Pediatric Renal Tumors

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Table of Contents

Introduction ........................................... 2
Wilms’ Tumor ........................................ 2
Bilateral Wilms’ Tumor ............................. 13
Mesoblastic Nephroma ........................... 15
Angiomyolipoma .................................... 16
Multicystic Dysplastic Kidney ................. 18
References ........................................... 20

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Christopher S. Cooper, MD

INTRODUCTION

Pediatric renal tumors are rare relative to adult tumors, and the most current methods of treatment may not be familiar to many urologists. Active research and advances in treatment of pediatric renal cancers continues to change urologic practice. A basic understanding of the pathology of these tumors, standard evaluation techniques, and risks and benefits of various treatment options helps the urologist to determine the treatment approach that will likely yield the best results for a particular patient.

This manual considers Wilms’ tumor as well as other kidney tumors, including mesoblastic nephroma, multicystic dysplastic kidney, and angiomyolipoma. Case-based discussions are used to highlight issues related to pathophysiology, patient presentation and evaluation, treatment options, and patient outcomes.

WILMS’ TUMOR

CASE 1 PRESENTATION

Patient 1 is a 2-year-old boy who initially presented to his primary care physician with a history of gross hematuria. He was treated with antibiotics for a presumed urinary tract infection, and the hematuria resolved. A voiding cystourethrogram revealed neither reflux nor bladder or urethral abnormalities.

The patient presents 1 month later with a history of recurrent gross painless hematuria and is referred to a urologist for evaluation. There is no other significant past medical, family, or surgical history. On physical examination, the patient is afebrile with a pulse of 113 bpm and a blood pressure of 127/65 mm Hg. The examination is remarkable for a palpable 5-cm mass in the right upper quadrant of the abdomen. The results of the physical examination are otherwise normal, and no adenopathy is detected.

- What imaging studies are appropriate in the evaluation of patient 1?

INITIAL EVALUATION

Evaluation of Gross Hematuria in Children

Any patient—child or adult—with a history of hematuria should undergo urinalysis to confirm the presence of erythrocytes in the urine and to exclude infection, proteinuria, or casts suggestive of medical renal disease. However, the imaging evaluation of children differs from that of adults. Because children are much less likely than adults to be affected by neoplasm, intravenous pyelogram (IVP) and cystoscopy—components of the standard evaluation in adults—are not routinely recommended in children.

Causes of hematuria in children include infection, medical renal disease, and congenital anomalies, as well as neoplasm. If the bleeding occurs only as spots in the underwear, the history is consistent with idiopathic anterior urethritis (urethrorrhagia), which is a benign, self-limited process and requires no further evaluation.1 In a child with gross painless total hematuria, a renal and bladder ultrasound should be obtained. A voiding cystourethrogram also should be obtained to evaluate the bladder and urethra.2

If a solid renal mass is detected on ultrasound, Wilms’ tumor is often suspected. Wilms’ tumor characteristically demonstrates a heterogeneous echo pattern on ultrasonography and can vary from predominately cystic to solid. Ultrasonography often permits assessment of the renal vein and inferior vena cava for the presence of tumor thrombus. If IVP is performed, an intrarenal mass may be manifested by distortion of the calyceal morphology. The use of IVP for evaluating patients with suspected Wilms’ tumor has declined, however, because of the increased availability of ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI).

MRI accurately evaluates the extent and size of renal tumors, including Wilms’ tumor, which often gives variable signal intensities. Areas of hemorrhage show increased signal intensity on T1- and T2-weighted pulse sequences. Regions of necrosis demonstrate a decreased signal on T1- but not on T2-weighted pulse sequences.3
CT also provides precise anatomic delineation of the renal and retroperitoneal anatomy.

Unfortunately, no imaging study can completely exclude the possibility of a renal mass harboring a malignancy. For this reason, even those tumors thought to be benign (e.g., angiomyolipoma or multicystic dysplastic kidney) require evaluation with serial imaging.

Differential Diagnosis of Pediatric Renal Masses

The most common renal mass in children is hydronephrosis. This can usually be diagnosed with renal ultrasonography; however, it can be difficult to differentiate from a multicystic dysplastic kidney or a cystic tumor (Figure 1). Other benign pediatric renal masses include congenital mesoblastic nephroma, multilocular cyst, angiomyolipoma, teratoma, polycystic kidney, glomerulocystic kidney, abscess, and xanthogranulomatous pyelonephritis (Figure 2A). The most common primary renal cancer in children is Wilms' tumor, followed in prevalence by renal cell carcinoma. Other primary renal cancers which occur more rarely are rhabdoid tumors, clear cell sarcoma, rhabdomyosarcoma, neuroblastoma, leiomyosarcoma, transitional cell carcinoma and anaplastic mesenchymal tumors (Figure 2B).

