yellow arrow) and no involvement of the left renal parenchyma. (C) Sagittal computed tomography nephrographic phase shows the large heterogeneously enhancing left adrenal lesion (arrowhead) with encasement of the left renal artery (white arrow) and abutment of the left renal vein (yellow arrow).

Papillary RCC is an aggressive malignant tumor with roughly 30% of cases found metastatic at the time of diagnosis [5]. In cases of metastatic RCC, the papillary subtype is associated with the lowest overall survival rates, when compared to clear cell and chromophobe subtypes. Here we present a unique case of synchronous papillary RCC initially diagnosed as papillary RCC with adrenal metastasis.

Case report

A 76-year-old male with history of hypertension, aortic stenosis, bilateral iliac artery aneurysms, celiac artery aneurysm, asthma, benign prostatic hyperplasia, ulcerative colitis, and no family history of genitourinary cancer initially presented for routine aneurysm surveillance with computed tomography angiogram (CTA) of the Aorta. This initial scan showed stable bilateral iliac artery aneurysms and was not remarkable for any adrenal abnormalities.

Six years later, he re-established care and underwent routine CTA of Aorta, which showed stable known aneurysms and

a new large hypodense mass superior and anterior to the left kidney measuring $7.7 \times 4.4 \times 8.9$ cm. Due to moderate suspicion for malignancy from the imaging appearance and interval development from the initial CTA, the patient was referred to surgical oncology for evaluation. He then underwent further characterization of the lesion with CT of the abdomen and pelvis, with adrenal protocol and a biochemical workup a week later. This new CT (Figs. 1–3) demonstrated a heterogeneous hypodense left adrenal mass with enhancement characteristics of absolute washout of 44% and relative washout of 22%, which are consistent with an indeterminate adrenal lesion. No aggressive features such as local invasion, hemorrhage, calcifications, or necrosis were reported. Additional findings on this CT showed a 1.2 cm hypoenhancing left posterior renal structure, suspicious for renal cell carcinoma (RCC), a small pancreatic tail hypodensity, and a stable benign small left hepatic lobe hypodensity.

The biochemical workup did not show any evidence of pheochromocytoma, Cushing's, or primary hyperaldosteronism. A CT of the chest with contrast was ordered to evaluate for metastatic disease, which did not reveal any evidence of metastasis.

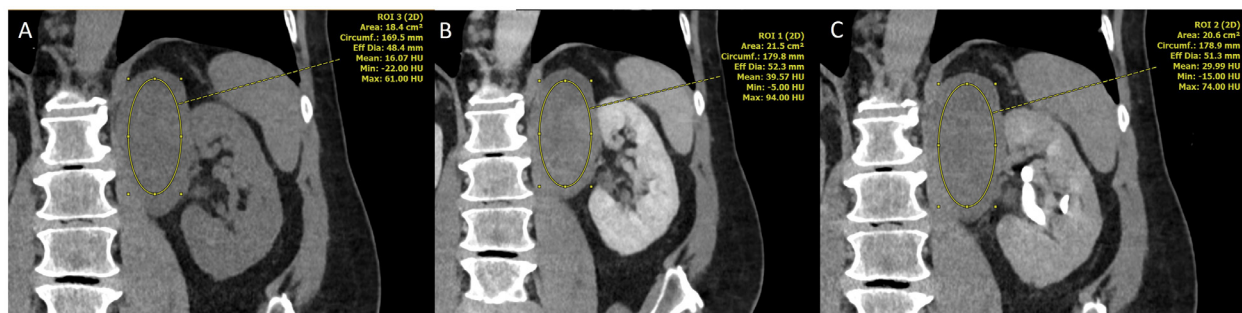


Fig. 3 – Seventy-six-year-old man with metastatic papillary renal cell carcinoma. Coronal computed tomography. (A) A large left adrenal mass measures 16.1 HU on noncontrast phase, (B) 39.6 HU on nephrographic phase, and (C) 30.0 HU on 15-minute delayed phase. These values correspond to an absolute washout of 40.9%, and a relative washout of 24.2%, which are both indeterminate.

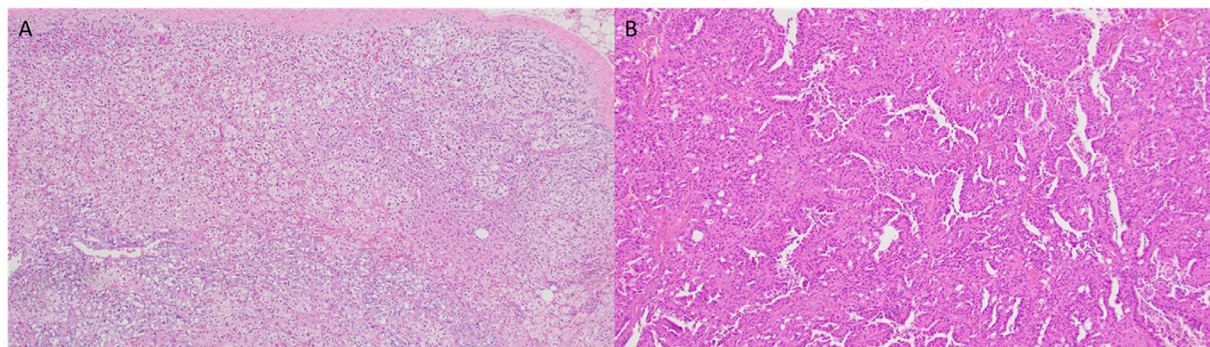


Fig. 4 – Seventy-six-year-old man with papillary renal cell carcinoma. Pathological study of biopsy specimens. Received separately were 2 fragments of tissue, 1 left adrenal gland and 1 fragment of tumoral tissue. (A) Demonstrates adrenal gland under H&E stain at 40x magnification, showing no significant pathologic findings. (B) H&E stained section of papillary renal cell carcinoma at 40x magnification, showing a tubulopapillary to papillary architecture of predominantly eosinophilic cells.

The patient underwent laparoscopic left adrenalectomy 1 month later which revealed a large left adrenal mass densely adhered to the left renal hilum. Histopathology of the removed 8 cm adrenal specimen showed papillary renal cell carcinoma (pRCC) with nuclear grade 2, positive lymphovascular invasion, negative margins, and a less than 0.5 mm capsule. Immunohistochemistry stains were positive for PAX8, AMACR, CD10, and CK7. The pathology slides were reviewed and the case was presented at genitourinary tumor board, where recommendation was made for a left nephrectomy. One month later, the patient underwent laparoscopic left radical nephrectomy with lymph node dissection.

Histopathological analysis of the removed left renal and nodal specimens revealed 2 para-aortic lymph nodes with metastatic RCC disease and WHO Grade 3 papillary renal cell carcinoma in the left kidney. After a second opinion pathological evaluation from an outside institution, it was determined that the adrenalectomy represented a tumor extending from the surface of the kidney and near the adrenal gland (Fig. 3), but the adrenal gland was not involved and was not a site of metastasis as previously reported on the initial pathology report.

Discussion

RCC metastasis has been documented in almost every organ site due to the aggressive nature of the tumor and its propensity to invade via hematogenous and lymphatic routes. The most common metastatic sites for papillary RCC include lymph nodes, lung, bone, and liver. Compared to these sites, the adrenal glands are less common and account for only 7% of all papillary RCC metastatic findings [6]. Moreover, RCC metastases to the adrenal glands are more commonly associated with clear cell subtype. The average size of adrenal metastatic lesions from RCC is 5 ± 0.2 cm, which is larger than the average size for adrenal adenomas, 2.0 ± 0.7 cm [7].

CT is an effective modality for evaluation of RCC with a sensitivity of 95–100% and specificity of 88–95%. In comparison to clear cell RCC, papillary RCC is less vascular and typically shows less enhancement than clear cell RCC in all post-contrast phases. Papillary RCC less than 3 cm tend to be homogenous and hypoenhancing in comparison to the renal parenchyma. Larger papillary RCCs tend to be more necrotic and heterogenous, however tumors still enhance less than

normal renal parenchyma in corticomedullary-phases. In pre-contrast images, these masses may also look similar to cystic renal lesions [8].

Options for metastatic pRCC are limited due to lack of response to conventional chemotherapy [3]. Prognosis can depend on the location of metastasis at the time of diagnosis. A retrospective study conducted by Dudani et al, showed pRCC with lymph node metastasis demonstrated median survival of 14.3 months (95% CI, 12.8–17.2 months) [6].

This case of papillary RCC is unique in several ways. The CT findings demonstrated a large mass with imaging characteristics more consistent with a primary adrenal mass, as well as an indeterminate 1.2 cm renal mass. Originally, pathological evaluation of the adrenalectomy disclosed this mass as papillary RCC, and in the setting of an associated indeterminate renal mass, was determined to be a metastatic lesion of papillary RCC. Metastasis to adrenal glands from papillary RCC is not uncommon, appearing in 7% of papillary metastasis, and thus an important consideration in a radiologist's differential. However, the metastatic rate of papillary RCC masses that are less than 4 cm is 1.7%, thus is unlikely in our case [9]. Additionally, adrenal metastasis has a variable appearance on CT, with masses typically displaying <50% washout. Metastases may also appear hypervascular with >120 Hounsfield units on portal venous phase. Some studies have identified adrenal metastatic lesions to be similar to lipid poor adrenal adenomas, with an average of 30–40 Hounsfield units on non-contrast CT [10]. None of these characteristics were identified with the mass in our case, which presented as a large heterogeneous hypodense mass. A study by Hussein et al, showed that adrenal masses greater than 4 cm with heterogeneous enhancement, as observed in our case, is the most predictive variable in predicting a primary adrenocortical carcinoma, thus supporting the initial radiological diagnosis [11]. Additionally, the large size of this mass is uncharacteristic of a metastatic lesion and is most consistent with a primary adrenal cancer.

The second opinion pathological evaluation of the adrenal specimen from an outside institution disclosed that the papillary RCC abutted the adrenal gland but was not a true metastasis. Retroperitoneal adenopathy is a consideration for RCC; however, the appearance on initial imaging was worrisome for a primary adrenal tumor. Thus, the radiological presentation is consistent of a bi-nodal papillary RCC with sites in the anterior superior region of the left kidney and at the site of the adrenal gland.

This case is a reminder of the variable presentation of renal masses on CT. CT is typically an acceptable modality for RCC identification and staging, with an accuracy of 95–100% in identifying renal masses and an accuracy of 91% for tumor staging [8]. A study by Nazim et al, showed that sensitivity and specificity of adrenal involvement on CT was 100% and 98% respectively [12]. Thus, CT imaging is an accurate and sensitive modality for identifying adrenal metastasis.

This data further supports the outside institution's pathological evaluation, which characterized the tumor as pushing against and effacing the adrenal gland, but not a true metastasis. Therefore, this case presents a unique presentation of papillary

RCC as a synchronous necrotic mass, arising in distinct areas of the kidney. It is also possible that the mass adjacent to the adrenal gland could have been a lymph node metastasis that was resected in surgery, however this is unlikely given the presentation on CT. Lymph node metastasis from RCC typically presents as small homogenous nodules in areas of lymphatic drainage, which is inconsistent with our case [13].

Patient consent

Written informed consent for publication of this case was obtained from the patient.

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