More than 57,000 people in the United States will be diagnosed with renal cell carcinoma (RCC) in 2009, with slightly more than 12,000 deaths occurring (Jemal et al., 2009). The clinical presentation of RCC may vary greatly. The kidneys are located within the retroperitoneum, surrounded by the body wall (see Figure 1). Tumor growth to large size with local extension may occur in the absence of symptoms. Less than 10% of patients present with the classic symptoms of kidney cancer—palpable mass, flank pain, and hematuria—which confer a poor prognosis (Zwiezig, 2002). Patients also may present with symptoms from systemic metastases (e.g., bone pain) or paraneoplastic syndromes (Moldawer & Figlin, 2008; National Comprehensive Cancer Network [NCCN], 2009). The latter may include hypercalcemia, erythrocytosis, cachexia, and fatigue. These syndromes are caused by dysregulated secretion of hormones or inflammatory mediators by the tumor. In these settings, the cancer may present in obscure ways, often mimicking other medical disorders such as hypercalcemia, erythrocytosis, cachexia, and fatigue. The five-year survival rates have been reported as 75%–95% for organ-confined disease, 65%–80% for perinephral fat or adrenal involvement, 40%–60% for vena cava thrombus, 10%–20% for lymph node involvement, and up to 5% for patients who develop metastatic disease following radical nephrectomy (Canda & Kirkali, 2006). The five-year survival rate for patients with metastatic RCC is less than 10% (Escudier et al., 2007). No systemic therapy has been proven to reduce the likelihood of relapse, which occurs most commonly in the lungs, bone, and brain (NCCN).

Diagnostic Methods

The initial evaluation of a patient with RCC should include a thorough history and physical examination, as well as routine laboratory tests (e.g., comprehensive metabolic profile, complete blood count) (NCCN, 2009; Nelson, Evans, & Lara, 2007). Because surgical planning is dependent on disease extent, radiographic imaging plays a key role in accurately determining tumor stage, adjacent organ involvement, and metastases prior to treatment initiation (Campbell, Novick, & Bukowski, 2006).

At a Glance

- Kidney cancer includes several distinct morphologic characteristics and histologic subtypes that guide surgical intervention and systemic treatment planning.
- Most kidney cancers are diagnosed incidentally at the time of diagnostic imaging for unrelated complaints.
- Imaging modalities such as computed tomography, ultrasonography, and magnetic resonance imaging are essential in establishing an accurate diagnosis of renal cell carcinoma and determining the course of treatment.
enlarged regional lymph nodes. In addition, some tumors, including avascular masses, inferior vena cava thrombus, and tumors with disease extension to the liver, cannot be accurately staged through CT scan (Bechtold & Zagoria).

**Magnetic Resonance Imaging**

Abdominal magnetic resonance imaging (MRI) plays an important role in the detection of renal masses (Ascenti et al., 2004). MRI may substitute CT in the detection of renal masses and staging when contrast material is contraindicated or if inferior vena cava involvement is suspected (Lawrentschuk, Gani, Riordan, Esler, & Bolton, 2005; NCCN, 2009). Accuracy in staging RCC ranges from 90%–100% (Curry et al., 2007). Soft-tissue contrast of MRI exceeds that of CT scan, for this reason, MRI more accurately delineates consistency and density of tissues where CT cannot. MRI may be more useful in detecting lesions smaller than 3 cm. Advantages of MRI over CT include multi-planar imaging, the ability to detect tumor extension, vascular patency, and distinction of collateral vessels from lymph node metastases (Curry et al.). Disadvantages of MRI include limited accessibility, unpredictable image quality, lack of clearly effective contrast agent, longer imaging time, and restrictive patient requirements (e.g., patients with claustrophobia may not have an MRI unless an open MRI is available) (Curry et al.).

**Ultrasonography**

Ultrasonography can be a useful screening tool for primary tumors as it is widely accessible, safe, rapid, and relatively inexpensive. In addition, ultrasonography does not require radiation (Yang et al., 2007). A study of ultrasonography (Yang et al.) concluded that determination of the tumor stage was correct in about 78% of patients, supporting the notion of its effectiveness in evaluation of proximal caval and right atrial tumor extension. However, ultrasonography is considered inferior to CT and MRI for overall staging and in evaluating early-stage tumors (McLennan, 2006). In addition, the technique requires a high level of operator skill, and bowel gas may obstruct imaging of the renal vein and infrahepatic inferior vena cava (Rezneck, 2004; Shirkhoda, 2005).

**Other Diagnostic Methods**

IV urography (IVU), also called excretory urography and IV pyelogram, was once considered the most accurate imaging modality for the initial evaluation of patients with suspected kidney tumors with an accuracy rate from 50%–70% (McDonald, Swagerty, & Wetzel, 2006; Shirkhoda, 2005). However, IVU is not as cost-effective as CT because it is less sensitive. CT is required as a complement to ensure the accuracy of the IVU results. In addition, follow-up ultrasonography tests must be performed every 12–18 months to ensure that the results are accurate (McDonald et al.; Siow et al., 2000). If the ultrasound is negative, a follow-up procedure may be appropriate.
Angiography is the most costly and invasive of the imaging methods. Accuracy varies from 36%–44% (Bechtold & Zagoria, 1997). When all methods of angiography are considered (i.e., rotational angiography, digital subtraction angiography, and inferior venacavography), this method is the least accurate means to stage RCC. When analyzed separately, the accuracy of inferior venacavography is similar to that of MRI (Lawrentschuk et al., 2005). Although use is rare, angiography may be used in certain clinical settings.

