Malignant Renal Masses in Pediatrics and the Role of the Pediatric Surgeon

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Grand Rounds
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Pre-Test

Intraoperative procedures performed during nephrectomy for unilateral Wilms’ tumor should include:

a. exploration of the contralateral kidney
b. sampling of perirenal, periaortic and pericaval lymph nodes
c. extensive hepatic resection in setting of tumor invasion
d. routine removal of the ipsilateral adrenal gland
e. partial nephrectomy if disease localized at the upper pole
A five-year-old boy is referred for evaluation of a large right-sided varicocele. He is asymptomatic. A scrotal ultrasound obtained by the pediatrician demonstrated normal testes bilaterally, with equal volume measurements.

The next step in management is:

a. observation and serial exams
b. doppler venography of the iliacs
c. abdominal CT or US
d. laparoscopic right varicocele ligation
e. venous embolization
A four-month-old presents with hypertension and a palpable right flank mass. Ultrasound and CT scan shows a solid right renal mass.

The most likely diagnosis is:

a. hydrenephrosis  
b. dysplastic kidney  
c. mesoblastic nephroma  
d. Wilms’ tumor  
e. neuroblastoma
A toddler presenting with a 14 cm mass originating from the upper pole of the left kidney also has multiple pulmonary nodules identified on CT scan.

Appropriate initial surgical therapy includes:

a. nephrectomy
b. laparoscopic biopsy
c. retroperitoneal lymph node dissection
d. resection of involved right hepatic lobe
e. thoracoscopic pulmonary nodule biopsy
• Pre-test
• Background and Challenges
• Malignant renal masses
  • Rapid review
• Putting it all together
  • Pediatric Surgeon
• Summary
• Post-test
Renal masses in children

- 10 Malignant
  - Several subtypes (RCC)
- 6-7% of all childhood tumors

Detection

- Incidental
- Routine physical examination
- Known clinical syndromes

Renal lesions in children

<table>
<thead>
<tr>
<th>Malignant</th>
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<tr>
<td>Wilms tumor</td>
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<tr>
<td>Clear Cell Sarcoma</td>
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<tr>
<td>Renal Cell Carcinoma</td>
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<tr>
<td>Clear cell</td>
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<td>Medullary carcinoma</td>
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<td>Multicyctic</td>
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<td>Chromophobe</td>
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<td>Collecting duct</td>
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<td>Translocation</td>
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<td>Xp11.2</td>
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<td>t(6;11)</td>
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<tr>
<td>Nephroblastomatosis</td>
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<td>Rhabdoid tumor</td>
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<td>Anaplastic sarcoma</td>
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<td>Congenital mesoblastic nephroma</td>
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<td>Desmoplastic small round cell tumor</td>
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<tr>
<td>Ewing sarcoma/PNET</td>
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<tr>
<td>Synovial sarcoma</td>
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Pieces of the Puzzle...

- Age?
- How did they present?
- Imaging modalities used?
The Challenges

- Malignant or Benign?
  - Thorough diagnostic evaluation
- To biopsy or not to biopsy?
  - What do you think it is?
  - What is the risk/benefit of biopsy?
- Pediatric surgeon
  - Is it resectable?
• Understand profile of malignant renal masses
  • Associated clinical and imaging features

• Goals
  • Accurate preoperative diagnosis
  • Precise oncologic surgery
  • Optimize patient care and outcomes
Approach

Renal Mass

History
Flank pain
Abdominal mass
   Fever
Hematuria
Pyuria

Physical Examination
Hypertension
Congestive heart failure
Palpable abdominal mass

Laboratory findings
Polycythemia
Hypercalcemia

Radiologic Imaging
Ultrasound
CT Abdomen and Pelvis
(+/- Head and Chest)
 +/- MRI

Multidisciplinary review by cancer specialists to determine optimal approach

Further workup required?
Benign or Malignant?
Resectability?
Staging systems

- NWTS/COG
  - WT
- AJCC/TNM
  - RCC
- Imaging studies
  - Localized vs metastatic, thrombus
- Surgical findings
  - Implants, invasion, palpable thrombus, rupture
- Pathologic findings
  - Cellular type, lymph nodes
Implications for Biopsy

