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A 20-year-old female with hemoptysis and high blood pressure: An unusual case of papillary renal cell carcinoma

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Female, 20
Final Diagnosis: Papillary renal cell carcinoma
Symptoms: Hemopthysis
Medication: Sutent
Clinical Procedure: CT guided biopsy
Specialty: Oncology

Objective: Rare disease

Background: Papillary renal cell carcinoma (PRCC) is a rare disease and is a carcinoma of the renal tubular epithelium, comprising only 10–15% of all renal cell carcinoma cases. The majority of cases occur in the sixth decade of life. PRCC rarely occurs before the fourth decade in the absence of family history. This paper describes an aggressive, sporadic case of PRCC in a 20-year-old female without family history and no risk factors.

Case Report: A 20-year-old African American female was admitted for hemoptysis with elevated blood pressure and was found to have left peri-hilar opacification on chest X-ray. Further radiological studies led to the discovery of a large complex left renal lesion within the collecting system, infiltrating the renal artery and causing severe hydronephrosis with para-aortic lymphadenopathy. An MRI also showed signal heterogeneity in the L2 and L3 vertebrae. Biopsies of the left renal mass and a right endobronchial lesion confirmed metastatic PRCC. Treatment was commenced with a tyrosine kinase inhibitor. Within a few weeks, the vertebral metastatic lesions progressed to cause spinal compression. After targeted radiotherapy, the patient was referred to Memorial Sloan Kettering Cancer Center for enrolment in a clinical trial.

Conclusions: PRCC rarely occurs in the second decade of life and even then, most such early cases occur in family clusters. PRCC also has a relatively benign course, constituting less than 10% of all metastatic renal cell carcinomas, further making this case a unique presentation.

MeSH Keywords: Carcinoma, Renal Cell • Hemoptysis • Hydronephrosis • Neoplasm Metastasis

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Background

Papillary renal cell carcinoma (PRCC) is a rare malignancy of the renal tubular epithelium, constituting 10–15% of all renal cell carcinomas. It was called "chromophil renal cell carcinoma" in the Mainz classification and has also been called "tubulopapillary carcinoma" [1].

In this report, we describe a 20-year-old African American female with metastatic papillary renal cell carcinoma who presented with a single episode of hemoptysis and high blood pressure, with no family history of cancer. This is a rare presentation of an uncommon disease.

Case Report

A 20-year-old African American woman with no significant past medical history arrived at the ER with a history of mild nonproductive cough for 2–3 weeks and 1 episode of hemoptysis on the admission day. History was negative for weight loss, night sweats, fever, enlarged glands or recent travel. Reviews of respiratory, cardiac, and abdominal symptoms were unremarkable. Hematologic review revealed a history of mild irondeficiency anemia secondary to menorrhagia. There was no evidence of pathological bleeding. The only significant finding on physical examination was a persistently elevated blood pressure of 160/107 with no significant difference when measured on the opposite arm. Abdominal examination was unremarkable. A chest X-ray revealed left peri-hilar opacification with medial displacement of the gastric bubble, raising concerns about splenomegaly (Figure 1). A follow-up chest CT with intravenous contrast showed soft-tissue masses clustered in and around the left lung hilum and multiple similar masses in and around the carina and anterior mediastinum. An incidental finding of severe left hydronephrosis was made on the inferior slices of the chest CT. The incidental renal findings were confirmed on abdomen CT without contrast, in addition to an osteolytic lesion on L3. Serum and 24-h urine catecholamines were sent but were negative. The patient was also sent for an abdomen and pelvis MRI with IV contrast, which revealed massive left hydronephrosis, multiple left renal cystic and solid lesions within the collecting system impairing renal perfusion and several mildly enlarged left para-aortic lymph nodes and osteolytic lesions on L2 and L3 vertebral bodies (Figure 2). The largest of the multiple solid left renal lesions seen on MRI measured 6.5 cm in diameter. CT-guided left renal biopsy was performed and the patient was discharged home. On follow-up, renal biopsy results confirmed papillary renal cell carcinoma. Biopsy stained positive for keratin AE1/AE3, CD 10, Vimentin, and PAX-2, and focally positive for cytokeratin 7 but negative for thyroid transcription factor 1 (Figure 3). Bronchoscopy with lavage revealed a left upper lobe friable bronchial lesion. Endobronchial biopsy