Continued Evaluation of Patient 1

Ultrasonograms of patient 1’s kidney and bladder are obtained. They reveal no abnormalities of the bladder; however, a solid renal mass is noted in the right kidney. An abdominal CT scan is performed, which reveals a large (5.5 cm × 5 cm × 5 cm) inhomogeneous lesion of the right superior pole with a thinned rim of parenchyma in the lower pole with hydronephrosis (Figure 3). There is no evidence of extrarenal invasion by the tumor. Functioning renal parenchyma is evident on the right side, but no contrast material is noted in
the renal pelvis, suggesting possible obstruction. Two small (< 0.5 cm) probable lymph nodes are present in the periaortic region. The left kidney and inferior vena cava appear normal. A presumptive diagnosis of Wilms’ tumor is made.

• What is a nephrogenic rest, and what is its importance in the development of Wilms’ tumor?
• What developmental anomalies are associated with Wilms’ tumor?

**EPIDEMIOLOGY**

Wilms’ tumor is the most common malignant renal tumor of childhood, accounting for 5% to 6% of all solid tumors in children. The annual incidence of Wilms’ tumor is 7 cases per 1 million children under the age of 15 years. This tumor is estimated to occur in 450 children in the United States each year. Boys and girls are affected almost equally, with a ratio of 0.97:1.0. Seventy-five percent of these tumors occur in children between the ages of 1 and 5 years, with 90% occurring in children younger than 7 years. The mean age at diagnosis is 36.5 months for boys and 42.5 months for girls, with an overall peak incidence occurring between 3 and 4 years of age.

**ETIOLOGY AND PATHOGENESIS**

The Wilms’ tumor 1 gene (WT1) is located in band 11p13 and is critical for normal genitourinary development. Mutations in this tumor suppressor gene are associated with the development of Wilms’ tumor and Wilms’-associated syndromes, including the Denys-Drash and WAGR syndromes, which are discussed in the following section. Mutations in band 11p15 (the WT2 gene) distal to the WT1 gene are associated with Wilms’ tumors occurring in the Beckwith-Wiedemann syndrome. The WT2 gene codes for a transcriptional factor protein that regulates the expression of other genes, including growth-inducing genes. Other genetic factors seem to play a role in the behavior of Wilms’ tumor since patients with a loss of heterozygosity for chromosome arms 16q, 7p, and 1p have a poorer outcome than patients without this loss of heterozygosity.

Current theory suggests that Wilms’ tumor originates from abnormal renal histogenesis, which results in abnormal proliferation of metanephric blastema without normal differentiation into tubules and glomeruli. A focus of abnormally persistent nephrogenic cells is termed a nephrogenic rest. Nephroblastomatosis is characterized by the presence of multifocal or diffuse nephrogenic rests. Nephrogenic rests may be precursor lesions to Wilms’ tumor. Genetic predisposition likely increases the incidence of nephrogenic rests, and a second factor may induce the transformation into malignancies.

Nephrogenic rests occur in 1% of infants studied in autopsy series. The incidence of nephrogenic rests in kidneys from children with Wilms’ tumor is as high as 41%. This incidence approaches 100% in children with bilateral synchronous Wilms’ tumors. Nephrogenic rests are classified as intralobar or perilobar, based on their position relative to the renal lobe. Intralobar nephrogenic rests (ILNRs) are located anywhere within the renal lobe, sinus, or pelvicaliceal system. Perilobar nephrogenic rests (PLNRs) occur in the lobar periphery. ILNRs present in a younger age group, are less common (0.1% of infants in autopsy series), and are often associated with aniridia or the Denys-Drash syndrome. PLNRs occur more frequently (0.87% of infant autopsy series) and are associated with hemihypertrophy and the Beckwith-Wiedemann syndrome.

Most nephrogenic rests regress or become sclerotic or obsolescent. Some rests grow and become hyperplastic, but these hyperplastic rests may later regress.
Unfortunately, any rest maintains neoplastic potential. The microscopic appearance of Wilms’ tumor and nephrogenic rests can be indistinguishable. Therefore, the diagnosis of Wilms’ tumor may depend on the shape and growth characteristics of the lesion. With hyperplasia, a rest tends to maintain its original shape, whereas a neoplasm is often spherical. Serial imaging studies evaluating the growth of a lesion may be required to determine its malignant potential.2

CLINICAL PRESENTATION

Most children with Wilms’ tumor present with an abdominal mass. These patients appear well and are asymptomatic, although nearly one-third present with abdominal pain. Gross hematuria may be a presenting symptom if the tumor involves the collecting system. Patients with tumor rupture or hemorrhage may present with an acute abdomen.13

Physical examination reveals a firm, nontender, smooth mass that rarely crosses the midline. Hypertension occurs in more than 60% of children with Wilms’ tumor. With tumor propagation into the vena cava, a child may develop a varicocele or even signs of congestive heart failure.

