Management of Carcinoma of the Kidney and Urinary Bladder

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Carcinoma of the Kidney

Tumors of the upper urinary tract constitute 1% to 2% of all cancers, and each year 11,000 new cases are diagnosed in the United States. Approximately half of these patients have metastatic disease at the time of diagnosis. Hypernephroma, or renal cell carcinoma, was first described in 1863 by Grawitz. These tumors arise from tubular epithelial cells and are correctly termed renal cell carcinoma or renal cell adenocarcinoma. There is evidence that further identifies the cell of origin as being from the proximal convoluted tubular epithelium. There does not appear to be a specific racial or ethnic incidence although it occurs three times more often in men than in women. Few epidemiological studies of this disease have been undertaken, although there is some association between the use of tobacco and an increased incidence of renal cell carcinoma. The classical triad of hematuria, pain, and a palpable mass are late findings with a poor prognosis which occurs in 10% of the patients and usually represents metastatic disease. Forty percent of the patients may have hematuria or other urinary complaints. Local effects of the tumors are hematuria, pain, and a flank mass, but the presenting symptoms may include a varicocele in the male which is produced by direct pressure of the tumor on the spermatic vein or because of stasis caused by an obstructing tumor thrombus in the vena cava. Systemic toxic effects such as hyperpyrexia may be of an intermittent or variable nature. Anemia or abnormal liver chemistries may also be present. Erythrocytosis, hypertension, and hypercalcemia may also be manifest.

Once a renal mass is found, a number of procedures can be followed in order to evaluate the patient before surgery. These include the use of intravenous excretory urography, retrograde pyelography, nephrotomography, renal angiography, and venacavography, along with sonographic examination of renal masses and the evaluation of renal masses by the use of computerized axial tomography.

The staging classification developed by Robeson is probably the most widely accepted: Stage 1—tumor confined within the kidney; stage 2—perirenal fat involvement confined within Gerota fascia; stage 3—a. gross renal vein or inferior vena cava involvement, b. lymphatic involvement, and c. vascular and lymphatic involvement; stage 4—a. adjacent organs other than the adrenal involved, and b. distant metastases. Renal vein involvement without perinephric involvement or lymphatic spread does not seem to alter the prognosis at 5-10 years where lymphatic involvement is an ominous sign.

Treatment

Surgical removal of the tumor for cure is the basic management of the patient with hypernephroma. The single, most significant advance in technique and its influence on survival were pointed out in 1968 by Robeson, who used the combination of early ligation of the renal artery and vein, complete

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removal of the perinephric envelope, and surgical extirpation of the lymphatic field. Caution in handling of the renal vein is important, especially if there is tumor involvement of the veins, as portions of renal vein tumor may break off and cause acute pulmonary embolization.

Preoperative Radiation

Several investigators have advocated the use of preoperative radiation in the management of renal cancer, but random clinical trials to date have not shown that this has improved long-term survival. In certain patients, however, a preoperative course of radiotherapy of 3,000-4,000 rads to the kidney in four weeks has markedly decreased the vascularity of the tumor. There is some evidence that postoperative radiotherapy may have a beneficial effect on survival statistics, especially if there has been extracapsular invasion and tumor has been left behind.

Chemotherapy

The use of chemotherapy in the management of metastatic renal carcinoma has proven particularly disappointing. Good results have been quoted by some investigators with the use of medroxyprogesterone (Provera) 100 mg t.i.d. and a number of other chemotherapeutic agents singly or in combination.

Special Management Problems

Involvement of the renal vein and vena cava are of interest because of the possible use of extracorporal circulation in order to approach the patient with tumor thrombus in the renal vein, the vena cava, and the atrium of the heart.

Carcinoma arising in a solitary kidney provides a real therapeutic dilemma. Procedures such as partial nephrectomy in situ, bench surgery with the removal of the kidney, perfusing the kidney for preservation, surgical excision of the tumor with repair of the kidney and autotransplantation back into the patient, and total extirpation with homotransplantation at a later date have all been used.

Approximately 12% of upper urinary tract malignancies are from renal pelvic tumors. These are often transitional cell carcinomas, but a few are of the squamous cell variety. The diagnosis is usually based on the appearance of a filling defect on intravenous urography or retrograde pyelography. A differential diagnosis from a nonopaque stone or blood clot may be difficult. As these tumors tend to be multiple, the therapy for them is total removal of the kidney and renal pelvis with removal of the entire ureter and a cuff of bladder. For those people who have undergone only partial removal of the ureter, recurrence in the stump of ureter has been high.

