58

Genitourinary Cancers

Robert Dreicer, Jorge Garcia, Timothy Gilligan, and Brian Rini

RENAL CELL CARCINOMA

Definition and Epidemiology

Renal cell carcinoma (RCC) represents 2% to 3% of all malignancies. It is the fifth most common cancer in men and the seventh most common cancer in women, with approximately 65,000 new cases diagnosed in the United States in 2013. Most patients do not have an identifiable risk factor. Smoking is an established risk factor for RCC, with a relative risk of two-fold greater than that of nonsmokers. Less certain risk factors include obesity and hypertension. RCC is also more common in patients with end-stage renal failure or polycystic kidney disease. A small number (3%) of cases of RCC are inherited.

The most recognized inherited RCC is von Hippel-Lindau (VHL) syndrome, an autosomal dominant disorder that is characterized by the development of multiple vascular tumors including clear cell RCC. The genetic event underlying VHL syndrome (inactivation of the *VHL* gene) also occurs in sporadic (noninherited) clear cell tumors, leading to RCC characterized by reliance on blood vessels for growth. Research into this syndrome has led to modified treatment options for advanced disease (see later discussion).

Pathology

The histologic subtypes of RCC are characterized by distinct genetic characteristics, histologic features, and clinical phenotypes. Clear cell RCC (75% of all RCCs) is the most common subtype and is characterized by *VHL* gene inactivation. Less common are the papillary, chromophobe, and unclassified subtypes and medullary RCC, which occurs almost exclusively in patients with sickle cell trait. Although these RCC subtypes are biologically distinct, the current surgical and medical approaches are uninfluenced by subtype.

Diagnosis and Differential Diagnosis

Masses in the kidney may be benign or malignant, with an increasing likelihood of malignancy with increasing size. Most clear cell RCC tumors are distinguishable based on their contrast enhancement. Other considerations for renal masses include benign tumors (e.g., oncocytoma), metastatic disease from another primary site (rare), angiomyolipoma, a lipid-containing benign tumor (most commonly occurring in young females), and infectious processes. The diagnosis is made on the basis of a biopsy or at the time of nephrectomy, although the radiographic appearance of each of the differential diagnoses is often characteristic.

Clinical Presentation

RCC is more common in males (2:1), and the median age at presentation is approximately 65 years. Most contemporary presentations are asymptomatic and incidental (identified on imaging studies ordered for other indications). Classic signs and symptoms include hematuria, flank pain, and a palpable abdominal mass. Systemic symptoms occur with metastatic disease or paraneoplastic syndromes. A renal mass is discovered, usually on computed tomography (CT) scanning, and has an appearance that is characteristic of RCC (i.e., highly vascular). Subsequently, a full staging work-up is performed, including CT scanning of the chest; CT head and bone scans are performed only as symptoms dictate. Diagnosis is usually made at the time of nephrectomy, although a biopsy of the renal mass may be indicated, such as in a patient with distant metastases in whom nephrectomy is not pursued or in a patient with a small renal mass that may be initially observed.

Treatment

Renal Masses

Some renal masses (approximately 20%) are not cancerous, so a diagnostic biopsy is indicated if the radiographic appearance is not classically consistent with RCC. One option for renal masses, even if proven to be RCC, is initial observation. Retrospective series have defined this approach in a select group of patients with renal masses smaller than 4 cm in diameter for whom surgery is not preferred. The growth rate is approximately 3 mm/year, and the reported incidence of development of metastases is very low. If surgery is pursued, then removal of either part of the kidney (partial nephrectomy) or the entire kidney (radical nephrectomy) is the standard of care, depending on factors such as the extent and anatomy of the tumor, native renal function, and surgical skill. Cancer outcomes are equivalent, although renal function is better preserved with partial nephrectomy. Another management option for renal masses is exposure to temperature extremes: freezing (cryotherapy) or burning (radiofrequency ablation). This approach is usually pursued in patients with contraindications to surgery. The long-term outcome awaits further data. To date no clinical trial evidence has demonstrated improvement in patient outcome, either before (neoadjuvant) or after (adjuvant) nephrectomy, regardless of risk of recurrence, despite l clinical trials.