Associated Anomalies

Fifteen percent of children with Wilms’ tumor have an associated anomaly.14 Associated anomalies may occur separately or as part of a defined syndrome. In children with Wilms’ tumor, the incidence of aniridia is 1 in 70, whereas the sporadic form of aniridia occurs in 1 in 50,000 people. One-third of children with the sporadic form of aniridia develop Wilms’ tumor.15 (A familial form of aniridia exists that is not associated with Wilms’ tumor.) Dermatological lesions, including hemangiomas, multiple nevi, and café-au-lait spots, occur in 7.9% of children with Wilms’ tumors. Genitourinary anomalies, including renal hypoplasia, ectopia, fusions, duplications, cystic disease, hypospadias, cryptorchidism, and pseudohermaphroditism, occur in 4.4% of children with Wilms’ tumors. Musculoskeletal anomalies are present in 3% of children with Wilms’ tumor.16

The WAGR syndrome includes Wilms’ tumor, Aniridia, Genitourinary anomalies, and mental Retardation.17 Children with the WAGR syndrome generally present before the age of 3 years.

Children with the Beckwith-Wiedemann syndrome develop enlargement of the adrenal cortex, kidney, liver, pancreas, and gonads. Other anomalies associated with Beckwith-Wiedemann syndrome include omphalocele, hemihypertrophy, microcephaly, mental retardation, hyperinsulinemic hypoglycemia, and macroglossia. Neoplasia occurs in 1 out of 10 children with this syndrome and may affect the liver, adrenal cortex, or kidney.18

Hemihypertrophy may occur isolated from the Beckwith-Wiedemann syndrome and consists of an asymmetry of the body. Its incidence is 1 in 14,300 people; the incidence increases to 1 in 32 (2.9%) in children with Wilms’ tumor. These children have increased genitourinary anomalies, adrenal cortical carcinomas, and hepatoblastomas. Children with Beckwith-Wiedemann syndrome, hemihypertrophy, or aniridia should undergo serial abdominal ultrasound examination every 3 months for 7 years, then every 6 months for 2 years, and then yearly until age 10 years.6

Denys-Drash syndrome occurs in association with a mutation in the WT1 gene. This syndrome includes Wilms’ tumor, testicular dysgenesis, male pseudohermaphroditism, and a nephropathy characterized by mesangial sclerosis that results in renal failure. Bilateral nephrectomy at the time of renal failure or tumor development and subsequent transplantation is indicated in patients with Denys-Drash syndrome because of the progressive nephropathy and high risk of Wilms’ tumors in the native kidneys.19 The transplanted kidney will not be at risk of Wilms’ tumor since it does not carry the associated gene mutation.

OPERATIVE TREATMENT

The goal of operative treatment is to provide a pathologic diagnosis, and, if possible, safely remove the tumor. Removal of the tumor may not be possible or indicated at the time of the first surgical exploration, as is discussed in the following section.

Preoperative Evaluation

Routine preoperative laboratory values should be obtained, including serum electrolyte level, blood urea nitrogen level, serum creatinine level, and hematocrit. The imaging evaluation should include, at a minimum, a chest radiograph to evaluate the lung fields and rule out significant metastatic disease. If the diagnosis of Wilms’ tumor is relatively certain, a preoperative chest CT may be appropriate to evaluate for pulmonary metastasis.35 Preoperative ultrasonography of the renal vein and inferior vena cava is recommended to identify vascular tumor extension, which occurs in 4% of children with Wilms’ tumor. One should consider obtaining consent for the patient to have a central line with an infusion port placed for subsequent chemotherapy. Preoperative consultation with the pediatric oncologists and radiation oncologists permits the development of a well-coordinated treatment plan.
Operative Approach

Although a variety of surgical incisions may be appropriate for nephrectomy, in this author’s experience, either a partial or full chevron-type incision beginning beneath the tip of the twelfth rib provides excellent exposure of even very large tumors.

Before excising the primary tumor, the extent of the tumor is evaluated, as well as the renal vessels, inferior vena cava, liver, and para-aortic lymph nodes. Despite the use of CT scanning, preoperative imaging has been reported to miss more than 7% of bilateral Wilms’ tumors; it is therefore recommended that the contralateral kidney be explored by opening Gerota’s capsule and inspecting the entire surface at the time of surgery. Biopsy of any suspicious lesion is required to rule out Wilms’ tumor or nephrogenic rests. Some authors have suggested that the lesions missed by preoperative CT scanning may be small and insignificant, and because these children will all receive chemotherapy, exploration of the contralateral kidney is not needed. The counterargument would suggest that the management of bilateral Wilms’ tumor is aimed at renal preservation; every effort—including surgical exploration—should be made to detect bilateral Wilms’ tumor early, thus reducing the need for nephrectomy, which is not indicated with bilateral Wilms’ tumors.

