RENA L C E LL C A RC INOMA

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PG 3RD YEAR
GENERAL MEDICINE
Epidemiology

- RCC is responsible for 2% - 3% of all malignancies in the adults.
- The peak incidence age is: 60 – 80 years old.
- Men : Women ratio of 2:1
- Arises from renal tubular cells
- Commonly sporadic
- Patients with a family history comprise about 4% of all cases of RCC.
**Etiology**

- Tobacco
- Obesity
- Chronic arterial hypertension
- Diabetes mellitus
- End-Stage Renal Disease on hemodialysis
- High fat, high protein diet, fried food, red meat
- Occupational exposure (asbestos, cadmium)
- Family history of RCC
- Analgesic usage
Genetic and hereditary conditions

- Von Hippel-Lindau (VHL) Disease
- Hereditary Papillary Renal Cell Carcinoma
- Birt-Hogg-Dube Syndrome
- Hereditary Renal Oncocytoma
- Polycystic Kidney Disease
Pathology

**Figure 40.3.1.** Kidney cancer is not a single disease, it is made up of a number of different types of cancers that occur in the kidney, each with a different histology, a different clinical course and caused by a different gene. (From ref. 178, with permission.)
Clinical Presentation

- Small tumors as incidental findings
- Hematuria
- Abdominal pain
- Palpable abdominal mass
Paraneoplastic syndromes

- Hypercalcemia
- Polycythemia
- Neuromyopathy
- Amyloidosis
- Stauffer syndrome
- Anemia
Diagnostic tests

- History & Physical Exam
- Laboratory: CBC, CMP, LDH, ESR, U/A
- CXR, Abdomino-pelvic CT Scan
- MRI if IVC thrombosis suspected
- Bone scan if bone metastases suspected
<table>
<thead>
<tr>
<th>PRIMARY TUMOR (T)</th>
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<tbody>
<tr>
<td>TX</td>
</tr>
<tr>
<td>T0</td>
</tr>
<tr>
<td>T1</td>
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<tr>
<td>T1a</td>
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<td>T1b</td>
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<td>T3</td>
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<td>T3a</td>
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<td>T3b</td>
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<td>T3c</td>
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<td>T4</td>
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<table>
<thead>
<tr>
<th>NODAL INVOLVEMENT (N)</th>
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<tbody>
<tr>
<td>The regional lymph nodes are the para-aortic and paracaval nodes. The juxtaregional lymph nodes are the pelvic nodes and the mediastinal nodes.</td>
</tr>
<tr>
<td>NX</td>
</tr>
<tr>
<td>N0</td>
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<tr>
<td>N1</td>
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<td>N2</td>
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<tr>
<th>DISTANT METASTASIS (M)</th>
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<tbody>
<tr>
<td>MX</td>
</tr>
<tr>
<td>M0</td>
</tr>
<tr>
<td>M1</td>
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(From ref. 180, with permission.)
# Table 29-1: Stage Definitions for Renal Cell Carcinoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
<th>TNM*</th>
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</thead>
<tbody>
<tr>
<td>I</td>
<td>Limited to kidney; 7 cm or less.</td>
<td>T1, N0, M0</td>
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<tr>
<td>II</td>
<td>Limited to kidney; more than 7 cm.</td>
<td>T2, N0, M0</td>
</tr>
<tr>
<td>III</td>
<td>Extends into major veins or perinephric tissues but not beyond Gerota’s fascia.</td>
<td>T1, N1, M0, T2, N1, M0</td>
</tr>
<tr>
<td>IV</td>
<td>Metastases or local invasion beyond Gerota’s fascia.</td>
<td>T3, N0, N1, M0, Any T4, any N2, any M1</td>
</tr>
</tbody>
</table>

TNM = tumor, node, metastasis.

* T3a directly invades the adrenal gland or perirenal and/or renal sinus fat; T3b grossly extends into the renal vein, its segmental branches, or the vena cava below the diaphragm; T3c invades the wall of the vena cava or extends into the vena cava above the diaphragm. N1 is defined as metastasis to a single regional lymph node irrespective of laterality, and N2 is any lymph node involvement beyond N1.

Source: Data from Guinan et al. (39). With permission.
Prognostic factors

- Symptomatic presentation
- Weight loss
- ESR > 30 mm/hr
- Corrected serum calcium >10
- Anemia
- Elevated alkaline phosphatase (>1.5 times upper limit)
- Tumor size, positive margins, liver & lung metastases,
Treatment options

- Surgery
- Rad. Nephrectomy
- Partial nephrectomy
- Nephron sparing surgery
- Minimal invasive methods (thermal ablative therapy)
- Immunotherapy
- Chemotherapy
- Radiotherapy
- Targeted agents
Localized RCC Treatment

- Surgery is the only curative therapy for stage I-III
- Radical nephrectomy is gold standard
- Partial nephrectomy in selected patients
- 20-30% of patients relapse within 2-3 years
  - Metastases to the lung most common 50%
  - Local recurrence is rare 2-3%
Laparoscopic radical nephrectomy is rapidly replacing the open radical nephrectomy with T1-2 tumor.

Open radical nephrectomy is mainly reserved for T3 tumor/tumor of >8 cm / tumor with R.V or IVC involvement.

Nephron sparing surgery will play a major role in small <4 cm peripheral tumor.
Targeted Therapy

- Highly vascularised tumor with increased VEGF and EGFR expression
- Tumor growth mediated via VEGF pathway and mammalian target of rapamycin (mTOR) pathway
VEGF Pathway Inhibition

- Tyrosine kinase (TK) inhibitors block the intracellular domain of the VEGF receptor
- Sunitinib
- Sorafenib
- Monoclonal antibody that binds circulating VEGF preventing the activation of the VEGF receptor
- Bevacizumab
mTOR Pathway Inhibition

- Temsirolimus (TMSR) is a rapamycin analog that inhibits mTOR kinase
- Benefit greater in non-clear cell RCC
Immunotherapy

- Spontaneous remissions have been documented.
- Increased risk of cancer in immunodeficient states
- Tumor infiltrating lymphocytes (TILs) have been found within tumors.
- Interferon alpha
- Interleukin-2 (IL-2)
Chemotherapy

- RCC is only minimally responsive to chemotherapy
- Vinblastine
- Floxuridine
- Mostly limited responses, rare to see increased survival
Radiation Therapy

- RCC relatively radioresistant
- Painful bone or recurrent abdominal metastases
- Brain metastases
Conclusion

- RCC is relatively rare but increasing incidence
- Associated with tobacco and inherited disorders
- Surgery is the only curative modality for Stage I, II, and III
- Stage IV disease holds poor prognosis despite advancements in molecular understanding
- IL-2, Sorafenib, Sunitinib, and Temsirolimus are FDA approved treatments for advanced RCC