THE AMERICAN JOURNAL of MEDICINE®

Beta-human Chorionic Gonadotropin-producing Renal Cell Carcinoma

To the Editor:

Our patient is a previously well 26-year-old African-American man who presented with several episodes of hematuria over the previous 8 months, and increasing right-sided flank and testicular pain. The patient's family history was significant for a paternal grandmother with gastric cancer, a paternal aunt who died at age 30 years from breast cancer, and a paternal cousin with lung cancer. The patient had an 8 pack-year smoking history and daily marijuana use. Laboratory testing revealed that β-human chorionic gonadotropin (bHCG) was elevated to 608 mIU/mL (male normal range 0-5 mIU/mL) and serum creatinine was elevated to 1.7 mg/dL from 1.0 mg/dL. Lactate dehydrogenase, alpha-fetoprotein, and C-reactive protein were within normal limits. Computed tomography of the abdomen revealed multiple large exophytic lesions arising from the kidneys bilaterally (**Figure A** and **B**) and enlarged retroperitoneal and left perinephric lymph nodes. Further imaging showed multiple small, indeterminate lung nodules (**Figure C**). Ultrasound of the testicles showed a small cyst in the left epididymis and trace left hydrocele (**Figure D**). Computed tomography-guided fine needle aspiration of the primary renal tumor (**Figure, E-G**) demonstrated epithelial membrane antigen-positive cells with bland nuclei and clear cytoplasm suggesting clear cell type renal cell carcinoma. TP53 sequencing with deletion/duplication analysis showed no mutation, which does not rule out mutations affecting gene expression or mRNA splicing. TP53 mutations are present in 20%-50% of renal cell carcinoma cases and over 50% of all human cancers. Our patient was not a candidate for surgical intervention due to the high burden of disease and evidence of distant metastases. He received 3 cycles of the tyrosine kinase inhibitor sunitinib. Five months after initial presentation, the patient demonstrated extension into the inferior vena cava and new metastatic disease in the liver and lumbar spine. The patient was subsequently switched to temsirolimus.

Renal cell carcinoma arises from the renal cortex and is the most common form of renal cancer (80%-85%). Abdominal imaging demonstrating a solid or complex renal mass raises suspicion for renal cell carcinoma. Advanced cases may present with hematuria, flank pain, and an abdominal mass. Renal cell carcinoma affects men more commonly than women (1.6:1), with a median age of diagnosis of 64 years, with 37 years of age representing the lower 2.5th percentile of age at diagnosis.[1] Treatment of renal cell carcinoma involves surgical removal of the affected kidney if metastases have not occurred. Metastatic renal cell carcinoma is relatively resistant to both radiation and medical therapy. Motzer et al[2] found a median survival of 26.4 months in stage IV renal cell carcinoma with sunitinib.

The patient's presentation described above was quite unusual; he was very young and presented with significant bilateral, synchronous disease. The atypical features in this case and significant family history suggest a possible underlying genetic abnormality (eg, van Hippel Lindau, Birt-Hogg-Dubé syndrome, tuberous sclerosis complex).

In the context of renal cell carcinoma, high bHCG levels suggest metastatic disease. Hotakainen et al[3] observed an elevation in bHCG in approximately 25% of renal cell carcinoma cases and an association with a negative prognosis in patients with metastatic disease.

The present case highlights the importance of considering renal cell carcinoma in a patient presenting with the classic signs, despite young age, and highlights the relationship between elevated bHCG and significant metastatic disease.

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Funding: None for all authors.
Conflict of Interest: None declared for all authors.
Authorship: All authors had full access to the data and contributed to the preparation, writing, and revision of the manuscript.