If the primary tumor has invaded surrounding organs and cannot be removed safely, the surgeon should wait until after treatment with chemotherapy, radiation, or both. If the tumor involves the upper pole and the kidney can be removed, the adrenal gland should be removed along with the kidney. In keeping with basic oncologic surgical principles, the renal artery and vein should be ligated prior to mobilizing the tumor, if possible, to avoid hematogenous spread. When manipulating the tumor, the surgeon should be cognizant of the possibility of tumor rupture with diffuse spillage and increased chance of abdominal relapse. Preoperative irradiation in addition to chemotherapy decreases this risk and should be considered if it is anticipated that the tumor will be difficult to remove safely. A formal lymph node dissection does not improve survival, although biopsies of hilar, para-aortic, iliac, and celiac nodes should be performed, as positive nodes portend a worse prognosis. Titanium clips should be used to identify any residual tumor or suspicious areas. Ferromagnetic clips can interfere with CT scanning and should not be used for hemostasis.

Operative Treatment of Patient 1

Patient 1 undergoes Doppler ultrasonography of the right renal vein and inferior vena cava, which demonstrates no evidence of a right renal vein or inferior vena cava thrombosis. A chest CT scan demonstrates no evidence of pulmonary metastases. The patient undergoes a right nephrectomy following a negative exploration of the left kidney. A limited retroperitoneal lymph node dissection is performed, and a permanent subcutaneous intravascular central line is placed for planned chemotherapy. Pathologic examination of the right kidney reveals a triphasic nephroblastoma with favorable histology, with tumor extending into the renal pelvis and protruding into the renal sinus but without sinus invasion. All margins are free of tumor; however, a microscopic focus of nephroblastic tubules is identified within an interaortocaval lymph node.

- What stage of Wilms’ tumor does patient 1 have?
- What histologic features are considered favorable in Wilms’ tumor?
- What additional treatment should patient 1 receive?

PATHOLOGIC CHARACTERISTICS OF WILMS’ TUMOR

Wilms’ tumor frequently consists of an encapsulated solitary tumor, which may occur in any part of the kidney. Hemorrhage and necrosis within the tumor are common. On occasion, a Wilms’ tumor may have a large cystic component. In patients with nephroblastomatosis, multiple lesions may occur. In nearly 20% of Wilms’ tumor cases, the renal vein is invaded by the tumor. The tumor rarely grows into the renal pelvis as it did in patient 1, where it caused both obstruction and hematuria (Figure 4). Gross assessment of nodal involvement is unreliable in Wilms’ tumor because the lymph nodes of patients without metastatic disease are frequently enlarged at the time of surgery.

Microscopically, Wilms’ tumor demonstrates a triphasic histology consisting of blastemal, epithelial, and stromal cells. The stromal component may differentiate into striated muscle, cartilage, or, rarely, fat or bone. The epithelial component varies from well-differentiated, resembling mature tubules (Figure 5A), to a very primitive appearance. Anaplasia, which is found in approximately 5% of all Wilms’ tumors, consists of a 3-fold variation in nuclear size with hyperchromatism and abnormal mitotic figures (Figure 5B). It occurs most often in older children. Diffuse anaplasia is diagnosed when anaplasia is present in more than one portion of the tumor or is found in any extrarenal or metastatic site. Anaplasia is considered an “unfavorable” histologic pattern; because tumors with anaplasia tend to be resistant to chemotherapy, its presence suggests a worse prognosis unless it is completely removed surgically. Diffuse distribution of anaplasia throughout the lesion
The rhabdoid tumor and clear cell sarcoma of the kidney were once considered forms of Wilms’ tumor with poor prognoses but are now considered separate entities. The rhabdoid tumor of the kidney is a rare tumor that occurs in children and young adults. It is characterized by the presence of rhabdoid cells, which are large, round cells with a granular cytoplasm and a star-like nucleus. The clear cell sarcoma of the kidney is a rare tumor that occurs in adults and is characterized by the presence of clear cells with abundant cytoplasm and a round or oval nucleus. The rhabdoid tumor and clear cell sarcoma of the kidney are now considered separate entities from Wilms’ tumor.