Fine-needle aspiration is relatively accurate in the subclassification of RCC and has been shown to have a limited role in the workup of patients with RCC (American Cancer Society, 2007; NCCN, 2009). This method may be considered in selected cases where imaging test results are inconclusive regarding the necessity of nephrectomy (NCCN). In one study evaluating accuracy, 74% of primary renal lesions were correctly classified with fine-needle aspiration. The most common error occurred when papillary and sarcomatoid RCC were misdiagnosed as clear cell (Renshaw, Lee, Madge, & Granter, 1997). Biopsy of the primary renal mass or metastatic lesion is appropriate in patients who present with metastatic disease, patients with unresectable primary tumors (because of size or extent of metastatic disease), and patients clinically not appropriate for nephrectomy because of other medical conditions.

Positron-emission tomography (PET) is not part of a routine workup but may soon have a larger role in renal tumor imaging (Chin, Lam, Figlin, & Belldegrun, 2006; NCCN, 2009). Preliminary studies show promise in the detection of lymph node involvement and improved differentiation of local recurrence and metastasis. Detection of malignancy in soft tissue masses is possible through PET before it can be detected through CT and MRI (Shvarts, Han, Seltzer, Pantuck, & Belldegrun, 2002). Some studies have shown PET-CT to be as good as conventional methods with the added advantage of examining all organ systems in one procedure without using contrast agents that can negatively impact renal function (Park, Jo, & Lee, 2009). Additional study is required for the clinical use of PET to become better defined. Patients presenting with a renal mass should have blood and urine tests to assess for anemia, electrolyte abnormalities, and hematuria. CT scans of the chest, abdomen, and pelvis and a bone scan should be performed to determine whether metastatic disease exists. In addition, patients will likely meet with a surgeon to discuss surgical options and a medical oncologist if they do present with metastatic disease. Collaboration between the surgeon and medical oncologist will determine the appropriate sequence of systemic anti-cancer therapy and surgery for patients who have metastatic disease at the time of their initial diagnosis.

Prognosis

Staging

The most important prognostic factor for patients with RCC is disease stage, or anatomical extent of disease (Chin et al., 2006). The tumor, node, metastasis (TNM) staging system uses primary tumor, regional lymph node involvement, and distant metastasis to assign a stage, which is correlated with prognosis (see Figure 2). Survival dramatically decreases between stages III and IV with systemic metastases. Five-year survival statistics are 96% for stage I, 82% for stage II, 64% for stage III, and 23% for stage IV (American Cancer Society, 2007). Lymph node involvement is an important prognostic indicator. Positive lymph node status is associated with a higher incidence of metastatic disease and, therefore, confers a poorer prognosis. About 20% of patients experience lymph node metastases, which carries a five-year survival rate ranging from 11%–35% (Chin et al.).

Grade

Nuclear grade follows staging in importance of patient prognosis. A higher nuclear grade correlates with a poorer prognosis (Motzer, Bander, & Nanus, 1996). The Fuhrman system takes into account nuclear size, shape, and prominence. Independent of
T stage, the five-year survival rate associated with Fuhrman grade 1 is 94%, 86% with grade 2, 59% with grade 3, and 31% with grade 4 (Moldawer & Figlin, 2008) (see Figure 3).

**Histologic Subtype**

Many types of cancer occur in the kidney, each with its own histologic pattern and genetic basis which determine the clinical course and prognosis (see Figure 4). About 90% of renal tumors are carcinomas and 85% are clear cell tumors. Other less common types include papillary, chromophobe, and Bellini duct tumors, with papillary as the largest subgroup of non-clear cell RCC (NCCN, 2009). Long-term survival is comparable with that of patients with clear cell histology, with five-year survival at 78% in patients with papillary subtype and 77% in patients with clear cell subtype (Schrader et al., 2009). The survival rate for metastatic papillary RCC is worse that for clear cell RCC (Cohen & McGovern, 2005). Chromophobic RCC makes up about 5% of kidney cancers. Patients with chromophoboc carcinomas generally have an excellent prognosis (Rodriguez-Jasso, Serrano-Brambila, & Maldonado-Alcaraz, 2008). Oncocytoma makes up less than 5% of kidney cancers and is rarely associated with metastases (Motzer et al., 1996).

**Molecular Markers**

Although not still considered standard practice, the clinical application of molecular markers as prognostic indicators for RCC may prove beneficial. Markers may predict responsiveness to therapies, predict recurrence, and act as a target for directed therapies (Chin et al., 2006). Markers play integral roles in angiogenesis, apoptosis, cell adhesion, regulation, and proliferation. Studies in carbonic anhydrase (CA) IX, a member of a family of proteins thought to regulate intra- and extracellular pH levels during hypoxic periods in tumor cells, have linked low CA IX with poor survival in patients with metastatic RCC (Chin et al.). Other molecular markers have been identified and are being examined (e.g., von-Hippel Lindau tumor suppressor gene, hypoxia-induced factor 1-α, CXCR3), but their role as prognostic tools has yet to be affirmed (Martignoni et al., 2007).

**Conclusion**

Kidney cancer is not just one but several types of cancer, each with a distinct histologic appearance, genetic basis, and clinical course. RCC is most often diagnosed incidentally at the time of radiologic imaging for unrelated complaints, which is fortunate as most asymptomatic tumors are small, confined, and curable. Molecular markers will likely play a larger role in determining patient prognosis as clinical trial data evaluating their use in RCC continue to emerge.

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