- Histology
  - Gold standard for diagnosis
- Biopsy risks
  - General anesthesia
  - Tumor spread (upstage → WT)
  - Sampling error
  - Inability to distinguish benign/malignant
Malignant renal tumors
- **Wilms tumor** (Nephroblastoma)
  - Most common
    - Pediatric renal malignancy
      - 6-7% all childhood cancer
    - Sporadic form
    - 2-5 years of age
    - Unilateral
      - < 13% bilateral
  - 1:10 000 newborns
WT associated genetic syndromes
- WAGR
  - WT +
  - ???
  - Genitourinary abnormality
  - Mental Retardation
  - Deletion on 11p13
  - Bilateral WT
• WAGR
  • WT +
    • Aniridia
    • Genitourinary abnormality
    • Mental Retardation
  • Deletion on 11p13
  • Bilateral WT
- Denys-Drash
- Pseudohermaphroditism
- Chronic renal failure
- WT1

Early syndrome
**********
• Denys-Drash
  • Pseudohermaphroditism
  • Chronic renal failure
  • WT1

Diffuse Mesangial Sclerosis

Early Nephrotic syndrome
Syndrome???

- Macroglossia
- Macrosomia
- Midline abdominal wall defects
- Neonatal hypoglycemia
- WT2
• Beckwith-Wiedemann
  • Macroglossia
  • Macrosomia
  • Midline abdominal wall defects
  • Neonatal hypoglycemia
  • WT2
Presentation
- Asymptomatic
- Abdominal pain/distention, hypertension

Imaging
- Ultrasound
- CT
Staging

Box 1: Wilms tumor staging system (COG)

1. Tumor limited to kidney and completely excised. The surface of the renal capsule is intact. Tumor was not ruptured before or during removal. There is no residual tumor apparent beyond the margins of excision.

2. Tumor extends beyond the kidney, but is completely excised. There is regional extension of the tumor; i.e., penetration through the outer surface of the renal capsule into perirenal soft tissues. Vessels outside the kidney substance are infiltrated or contain tumor thrombus. There is no residual tumor apparent at or beyond the margins of excision.

3. Residual nonhematogenous tumor confined to abdomen. Any one or more of the following occur:
   a. Lymph nodes are involved with tumor.
   b. There has been peritoneal contamination by tumor such as by biopsy or rupture of the tumor before or during surgery, or by tumor growth that has penetrated through the peritoneal surface.
   c. Implants are found on the peritoneal surfaces.
   d. The tumor extends beyond the surgical margins either microscopically or grossly.
   e. The tumor is not completely resectable because of local infiltration into vital structures.

4. Hematogenous metastases. Deposits beyond stage III; i.e., lung, liver, bone, and brain.

5. Bilateral renal involvement at diagnosis. An attempt should be made to stage each side according to the above criteria on the basis of extent of local disease.
Treatment

- Unilateral and resectable
  - Nephrectomy + lymph node sampling
- Unilateral and unresectable
  - Chemotherapy then surgery

Situations requiring nephron sparing approach

- Bilateral WT
- Solitary or Horseshoe kidney
- Clear cell sarcoma
  - 2nd MC
  - 3-5%
  - < 4 years of age
  - Aggressive
    - Likes Bone and brain
    - Compresses renal parenchyma
    - Displaces collecting system
• Typical presentation
• Large, unilateral, well circumscribed mass
- Cytogenetic abnormalities
  - Translocations
    - T(10;17)(q22;p13/p12)
  - Deletions
    - 14q24q31
- Lymph node metastases
  - 29%
- Treatment
  - Radical nephrectomy + Lymph nodes
  - Chemotherapy and radiation
Renal cell carcinoma

- MC renal tumor adolescents
- 10-11 years of age
- Several subtypes
- Greater frequency
  - Childhood cancer survivors
  - Von Hippel-Lindau disease
  - Mutation gene???
Renal cell carcinoma

- MC renal tumor adolescents
- 10-11 years of age
- Several subtypes
- Greater frequency
  - Childhood cancer survivors
  - Von Hippel-Lindau disease
    - vHL-tumor suppressor gene
    - Short arm chromosome 3
Renal cell carcinoma