Staging of Wilms’ Tumor

Stage I Wilms’ tumor is confined to the kidney and completely excised without rupture or biopsy. Stage II Wilms’ tumor may extend beyond the kidney but is completely excised; however, it may have invaded vessels, or a local confined tumor spill may have occurred. This group also includes cases in which the kidney has been biopsied. Patients with stage III Wilms’ tumor have tumor left within the abdomen following surgery. This can include positive lymph nodes, positive surgical margins, peritoneal metastases, or diffuse unconfined tumor spillage. This also includes all patients with tumors found to be inoperable at the initial surgical exploration. Stage IV disease consists of metastases spread hematogenously (eg, lung, liver, bone, brain). Patients with bilateral Wilms’ tumor are considered to have stage V disease.

Benign Tumors Requiring Differentiation from Wilms’ Tumor

The cystic nephroma, or multilocular cystic nephroma, is round and smooth externally with multiple cysts internally. The septa of the cysts in the pediatric tumor are composed of fibrous tissue and may contain well-differentiated tubular structures. It usually occurs in only a single kidney, and its incidence reflects a bimodal age peak distribution. The peak incidence in the pediatric age group is between 3 and 24 months of age, and two-thirds of cases occur in boys. This tumor has the potential to develop into a classic Wilms’ tumor, although without this transformation, it remains benign. Treatment of the cystic nephroma requires local excision; however, the kidney may be preserved. The second peak incidence of cyst (ie, nephroma) occurs in adults, usually female, older than 40 years. In adults, the tumor frequently has mature fibrous tissue in the wall and also follows a benign course.

The cystic, partially differentiated nephroblastoma (CPDN) mimics the cystic nephroma and may be a variant of it. The septa of the CPDN contain blastema and may or may not contain other embryonal or epithelial cell types. A cystic Wilms’ tumor differs from both a cystic nephroma and a CPDN; a cystic Wilms’ tumor includes solid portions demonstrated radiographically.
and grossly that contain Wilms’ tumor. Frozen-section analysis is essential to plan surgical treatment for children with cystic renal tumors; unlike cystic nephroma, CPDN has been reported to recur locally, and thus nephrectomy is indicated for its treatment.

POSTOPERATIVE TREATMENT

In 1966, Farber published results demonstrating that the addition of single agent chemotherapy (daclarubicin) to radiation therapy and surgery increased survival for children with Wilms’ tumor from 40% to 89%. Since that time, several large multi-institutional studies conducted by the National Wilms’ Tumor Study Group (NWTSG) and the International Society of Pediatric Oncology (SIOP) have led to improvement in treatment and survival of children with Wilms’ tumor. At present, all children in NWTSG protocols currently receive chemotherapy. The treatment protocol currently used by the NWTSG is summarized in Table 1. The approach of a primary nephrectomy before adjuvant chemotherapy or radiation therapy is recommended by the NWTSG with the exception of bilateral tumors, tumors in a solitary kidney, or those that are not safely resectable because of size or invasion of surrounding structures, including the suprahepatic inferior vena cava. This approach differs from the SIOP protocols, which routinely recommend preneoprectomy chemotherapy without an initial biopsy as well as postneoprectomy chemotherapy or radiation therapy. No clear survival benefit has been demonstrated with the SIOP protocol, despite a reduction in the incidence of tumor rupture. A disadvantage of preoperative chemotherapy is the loss of accurate staging, including staging of the regional lymph nodes.

Table 1. Summary of Current NWTSG Treatment Protocols for Wilms’ Tumor, Stages I–IV.

<table>
<thead>
<tr>
<th>Disease Stage</th>
<th>Treatment Protocol</th>
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<tbody>
<tr>
<td>Stage I</td>
<td>Dactinomycin and vincristine</td>
</tr>
<tr>
<td>Stage II</td>
<td>Favorable histology: as with stage I disease Unfavorable histology: dactinomycin, vincristine, doxorubicin, cyclophosphamide, etoposide, and irradiation</td>
</tr>
<tr>
<td>Stage III, IV</td>
<td>Favorable histology: dactinomycin, vincristine, doxorubicin, and irradiation Unfavorable histology: as with stage II disease with unfavorable histology</td>
</tr>
</tbody>
</table>

NWTSG = National Wilms’ Tumor Study Group.

Irradiation of the operative site or the whole abdomen is performed 1 to 3 days following surgery. The current NWTSG recommendation is 10.8 Gy as the abdominal dose for Wilms’ tumor with favorable or unfavorable histology regardless of age. Supplemental radiation is directed to regions with residual tumor. Pulmonary metastases seen on chest radiograph necessitate radiation to both lungs regardless of the number or location of metastases.

Postoperative Treatment of Patient 1

Patient 1 is diagnosed with stage III Wilms’ tumor due to the microscopic focus of nephroblastic tubules identified within the lymph node. Because the histology is favorable, he is treated with dactinomycin, vincristine, and doxorubicin, as well as 10.8 Gy of radiation directed to the right side of the abdomen. Trimethoprim-sulfamethoxazole is initiated for Pneumocystis carinii pneumonia prophylaxis.

- What are the potential complications of treatment for Wilms’ tumor?
- How should patient 1 be monitored following treatment of his Wilms’ tumor?

COMPLICATIONS OF TREATMENT

Table 2 lists common complications associated with the treatment of Wilms’ tumor in children. Complications from surgery may occur in 8% to 20% of children. The most frequent complication is small bowel obstruction (3.7% of children). Other complications include significant intraoperative bleeding, injury to visceral organs, vascular injuries, and tumor rupture. Deaths related to surgical complications occur in 0.5% of children. Risk factors for surgical complications include advanced-stage local disease and intravascular extension of the tumor.

Several potential complications of chemotherapy and radiation therapy for Wilms’ tumor exist. Damage may occur to the remaining kidney as well as to the heart, lungs, liver, bones, and gonads. In addition, second malignant neoplasms may be induced. Renal failure was noted in 0.25% of children with unilateral Wilms’ tumor. The most common cause was unrecognized renal disease (Denys-Drash syndrome) followed by radiation nephritis. Patients treated with nephrectomy and abdominal irrigation are at increased risk for renal dysfunction, which appears to be dose-related. In one study, 73% of patients who received greater than 24 Gy of radiation to the remaining kidney developed an impaired creatinine clearance, compared to 19% of those who received less than 12 Gy.
Cardiac abnormalities occur in up to 25% of Wilms’ tumor survivors treated with doxorubicin. Doxorubicin is known to cause a dose-related cardiomyopathy that can cause congestive heart failure. Radiation also may cause cardiac damage and contribute to the development of congestive heart failure. In one study, 1.7% of children with Wilms’ tumor treated with doxorubicin had developed congestive heart failure by 15 years after their initial diagnosis; 50% of these developed heart failure by 8 years after diagnosis. The incidence of heart failure increased to 5.4% in those patients who received whole-lung irradiation. Pulmonary pneumonitis occurs in approximately 20% of children with Wilms’ tumor treated with whole-lung irradiation.

One of the most common complications of treatment in Wilms’ tumor patients is acute hematologic toxicity due to the suppressive effects of chemotherapy on the bone marrow. Chemotherapy also frequently induces an acute gastrointestinal toxicity manifested by nausea, vomiting, and diarrhea. Infertility, which occurs more frequently in males than in females, may result following chemotherapy and radiation owing to effects on the rapidly dividing germ cells. Dactinomycin is hepatotoxic; the incidence of hepatotoxicity in the National Wilms’ Tumor Study 4 ranged from 2.8% to 14.3%.

One of the most distressing complications of treatment of Wilms’ tumor is second malignant neoplasms, which occur in 1.6% of survivors by 15 years after diagnosis. Abdominal irradiation increases the risk of second malignant neoplasms, and doxorubicin potentiates this effect. These tumors often arise in the irradiated field and may include sarcomas, adenocarcinomas, bone tumors, breast cancer, and thyroid cancer.

**PROGNOSIS**

Prognosis of children with Wilms’ tumor depends on several factors, including the stage and grade of the tumor. The overall 4-year survival rate (suggesting cure) of children with unilateral Wilms’ tumor with favorable histology exceeds 90%. The 4-year postnephrectomy survival results from the NWTSG are shown in Table 3.

The most important prognostic factor in Wilms’ tumor is histology. The relapse rate of children with anaplasia is 4 times greater than that of children without anaplasia, and the death rate is 9 times greater. When anaplasia is well-circumscribed and focally contained within the primary tumor, it is not considered unfavorable. Focal anaplasia in a stage I Wilms’ tumor does not alter the prognosis when treated with nephrectomy.

Hematogenous metastases also worsen the prognosis and are present at diagnosis in 10% to 15% of Wilms’ tumor patients. Metastatic disease to the lungs occurs most often (85%), followed by metastases to the liver, bone, or brain. A tumor with renal vasculature invasion carries a higher risk of local relapse. When metastatic or recurrent disease is encountered and the patient has only received dactinomycin and vincristine, doxorubicin is routinely given. For those who have already received 3-agent chemotherapy, no well-established regimen exists.

**PRINCIPLES OF FOLLOW-UP**

Follow-up of Wilms’ disease patients is directed at detecting complications of treatment and recurrence of cancer. Physical examination should include palpation of the abdomen; any suspicious findings should be evaluated with diagnostic imaging. Follow-up also should include measurement of blood pressure, urinalysis to check for protein, and serum creatinine level. For patients with low-stage disease, evaluation of the abdomen with physical examination and of the lungs with a chest radiograph for recurrence may be all that is required as the lungs are the most likely site of relapse.

In children at risk for abdominal recurrence, such as those with a history of higher stage disease or contralateral nephrogenic rests, abdominal ultrasonography should be performed every 3 months for at least 4 years. For patients with a history of hematogenous metastasis (brain, lung, liver, or bone), the site of metastasis should be evaluated with imaging every 3 months for the first year after therapy is completed, every 6 months...

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**Table 2. Complications from Treatment for Wilms’ Tumor in Children**

<table>
<thead>
<tr>
<th>Surgical complications</th>
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<tbody>
<tr>
<td>Bone marrow toxicity</td>
</tr>
<tr>
<td>Cardiomyopathy/congestive heart failure</td>
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<tr>
<td>Gastrointestinal toxicity</td>
</tr>
<tr>
<td>Hepatic toxicity</td>
</tr>
<tr>
<td>Infertility</td>
</tr>
<tr>
<td>Pulmonary pneumonitis/reduced lung capacity</td>
</tr>
<tr>
<td>Renal insufficiency/failure</td>
</tr>
<tr>
<td>Secondary neoplasms</td>
</tr>
<tr>
<td>Vertebral hypoplasia and scoliosis</td>
</tr>
</tbody>
</table>

*(continued on page 13)*
for the next 2 years, and then yearly, for a total follow-up of 5 years. For example, an MRI of the brain should be performed for evaluation of a child with a previous history of brain metastases. Irradiated bone should be monitored for the life of the patient for the development of any radiation-associated neoplasms.

CASE 1 CONCLUSION
At 1 year following the completion of therapy, patient 1 has had no evidence of recurrent or metastatic disease. His chest radiograph, abdominal ultrasonograms, and results of urinalysis have been normal, and his serum creatinine level is 0.4 mg/dL. After 4 years he will be considered to be in complete remission.

BILATERAL WILMS’ TUMOR

CASE 2 PRESENTATION
Patient 2 is a 30-month-old girl who was noted by her mother and confirmed by her physician to have a rightsided abdominal mass. Following confirmation of a solid mass in the right kidney by ultrasonography, an abdominal MRI is obtained (Figure 6). The MRI demonstrates a large, 7-cm inhomogeneous mass in the right kidney, as well as a smaller, 2-cm mass in the left kidney. No evidence of adenopathy or inferior vena cava involvement is noted. A presumptive diagnosis of bilateral Wilms’ tumor is made.

• What is the next step in the treatment of patient 2?

MANAGEMENT OF BILATERAL WILMS’ TUMOR
Bilateral Wilms’ tumors occur in 5% to 8% of children with Wilms’ tumor. The role for primary exenterative renal surgery in the treatment of bilateral Wilms’ tumor has diminished with the advent of effective chemotherapy. Prior to the 1960s, it was common practice to perform aggressive surgical excision of the larger tumor at initial laparotomy. In 1966, after reviewing the experience with bilateral Wilms’ tumor at the Children’s Hospital of Philadelphia, Bishop and colleagues recommended performing bilateral renal biopsies, followed by treatment with chemotherapy and irradiation, and subsequent partial nephrectomy of the least-involved side. By 1989, the NWTSG suggested that the practice of initial resection of all tumors should be replaced by initial biopsy and staging, followed by chemotherapy and subsequent surgery. The chemoresponsiveness of many large tumors have allowed partial nephrectomies in kidneys that would not otherwise have been salvageable. Nephron-sparing surgery is important because the risk of renal failure in patients with bilateral tumors is 15% at 15 years. At present in the United States, the treatment of bilateral disease (stage V) most often employs biopsy followed by chemotherapy and bilateral partial nephrectomies.

Initial Treatment of Patient 2
Patient 2 undergoes exploration and biopsy of both kidney tumors, which reveals bilateral favorable-histology Wilms’ tumor. She is treated with vincristine and dactinomycin. Repeat MRI reveals shrinkage of the right-sided tumor with no change in the left renal tumor. At this point, it is elected to perform bilateral partial nephrectomies.

• What surgical technique is used for partial nephrectomy for bilateral Wilms’ tumor?
• Can brachytherapy be performed for Wilms’ tumor?

Partial Nephrectomy for Bilateral Wilms’ Tumor
Partial nephrectomy is most often performed in patients with synchronous bilateral Wilms’ tumors, but also is indicated in patients with a solitary kidney or renal insufficiency, and those with an associated syndrome that may predispose them to bilateral Wilms’ tumors (eg, Beckwith-Wiedemann syndrome).

The surgical incision most often employed is a transverse abdominal incision extending between the tips of the twelfth ribs. This facilitates mobilization of the ascending and descending colon and permits bilateral kidney inspection. The renal artery and vein may be encircled with vessel loops to provide rapid access and clamping of the blood supply if required during a partial nephrectomy. Ice slush and arterial clamping are

Table 3. Four-Year Survival Rates in Wilms’ Tumor Patients After Nephrectomy and Chemotherapy with or Without Radiotherapy

<table>
<thead>
<tr>
<th>Disease Stage</th>
<th>Favorable Histology (%)</th>
<th>Unfavorable Histology (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>96</td>
<td>68</td>
</tr>
<tr>
<td>II</td>
<td>91</td>
<td>55</td>
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<td>91</td>
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<tr>
<td>IV</td>
<td>80</td>
<td>4</td>
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Data from Neville and Ritchey and D’Angio et al.
used by some surgeons for cooling of the kidney prior to tumor removal. Alternatively, manual compression of the kidney often provides adequate vascular control, and blood loss should be minimal.

After the tumor is identified, an incision is made in the capsule around the neoplasm. With large tumors, the line of incision should be placed such that enough renal capsule is preserved following tumor removal to permit approximation of the capsular edges. By carefully dissecting through the incision, the surgeon frequently finds a rim of compressed normal tissue above an encapsulated Wilms’ tumor. The plane of the tumor capsule may be bluntly developed with the back of a lacrimal duct probe. This technique often permits enucleation of the tumor with maximum preservation of the surrounding normal renal parenchyma. Alternatively, a wedge of tissue including the tumor can be excised.

Biopsies of the tumor bed may be obtained and sent for pathologic analysis to evaluate for the presence of tumor tissue at the margin of resection. Arterial bleeding may be controlled with figure-of-8 absorbable sutures. Entrance into the collecting system also should be closed using absorbable suture. Careful approximation of Gerota’s fascia or omentum over the kidney prior to wound closure helps to maintain tissue planes and simplify re-exploration and repeat partial nephrectomy if required. This technique helps decreases scarving and adhesions to the kidney and has been shown to permit multiple repeat partial nephrectomies in patients with bilateral Wilms’ tumor.

Role of Brachytherapy

Brachytherapy has been used for children with Wilms’ tumor, and some of the preliminary results with brachytherapy in treating local disease have been encouraging. In one series, 7 children with bilateral Wilms’ tumor, 5 of whom had failed to respond to multiple chemotherapeutic agents, were treated with brachytherapy. None of these children, including 2 with anaplasia, had evidence of local recurrence. The success of brachytherapy in these patients with chemoresistant tumors demonstrates its potentially valuable contribution to the nephron-sparing management of patients with bilateral Wilms’ tumor.

The technique for brachytherapy involves placement of a catheter in the tumor bed following tumor resection. The balloon is inflated until it just fills the tumor bed. The catheter is then secured in place with absorbable sutures and brought out through a separate flank incision. Plain film radiographs are obtained at the end of the surgical procedure to verify the position of the catheter as well as the position of a plastic tandem catheter that is inserted through the catheter lumen. The radiation oncologist and dosimetrist determine the appropriate activity of cesium 137 or iridium 192 needed to treat the residual tumor volume with adequate margin. The radionuclide is inserted through the tandem catheter with a pusher during the postoperative period.

**PROGNOSIS FOR PATIENTS WITH BILATERAL WILMS’ TUMOR**

The survival rate for children with bilateral Wilms’ tumors with favorable histology managed with partial nephrectomy is approximately 75%. The survival rate is severely decreased for children with bilateral Wilms’ tumor and anaplasia (10% to 26%). This relates to the lower effectiveness of chemotherapy for anaplastic tumors. Unfortunately, the role of nephron-sparing surgery for children with bilateral Wilms’ tumors and either focal or diffuse anaplasia appears limited. In the first published report of survival of patients with bilateral, unfavorable-histology Wilms’ tumor, only 4 of the 15 children who had diffuse anaplasia (by the current definition) survived. In two of the 4 surviving patients, follow-up continued for 7 months only.) In this series, 3 of the 4 children with diffuse anaplasia who survived had stage I disease; only 1 of 11 children who had diffuse anaplasia and a higher disease stage survived. Subsequent series have confirmed the dismal outcome for children with bilateral Wilms’ tumor and diffuse anaplasia. Perhaps a more aggressive surgical approach, including bilateral nephrectomy and transplantation, would increase the survival rate in this group, although this remains unknown.
CASE 2 CONCLUSION

Pathologic analysis of patient 2’s tumor tissue reveals favorable histology Wilms’ tumor in the right kidney and an anaplastic tumor in the left kidney. She is treated with additional chemotherapeutic agents, including doxorubicin, cyclophosphamide, and etoposide. