Renal Cell Carcinoma

Background

1. General information
    - Accounts for 2-3 % of all malignancies
    - 5 variants
        - 75-85% clear cell tumors
        - 12-14% chromophilic
        - 4-6% chromophobic
        - 2-4% oncocytic
        - 1% collecting duct

Pathophysiology

1. Pathology of disease
    - Spreads by extension and vascular invasion
    - Metastatic disease noted in 23-33% of all newly diagnosed cases
    - Most common sites of metastasis in order of decreasing frequency
        - Lung, bone, upper abdominal (adrenals, contra-lateral kidney & liver), brain and skin
2. Incidence, prevalence
    - Peak age 60-80 years
    - Men > women 2:1
    - 54,000 new cases / year and 13,000 deaths / year in the United States
        - Recent increase in incidence, likely secondary to early detection
3. Risk factors
    - Smoking
    - Obesity
    - Occupation exposure to cadmium, asbestos or petroleum products
    - Acquired cystic kidney disease (polycystic kidneys)
    - Analgesic abuse
    - Nephropathy
    - End stage renal disease on dialysis
        - After 3 years of dialysis, nearly 80% of patients develop acquired cystic kidney disease
        - This causes a 50-fold increase risk for developing renal cell carcinoma, compared to the general population
    - Genetic predisposition (Von Hippel-Lindau disease, tuberous sclerosis)
4. Morbidity / mortality
    - Based on tumor size and presence of metastasis

Diagnostics

1. History
    - Classic triad of hematuria, abdominal or flank pain, flank mass occurs in 5-10%
    - Other symptoms include fever, weight loss, sweats, malaise, anemia, and paraneoplastic symptoms
        - A number of ectopic hormones can be produced including parathyroid hormone-related protein, gonadotropins, renin, erythropoietin and ACTH-like substances

        - These can cause hypercalcemia, hepatic dysfunction, in the absence of liver metastasis (stauffer's syndrome), hypertension and Cushing's syndrome
        - Less commonly erythrocytosis and amyloidosis
    - Incidental diagnosis made on radiological procedures is increasingly common
2. Physical examination
    - Flank mass present 20-40%
    - 11% with scrotal varicoceles
3. Diagnostic testing
    - Laboratory evaluation
        - UA with cytology, CBC, LFTs, calcium
    - Diagnostic imaging
        - CT scan of abdomen and pelvis
        - Renal ultrasound may help delineate if cystic or solid
    - Pre-op needle biopsy of primary lesion NOT recommended due to concerns of seeding peritoneum and poor specificity
4. Other studies
    - Tumors > 3cm, consider MRI of abdomen/pelvis to evaluate renal vein & IVC for caval thrombus
    - CT chest to evaluate for pulmonary metastasis
    - Bone scan if bone pain present
    - MRI brain for neurological symptoms
5. Tumor staging based on clinical and radiographic presentation
    - TNM system

Differential Diagnosis

1. Key differential diagnoses
    - Pyelonephritis
    - Renal abscess
    - Renalcysts
    - Benign tumors
        - Angiomyelipoma, adenoma, oncocytoma
    - Metastatic disease
2. Extensive differential diagnoses
    - Other malignancies including Wilms tumor, sarcoma, lymphoma, carcinoid, transitional cell carcinoma of renal pelvis

Therapeutics

1. Acute treatment
    - Surgical management
    - Surgery type based on tumor size and presence or absence of metastasis (TMN system)
        - Lesions > 4cm are treated with radical nephrectomy
        - Cortical lesions < 4cm can be treated with partial nephrectomy (nephron sparing)
        - Small lesions can be treated with cryoablation / radiofrequency ablation
    - Isolated metastasis if possible can be treated with solitary resection

- Immunotherapy and molecular targeted therapy can be useful for treatment of metastatic disease

2. Long-term care
   - Clinical monitoring
   - Re-occurrence in 20-50%
     - Occurs within first 2-5 years post treatment but up to 10% re-occur after 5 years

Follow-Up

1. Post treatment surveillance is critical but evidence to support them is not clear
2. Surveillance protocols are based on tumor size, stage, nuclear grade and metastasis
3. For T1 primary tumors physical exam, labs such as CBC and liver function studies & chest x-ray are recommended at least twice a year for 2-3 years then yearly to 5 years
4. T2 primary tumors are monitored with history and physical exams, labs and chest x-ray every 6 months for 3 years then annually till 5 years out
   - Abdominal CT can be done annually for 3 years or at year 2 and 5 post resection
5. T3 or T4 primary tumors have protocols recommending history and physical, labs and chest x-ray every 6 months for a few years then annually
   - Abdominal CT scans recommended every 3-6 months for the first 3 years after surgery
   - Following this, abdominal CT scans every 1-2 years
6. Renal cell carcinomas treated with ablation therapies require close monitoring with CT scan or MRI to evaluate the ablation zone
   - There is a 10% risk of residual or recurrent disease with this treatment method that may require treatment with salvage or recurrent ablative therapy
   - Three or four CT or MRI studies done in the first year at the 1, 3, 6 and 12 month post ablation are recommended
   - Long-term surveillance protocols are still unknown

Prognosis

1. Overall 5 year survival rate 62%
2. Advanced or metastatic disease is associated with a poorer prognosis with 5 year survival of 13-50%

Prevention

1. Screening for high risk individuals may be considered for those with inherited conditions associated with RCC, strong family history & those with ESRD on dialysis >3years

Patient Education

1. "What You Need to Know About Kidney Cancer" National Cancer Institute
   - http://www.cancer.gov/pdf/WYNTK/WYNTK_Kidney.pdf Accessed 3.26.2009

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