- MC renal tumor adolescents
- 10-11 years of age
- Several subtypes
- Greater frequency
  - Childhood cancer survivors
  - Von Hippel-Lindau disease
  - Cystic or ESRD
  - Sickle cell hemoglobinopathies
  - Pediatric renal transplant recipients
• Classic triad
  • Gross hematuria, flank pain, palpable mass
• MC mets
  • Lungs and bones
Imaging

- Usually invades tissue locally
- Regional lymphadenopathy, vascular invasion
Treatment

- Surgery
  - Radical nephrectomy
  - Regional lymphadenectomy
- Cytotoxic therapies
  - Generally resistant
- Radiotherapy
  - Poorly responsive
- Rhabdoid
  - < 2% of all pediatric renal malignancy
  - < 2 years of age
  - Highly aggressive
    - Lethal
Distinct clinical presentation
- Fever, hematuria, young age, advanced disease
- Hypercalcemia
Distinct clinical presentation
- Fever, hematuria, young age, advanced disease
- Hypercalcemia ➔ Parathormone
Imaging

- Hemorrhage, necrosis, calcifications
• Germline mutation ~35%
  • *SMARCB1*

• Treatment
  • Chemotherapy
  • Radical nephrectomy
• Congenital Mesoblastic Nephroma
  • MC solid renal tumor in infancy
    • < 3m
    • 90% < 1 year of age
  • Low grade fibroblastic sarcoma
- Manifestations
  - Hypercalcemia, CHF, hypertension
- Prenatal ultrasound
  - Polyhydramnios
• Imaging
  • Large, heterogeneous intrarenal mass
Treatment

- Radical nephrectomy
  - Complete surgical resection adequate
  - If incomplete then adjuvant chemotherapy
Rarer than rare

- DSRCT
  - t(11;22)(p13;q12) translocation
- Ewing sarcoma/PNET
  - t(11;22)(q24;q12) translocation
    - ~90%
- Synovial sarcoma
  - t(x;18)(p11;q11) translocation
Rarer than rare

- DSRCT
  - t(11;22)(p13;q12) translocation
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Wagyu beef
Putting it all together...

- Known renal mass
  - Age
- Imaging
  - Assessment
    - Primary tumor
    - Vascular extension
    - Metastatic disease
• Associated Medical Conditions
  • HTN, hypercalcemia
• Approach to resection
  • Oncologic principles
Oncologic principles

- Adequate exposure
- Full visual and manual exploration
  - Abdominal cavity
- Dissection
  - Colon mobilization
  - Systematic mobilization of kidney/mass/ureter
- Vascular
  - Clearly identify
  - Feel
  - Ligate and Divide
- DO NOT Rupture!!!
Case 1
2yM

- 1m history “lazy eye”
- Eval by local optometrist/ophthalmologist
- Concern for widespread retinopathy
- Plan HTN work-up
- Metastatic work-up negative
- Impression
  - 2yM with unilateral multinodular right renal mass
OR

- Laparotomy
- Right radical nephrectomy, resection associated adenopathy
Pathology

- Multifocal WT
- Focal anaplasia confined to upper pole tumor
- 12/12 LN negative for tumor
Case 2
- 3yM
- Ex-27 weeker
- h/o UTI
- Metastatic work-up negative
- **Impression**
  - 3yM with unilateral solid right renal mass
OR
- Laparotomy
- Right nephrectomy, resection of associated adenopathy
Pathology

- WT, favorable histology
- 4/4 LN negative
Case 3
19yM

- ALL s/p SCT 2010
- ESRD (BK virus) on hemodialysis
- GVHD
- Chronic lung disease
- CT bone density 2013
  - Incidental left renal mass
• Metastatic work-up negative
• Impression
  • 19yM h/o ALL, ESRD with unilateral solid left renal mass
OR

- Left radical nephrectomy

Pathology

- RCC with Xp11.2 translocation
- Extensive invasion
  - Renal sinus and soft tissues
- Inked resection margins negative for tumor
• Routine follow up ultrasound
Metastatic work-up negative