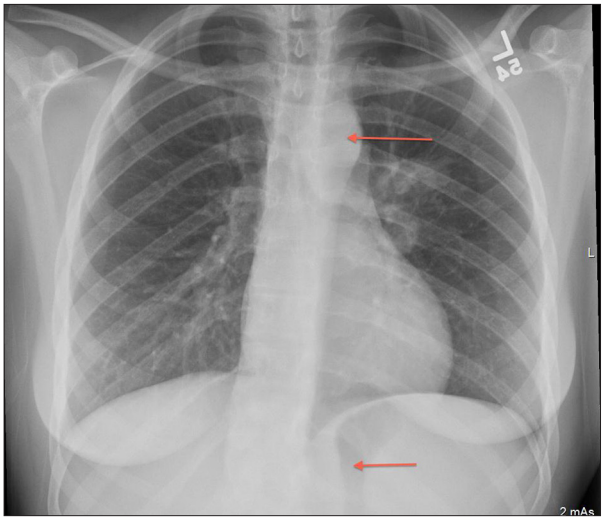

Figure 1. Posterior-anterior view chest X-ray showing left perihilar opacity and medial displacement of the gastric bubble.

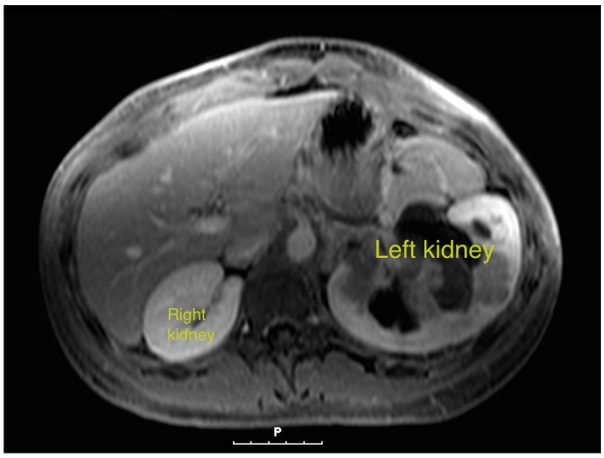

Figure 2. Abdominopelvic MRI with gadolinium slide showing left renal mass with hydronephrosis and infiltration of the renal artery

samples and bronchopulmonary lavage both confirmed metastatic carcinoma with papillary features compatible with renal origin. The patient and her parents state that there is no history of renal cell carcinoma or any other cancers in their family to the best of their knowledge. The patient has never smoked, urine toxicology was negative, and her BMI was within normal limits. Treatment was commenced with oral Sutent (sunitinib malate) 50-mg capsule daily, which is a multi-receptor tyrosine kinase inhibitor. The patient was re-admitted a few weeks later with severe lower back pain and right lower extremity weakness. Imaging studies could not rule out cord compression but did not show fracture (Figure 4). The patient received targeted radiotherapy to the L2/L3 vertebral area, physiotherapy and a back brace with subsequent significant clinical improvement. Urology determined surgery was not indicated based on tumor

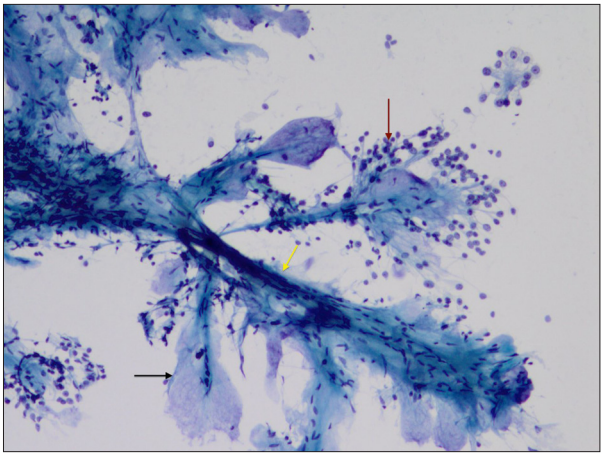

Figure 3. Cellular smear from patient's renal biopsy showing papillary projections (black arrow), fibrovascular core (yellow arrow) and malignant cells (red arrow)

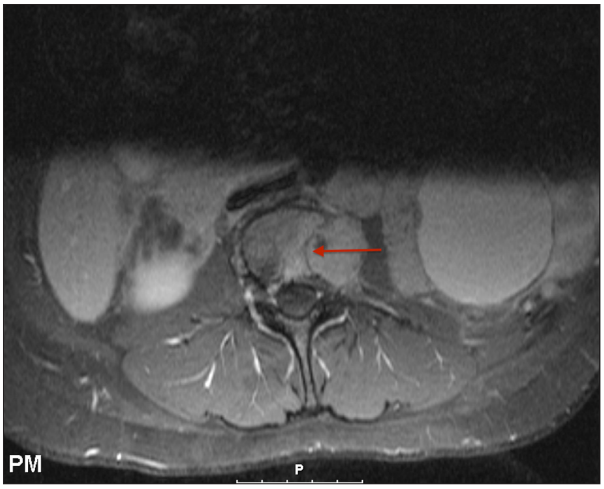

Figure 4. MRI of the lumbar spine showing osseous extension of primary tumor into left side of L3 vertebra.

size (multiple left renal lesions, the largest of which was 6.5 cm) and distant metastasis. The patient was referred to Memorial Sloan Kettering Cancer Center (MSKCC) where she was enrolled in an interleukin-2–based therapy clinical trial.

