PRIMER ON KIDNEY DISEASES

Second Edition

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rected. Infection usually cannot be eradicated in patients with nephrolithiasis without removal of the calculi, either by surgical means (in the case of larger or staghorn calculi) or by lithotripsy (in the case of smaller stones). Patients with indwelling catheters will continue to develop episodes of infection despite treatment of individual episodes as they arise. Infections caused by pseudomonas and enterococci are especially prone to recurrence. Chronic and recurrent infections of the urinary tract may lead to suppurative sequelae or to loss of functioning renal tissue with subsequent impaired renal function.

Prevention

Urinary catheters should not be used unless they are medically indicated. Sterile insertion and maintenance of a closed catheter system can reduce the incidence of catheter-associated urinary tract infections. Condom catheters may be an alternative. As the prevalence of infection increases with the duration of catheterization, catheters should always be removed as soon as possible. In particular, the junction between the distal catheter and the collecting system should remain closed, downhill gravity drainage should be maintained at all times, and sterile technique should be used whenever urine is drained from the collecting bag. Detailed guidelines for prevention of catheter-associated infections have been published elsewhere. Antimicrobial prophylaxis has no value in chronically catheterized patients or in most patients with intermittent asymptomatic bacteriuria. Antimicrobial prophylaxis should be provided to patients undergoing prostatic surgery or other urological procedures since such prophylaxis prevents postoperative urinary tract infection and urosepsis. All pregnant women should be screened for bacteriuria in the first trimester and treated if positive.

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RENAL AND URINARY TRACT NEOPLASIA

ROBERT R. BAHNSON

It is estimated that in 1996, approximately 83,000 individuals will be diagnosed with cancer of urinary organs (bladder, kidney, and other urinary) and roughly 24,000 deaths from urinary neoplasia will occur. In addition, more than 317,000 men will be diagnosed with cancer of the prostate and more than 41,000 will die from this common malignancy (Table 1). Neoplasms of the kidney, renal pelvis, ureter, bladder, and prostate will be discussed separately highlighting their etiology, pathology, diagnosis, staging, and treatment.

RENAL NEOPLASMS

Etiology

The most common cancer of the kidney is renal cell carcinoma. The tumor is more common in men, with a male : female ratio of roughly 2 : 1. It is generally a tumor of adults, with peak incidence between the fifth and seventh decades of life. A recessive oncogene located on chromosome 3p (short arm) is associated with the formation of

TABLE I

	Estimated new cases of urinary organ cancer			Estimated deaths from urinary organ cancer		
	Bladder	Kidney and other urinary	Prostate	Bladder	Kidney and other urinary	Prostate
Men	38,300	18,500	317,000	7800	7300	41,400
Women	14,600	12,100		3900	4700	
Total	52,900	30,600		11,700	12,000	

both sporadic and familial renal cell carcinoma. This observation is supported by findings of loss of chromosome 3p alleles in renal cell carcinomas from patients with von Hippel-Lindau (VHL) disease. VHL syndrome is a hereditary disease characterized by spinal and cerebellar hemangioblastomas, retinal angiomas, pheochromocytomas, renal and pancreatic cysts, cystadenomas of the epididymis, and renal cell carcinomas. From 28 to 45% of VHL patients will develop renal cell carcinomas of the clear cell type. The tumors in these patients occur early in life (mean age at diagnosis is 39 years) and are frequently multiple and bilateral. No definite causal relationship between environmental carcinogens and the development of renal cell carcinoma has been documented.

Patients with chronic end stage renal disease (ESRD) often develop acquired cystic disease of the kidney (ACDK). Approximately 1 to 4% of these patients develop renal carcinoma. This rate is roughly three to six times greater than that of the general population.

Pathology

The proximal tubular cell has been identified by electron microscopy and monoclonal antibodies as the origin of renal cell carcinoma. The tumor is generally composed of four common histologic types: clear cell, granular cell, tubulo papillary, and sarcomatoid. These cells grow in solid sheets, trabecular patterns, or less commonly in papillary configurations. The sarcomatoid renal cell carcinoma is also known as the bone-metastasizing variant because of its predilection for bony metastases. This histologic subtype is characterized by aggressive clinical behavior and a poor prognosis.

Diagnosis

Renal cell carcinoma has often been called the internist's tumor due to the variety of its presentation and the uncommon number of systemic syndromes that have been reported to occur in patients with the disease (Table 2). The classic triad of flank pain, palpable mass, and hematuria is present in only 10% of patients and is often an indication of advanced disease. The majority of clinically confined renal tumors are now discovered serendipitously by ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI). As an initial radiologic test, ultrasound can distinguish cystic, solid, and complex renal masses. Any mass that does not meet the criteria for simple cyst should be further evaluated by CT. As a single diagnostic imaging study, CT scanning is probably the best method to evaluate a suspected renal mass lesion as it gives fairly reliable information about the local extension of tumor, lymph node involvement, and presence of tumor thrombus in the renal vein or inferior vena cava. Renal arteriography is seldom necessary unless required for the planning of parenchyma sparing surgery.

The issue of screening for renal cell carcinoma in VHL and ACKD is controversial (see Chapter 45). Since renal involvement in VHL occurs in 28 to 66% of patients and bilateral renal cell cancers develop in 63 to 75% of those with renal lesions it has been recommended by some that such lesions be followed by annual CT examinations. ACKD increases significantly in frequency after 3 years of dialysis. As in VHL, CT is probably the best imaging technique. Clearly any patient with VHL or ACKD with symptoms or hematuria should undergo a complete imaging evaluation.