Bladder Cancer

Carcinoma of the urinary bladder accounts for 4% to 5% of all new cancers. Approximately 30,000 new cases of bladder cancer are found in the United States each year resulting in over 9,500 deaths. The incidence is three times more prominent in men than in women and four times more common in whites than in non-whites. Age distribution reveals a peak in patients 75-84 years of age, and 80% of these tumors occur after age 50.

The known and suspected causes of bladder cancer are grouped into four categories: 1) Industrial chemicals; 2) metabolites of foodstuffs; 3) tobacco tar; and 4) chronic mechanical irritation and infection.

All but 3% to 4% of bladder tumors originate in the transitional cell epithelium. Transitional cell carcinoma of the bladder occurs in approximately 90% of the patients, with squamous cell carcinoma accounting for 6% to 7% and adenocarcinoma 1% to 2%. Transitional cell carcinomas may be very small and papillary in character but may be multiple, large and sessile tumors; the surface may be intact or ulcerated, crusted, and bleeding. Squamous cell cancer, on the other hand, is usually flat, ulcerated, and sometimes necrotic; adenocarcinoma appears grossly as transitional or squamous and must be differentiated microscopically.

Diagnosis

Painless, gross hematuria is found in 75% to 85% of the patients presenting with carcinoma of the bladder. As the tumor enlarges, other symptoms such as frequency, urgency, dysuria, and decrease in caliber or force of the urinary stream may be present. These symptoms may be secondary to infection of the bladder or may be irritations caused by the tumor. As the tumor progresses, the suprapubic pain and a palpable mass may become prominent, these being associated with obstructive uropathy and uremia.

The diagnosis is made at the time of cystoscopy when a tumor is seen and biopsies can be obtained. It is important that a rectal and bi-manual examination be done to assess the size of the mass. A palpable,

hard, indurated mass is usually a sign of an advanced tumor and a poor prognosis.

Intravenous urography is an important step in the assessment of the patient with bladder cancer. The urogram will indicate the functional status of the kidneys and the possibilities of ureteral obstruction. By using triple-phase contrast studies of the bladder, one can ascertain fixation of the bladder wall and the possibility of invasion. If this is combined with pelvic arteriography in conjunction with perivesical and intravesical gas or with computerized axial tomography, a better evaluation of the size of the tumor may be found.

Grading and Staging

All tumors can be graded histologically based on the degree of cellular anaplasia. Grade I or well-differentiated tumor has a much better prognosis than a grade III or IV or poorly differentiated tumor. Staging in the United States has usually been by the A, B, C, D classification of Jewett and Strong, and Marshall. Recently the TNM (Tumor, Nodes, Metastasis) classification of the International Union Against Cancer has been publicized in order to get physicians in the United States to switch to that classification of all tumors. In general, however, a stage O tumor is one that is localized only to the mucosa; stage A is limited to the submucosa, and stage B_1 indicates that the tumor has invaded the bladder muscle but is less than half-way through the bladder wall. Stage B_2 tumors extend through the bladder muscle but do not invade the perivesical fat, and stage C indicates perivesical fat involvement or involvement of the capsule of another organ. Stage D_1 tumors are those that have spread to the regional pelvic lymph nodes or have invaded the pelvic wall or rectus muscle or both. Stage D_2 tumors exist when the tumor has spread beyond these limitations and is outside the pelvis and the immediate bladder area. Metastases occur most often to the regional lymph nodes, lungs, liver, and bone.

Treatment

The treatment of the patient with a superficial tumor is usually by means of endoscopic surgery with transurethral resection. Careful follow-up examination with repeat cystoscopies every three months for one year, and every six months for five years, and every year thereafter are necessary in order that any residual or recurrent tumors may be promptly found and the appropriate treatment instituted. For the patient with multiple recurring tumors, the use of intravesical therapy (ThioTepa), partial or total removal of the bladder, or radiation are possible therapeutic choices. For the patient with invasive transitional cell carcinoma, endoscopic procedures are not adequate. One cannot endoscopically tell the degree and extent of the tumor, therefore, an open surgical procedure with removal of the entire tumor or radiation therapy is indicated. It would appear as of this writing, that the best results are obtained from preoperative radiation followed by open surgical extirpation of the tumor, usually a radical cystectomy with urinary diversion. There is some discussion about whether 2,000 rads in one week, 4,000 rads in 4 weeks, or 4,500 rads in 6 weeks followed by either immediate or delayed cystectomy is best.

Chemotherapy

Long-term survival is rare once the tumor has spread beyond the confines of the bladder. One means of destroying metastases, however, may be through the use of combinations of chemotherapeutic agents. Drugs used in the management of patients with transitional cell carcinoma of the bladder have been 5-fluorourocil, bleyomycin, adriamycin, cyclophosphamide (Cytoxan) and the cis-platinum compounds.