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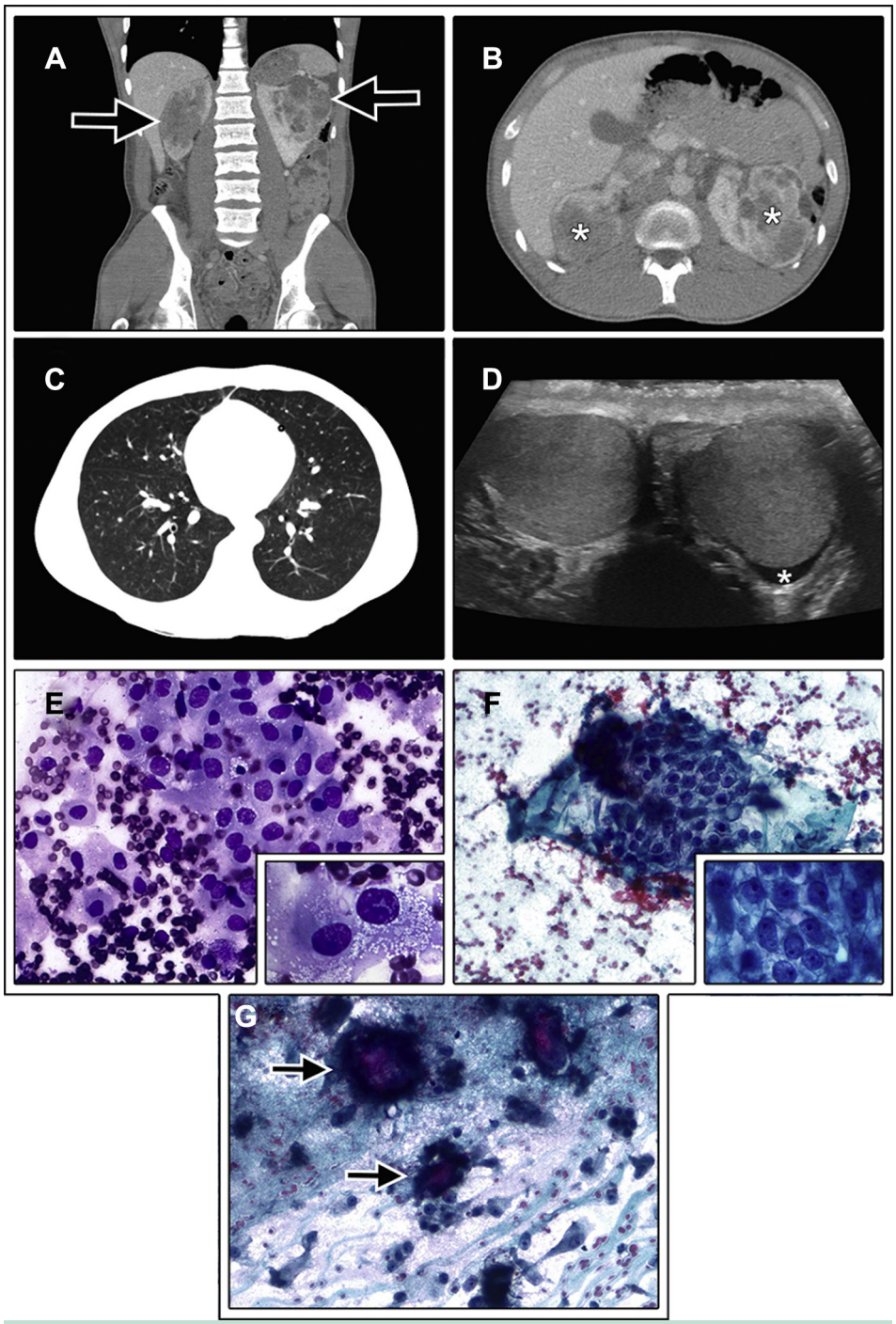

Figure (**A**) Coronal abdominal computed tomography (CT) with contrast shows large mixed cystic/solid lesions in both the right and left kidneys (arrows). (**B**) Axial abdominal CT with contrast showing bilateral complex masses (asterisks) and enlarged adjacent retrocaval and left perinephric lymph nodes, concerning for local metastatic disease. (**C**) Axial chest CT demonstrates multiple indeterminate pulmonary nodules. (**D**) Testicular ultrasound reveals a left hydrocele (asterisk). (**E**) Fine-needle aspiration (FNA) smear of renal tumor shows cluster of smooth-bordered cells typical of renal cell carcinoma. Cells with bland nuclei and clear cytoplasm favor clear cell type (Diff-quick stain 20×; inset - 40×magnification). (**F**) FNA smear of renal tumor (Papanicolaou stain, 20×; inset, 40×magnification). (**G**) FNA smear of renal tumor demonstrates calcifications (arrows) (Papanicolaou stain, 20×). Contrast and brightness of images have been optimized for display. TP53 sequencing showed dup/del and mutation, which does not rule out mutations affecting gene expression or mRNA splicing.

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http://dx.doi.org/10.1016/j.amjmed.2015.10.035

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