Staging

Staging of kidney carcinoma is best performed using the tumor, node, metastases (TNM) classification agreed on by the International Union Against Cancer and the American Joint Committee on Cancer (Table 3). Cost effective clinical staging of patients can be accomplished with a history and physical exam, chest X ray, liver function tests, and serum calcium determination. The most frequent sites of metastases in decreasing order of frequency are lymph nodes, lung, liver, and bone. Patients with a palpable liver or abnormalities of liver functions should have further radiographic or radionuclide imaging of the liver. Symptoms of skeletal involvement or an increase in serum calcium or alkaline phosphatase should prompt a radionuclide bone scan.

Treatment

The only successful treatment for patients with localized renal cell carcinoma is surgical extirpation. Radial nephrectomy, removal of the kidney with its surrounding fascial envelope (Gerota's) and the ipsilateral adrenal gland, is the preferred surgical approach. The 5-year survival of patients with node negative tumors without metastases ranges from 47 to 82%. The presence of positive lymph nodes or distant metastasis augurs poorly for survival beyond 2 years. Regrettably, radiation therapy and chemo-

TABLE 2
Incidence of Systemic Syndromes in Patients with Renal Cell Carcinoma

Syndrome	%
Raised erythrocyte sedimentation rate	55.6
Hypertension	37.5
Anemia	36.3
Cachexia, Weight loss	34.5
Pyrexia	17.2
Abnormal liver function	14.4
Raised alkaline phosphatase	10.1
Hypercalcemia	4.9
Polycythemia	3.5
Neuromyopathy	3.2
Amyloidosis	2.0

therapy have been of limited value in this disease. Several studies have failed to confirm an advantage to treated patients who received either pre- or postoperative radiotherapy. Multiple, single agent, and combination chemotherapy trials have proven that renal cell carcinoma is highly resistant to commonly employed cytoxic agents. The single most active drug appears to be vinblastine, but objective response rates are too low to justify its routine use.

The most promising therapy of metastatic renal cell carcinoma in the past decade has been immunotherapy. Nonspecific active, systemic immunotherapy with bacillus Calmette-Guerin (BCG) or *Cornybacterium parvum* has shown only modest success. Cytokine therapy utilizing interferons has shown response rates reported in the 15 to 20% range. Most patients who respond have undergone nephrectomy, have an excellent pretreatment performance status, and have limited pulmonary metastases. Rosenberg and colleagues at NCI have used adoptive immunotherapy with lymphokine-activated killer (LAK) cells and interleukin-2 (IL-2). They reported a 35% objective response rate in 72 patients with renal cell carcinoma. Since then, efforts of this group have focused on using genetically altered tumor infiltrating lymphocytes (TIL) which are grown from single-cell tumor suspensions cultured in IL-2. Response rates of 0 to 33% have been reported in five trials of combination IL-2/TIL in patients with metastatic renal cell carcinoma.

Other Renal Tumors

Renal Oncocytoma

Oncocytomas constitute approximately 5% of solid renal neoplasms and invariably pursue a benign course. Microscopically these tumors are composed of polygonal cells with intense eosinophilia, granular cytoplasm, and abundant mitochondria. Grossly, on cut section, these tumors have brown pigmentation and are often associated with a central scar. The origin of these tumors is thought to be the distal collecting tubule. Because preoperative diagnosis is difficult and because oncocytomas can coexist with renal cell carcinoma, the treatment of choice is radical nephrectomy.

Angiomyolipoma

Angiomyolipomas are hamartomas composed of blood vessels, adipocytes, and abundant smooth muscle. They are seen commonly in patients with tuberous sclerosis and have a tendency to multiplicity and bilaterality. The fat content of these lesions often permits radiographic diagnosis with CT imaging. Asymptomatic tumors under 4 cm may be observed with radiographic monitoring. Symptomatic lesions can often be treated with angioinfarction. If surgery is required, excision of the lesion using renal parenchymal sparing techniques should be attempted because of the tendency toward multiplicity and bilaterality.

Sarcomas

Sarcomas represent less than 5% of all malignant tumors of the kidney. The most common sarcoma is leiomyosarcoma. Others include osteogenic sarcoma, liposarcoma, carcinosarcoma, fibrosarcoma, rhabdomyosarcoma, and malignant fibrous histiocytoma. The treatment of choice for all of these tumors is radical nephrectomy, if possible.

Metastatic Tumors

Because of their rich vascularity, the kidneys are frequently the site of metastatic spread. These tumors are often asymptomatic and discovered only at autopsy. Lymphoma is probably the most common metastatic neoplasm of the kidney; it may involve the renal parenchyma diffusely. With the exception of lymphomatous involvement which may respond to systemic therapy, treatment is usually unnecessary since the patient's prognosis from their primary tumor is almost uniformly poor.

RENAL PELVIC AND URETERAL TUMORS

Epithelial tumors of the upper urinary tract are uncommon. They show a male to female predominance of roughly 2:1 and are more common among whites than African-Americans. Tumors of the upper urinary tracts are common in patients with Balkan nephropathy and are more frequently bilateral. These upper tract tumors are commonly associated with bladder tumors which occur in 40 to 75% of patients at some point in time. Patients with bladder tumors have a slight (2 to 13%) chance of developing ureteral or renal pelvic tumors.

Etiology

An increased risk of renal pelvic and ureteral tumors has been reported for patients who smoke, abuse analgesics (particularly phenacetin), and who have been occupationally exposed to chemicals, petrochemicals, plastics, coke, coal, asphalt, and tar. Among these, cigarette smoking is the major risk factor for carcinoma of the upper urinary tract.

Pathology

Transitional cell carcinoma accounts for more than 90% of all upper tract urothelial tumors. The remaining 10%

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