Impression

20yM h/o ALL, ESRD, left RCC s/p radical nephrectomy with new solid right renal mass
OR

- Right radical nephrectomy

Pathology

- RCC with Xp11.2 translocation
- Inked resection margins negative for tumor
Case 4
4yF Ecuador

- Abdominal mass (age 2)
- Imaging
  - Large left renal mass
- Planned resection → biopsy
  - Chemotherapy
    - 8 months
    - Completed treatment 2 years ago
- Referred
- Metastatic work-up negative
- Impression
  - 4yF left renal mass
• OR
  • Laparotomy
  • Left nephrectomy, resection associated adenopathy
- Pathology
  - WT extensive treatment effect
  - All resection margins negative
  - 5/5 LN negative
  - Accessory spleen negative
Summary

- Malignant renal masses in Pediatrics
  - Rare (WT>CCSK>RCC>Rhabdoid>CMN)
  - Fundamental differences in profiles
- Thorough evaluation
  - H&P, Laboratory data, Radiologic imaging
- Staging
- Multidisciplinary team
- The role of the Pediatric Surgeon...
“... The most important role for the surgeon is to ensure complete tumor removal without rupture and assess the extent of disease”
Let’s get outta here

Vamos!!!!
References

- Photo WT1 Diffuse Mesangial Sclerosis: http://www.humpath.com/spip.php?article3297
- Photo BWS: http://healthfoxx.com/beckwith-wiedemann-syndrome-pictures-prognosis-management/


Post-Test

Intraoperative procedures performed during nephrectomy for unilateral Wilms’ tumor should include:

a. exploration of the contralateral kidney
b. sampling of perirenal, periaortic and pericaval lymph nodes
c. extensive hepatic resection in setting of tumor invasion
d. routine removal of the ipsilateral adrenal gland
e. partial nephrectomy if disease localized at the upper pole
Discussion

The correct answer is B.

Radical nephrectomy is the standard procedure for most unilateral Wilms’ tumors (WT). During nephrectomy, careful technique must be observed to ensure en-bloc resection of the tumor with minimal risk of rupture. For unilateral disease, there is no role for partial nephrectomy, with partial nephrectomy limited to select cases of bilateral disease. Risk factors for local tumor recurrence include tumor spillage, as well as unfavorable histology, incomplete removal of tumor, and absence of lymph node sampling.

Surgical exploration should follow guidelines advocated by surgical study groups, with the Children’s Oncology Group (COG) guiding practices in North America. Although routine exploration of the contralateral kidney was originally recommended by COG, this is not currently advocated as long as preoperative CT imaging does not suggest bilateral disease.

Formal lymph node dissection is not currently recommended, although lymph node sampling from the ipsilateral renal hilal, pericaval, and paraaortic areas should be done for staging. The absence of lymph nodes in the specimen mandate treatment as Stage III disease.

In case of tumor extension into the renal vein or subhepatic vena cava, the thrombus should be removed en bloc with the kidney. Patients with tumor extension into either the intrahepatic or suprahepatic vena cava should be biopsied only, and managed with chemotherapy to facilitate shrinkage of the intravascular thrombus prior to resection.

Although the adrenal gland should be removed if required to obtain gross total tumor resection, removal is not mandatory for all tumors. In the presence of invasion of other adjacent organs, resection of a small portion of diaphragm, psoas muscle, pancreas or diaphragm is acceptable. However, if resection of multiple organs or extended liver resection is required to allow for complete tumor removal, primary resection is not indicated. Biopsy followed by chemotherapy may allow for a safer delayed resection.

Although controversial, preoperative chemotherapy prior to resection, as advocated in Europe under SIOP, is gaining interest in North America, particularly for large bulky tumors. A comparison of NWTS-5 and SIOP-93-01 trials demonstrated that the overall complication rate for the SIOP patients, particularly for tumor spillage and local recurrence, was lower compared to NWTS patients.

References


Level of evidence: II
A five-year-old boy is referred for evaluation of a large right-sided varicocele. He is asymptomatic. A scrotal ultrasound obtained by the pediatrician demonstrated normal testes bilaterally, with equal volume measurements.