Discussion

PRCC is an uncommon disease and metastasis is rare. It was estimated that there would be 64 770 newly diagnosed cases of renal cell carcinoma (RCC) in the United States in 2012 [2]. On average, 10–15% of all cases of RCC are PRCC. By extrapolation, in 2012 there would only be 6477 to 9715 new cases of PRCC in the United States in 2012 [2].

The median age at diagnosis of renal cell carcinoma in general is 64 years [2]. Only 1.7% of all RCC between 2005 and 2009 in the United States were diagnosed between the ages of 20 to 34 years. A study on the incidence and long-term prognosis of PRCC in the United States involving 122 patients with PRCC also showed a median age of 63.46 years for PRCC [3]. Our patient was diagnosed at the age of 20 years, which is more common in family clusters [2]. However, our patient and her parents denied any history of cancer or unexplained medical deaths in their family, making this a highly unusual and rare presentation for a patient of this age.

PRCC may be sporadic or hereditary [3]. Hereditary forms are associated with mutations in the c-met oncogene, which occurs in only 5–13% of sporadic cases [4]; 75% of sporadic cases of PRCC demonstrate trisomy 7 [5]. However, the molecular and genetic features of PRCC are complex and usually involve several different chromosomes and abnormalities, the most common of which are gains of chromosome 7 and/or 17 or loss of chromosome Y [5]. PRCC may also be classified based on histological features and gene expression profiles into type 1 or type 2 tumors [3]. There is evidence that this particular classification has prognostic implications. One study found type 1 tumors have significantly better overall and disease-free survivals compared to type 2 [6]. Microscopically, type1 PRCC demonstrates papillae covered by single-layered, small cells with pale cytoplasm and round-to-ovoid nuclei, a pattern characteristic of hereditary PRCC but also seen in sporadic cases. In contrast, type 2 tumors show pseudostratified, large cells with relatively abundant eosinophilic cytoplasm; they are associated with poorer clinical outcomes [5].

Since the 1970s, PRCC has been associated with a more favorable outcome and benign course [7]. However, recent studies have shown a similar prognosis for PRCC and clear renal cell carcinoma (CRCC) when taking stage and grade into consideration [8]. These discrepancies are likely due to the more aggressive PRCC subtype 2. The tumor stage at diagnosis of subtype 2 of PRCC is significantly higher than type 1 [8]. Vascular invasion and distant metastasis by PRCC was reported in one study to be more common in type 2 than in type 1 [8]. Our patient presented with renal artery infiltration causing secondary hypertension and metastasis to the lumbar spine, paraaortic lymph nodes, pulmonary hilar lymph nodes, and right bronchial system. As a whole, PRCC typically constitutes less than 10% of all metastatic renal cell carcinomas [9], making this case even more unique. Mode of presentation of PRCC tends not to be significantly different from other RCCs. Male predominance occurs in both, but is 5:1 in PRCC compared to 1.6:1.0 in RCC as a whole [10]. Approximately 50% of RCC cases are incidental findings with minimal or no symptoms [10].

Immunotherapy with cytokines or tyrosine kinase inhibitors is the main treatment for metastatic PRCC and usually only achieves major responses in 10–20% of cases [10]. Because metastatic PRCC is rare, it is difficult to find large clinical trials

addressing treatment and outcome. A review of cases of metastatic PRCC performed by MSKCC covering 1985 to 2005 identified only 38 cases [11]. Of these 38 cases, 30 were treated at MSKCC with various systemic therapies including cytokines (such as interferon, interleukin-2, and combinations of these) and the multi-targeted tyrosine kinase inhibitor sunitinib (which was used in our patient) [11]. The average survival time of this group was 8 months with a 3-year survival rate of 7% [11].

Conclusions

We presented a rare case of a 20-year-old African American female with hemoptysis and high blood pressure leading to the finding of metastatic PRCC. PRCC rarely occurs in the second decade of life and even then, most such early cases occur in family clusters. PRCC also has a relatively benign course, accounting for less than 10% of all metastatic renal cell carcinomas, again making this case a unique presentation.

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