The next step in management is:

a. observation and serial exams
b. doppler venography of the iliacs
c. abdominal CT or US
d. laparoscopic right varicocele ligation
e. venous embolization
Discussion

The correct answer is C.

Varicoceles (dilation of the veins of the spermatic cord or pampiniform plexus) are a relatively common finding in adolescent boys, with an incidence estimated as high as 15%. In contrast, varicoceles are uncommon in five-year-old boys, and a right-sided varicocele may indicate proximal venous compression by a neoplasm. A screening study (US or CT) is a reasonable approach.

An underlying coagulopathy or congenital venous abnormality is possible but unlikely. The incidence in children under the age of 10 years is about 1%. The majority of varicoceles are found on the left, as a result of drainage of the left internal spermatic vein into the left renal vein, and drainage on the right directly into the inferior vena cava. Indications for treatment of varicocele include a discrepancy in testicular volume (by ultrasound) of >20%, symptoms, and fertility problems or abnormal findings on semen analysis in older patients. Varicoceles are treated by laparoscopic ligation of the veins (and sometimes the artery as well – Paloma procedure), trans-inguinal ligation of the veins, a microsurgical approach, or obliteration of the veins by interventional radiology. However, the child presented has no indication for varicocelectomy.

References

A four-month-old presents with hypertension and a palpable right flank mass. Ultrasound and CT scan shows a solid right renal mass.

The most likely diagnosis is:

a. hydrenephrosis
b. dysplastic kidney
c. mesoblastic nephroma
d. Wilms’ tumor
e. neuroblastoma
Discussion

The correct answer is C.

Only ten percent of renal tumors present in patients less than six months of age. Although hydronephrosis is the most common newborn flank mass, sonographically, hydronephrosis and dysplastic kidneys are cystic. The majority of solid renal masses are Wilms’ tumors but usually occur between one and four years of age. In this age group congenital mesoblastic nephroma occurs twice as frequently as Wilms’. Paraneoplastic syndromes such as hypertension or hypercalcemia are common in infants with CMN.

This tumor is generally cured by nephrectomy. In order to avoid local recurrence generous margins should be obtained due to the tumor’s tendency to infiltrate the renal hilum and surrounding tissue. Chemotherapy has been effective in those rare patients with metastases.

References

A toddler presenting with a 14 cm mass originating from the upper pole of the left kidney also has multiple pulmonary nodules identified on CT scan.

Appropriate initial surgical therapy includes:

a. nephrectomy
b. laparoscopic biopsy
c. retroperitoneal lymph node dissection
d. resection of involved right hepatic lobe
e. thoracoscopic pulmonary nodule biopsy
Discussion

The correct answer is A.

This child has stage IV disease due to the pulmonary metastasis. Treatment regimes differ between NTWS and SIOP. In North America most of the children with stage IV disease will undergo upfront surgical resection. Indications for pre-operative chemotherapy include those with bilateral tumors, inferior vena cava and intra-atrial involvement and patients with massive tumors that the operating surgeon feels are not initially resectable. This decision however often cannot be made without initial exploration. It is vital for the operating surgeon to remove the primary tumor completely, without spillage and to assess the extent of tumor spread. Visual assessment of lymph nodes is not adequate and ipsilateral nodes along the IVC or aorta need to be removed for histologic inspection.

The controversy over preoperative chemotherapy exists because in Europe many children treated under SIOP protocols will be managed in this manner. However there is evidence to suggest that this methodology may have adverse effects on staging and histologic evaluation which may lead to under treatment of the disease. For example SIOP studies suggest a higher recurrence in infra-diaphragmatic recurrence for those children with stage III disease who did not receive post-operative radiation therapy.

The child in this scenario should undergo up front surgical resection and then based on histology undergo therapy for favorable or unfavorable disease. Biologic markers showing loss of heterozygosity (LOH) on 1p and 16q also are used in determining the regimen. Stage IV disease without LOH require 3 drug chemotherapy to include doxorubicin, vincristine and actinomycin D. If pulmonary disease responds rapidly no pulmonary radiation therapy (XRT) is needed. Slow or incomplete response or those with 1p and 16q LOH require pulmonary XRT.

References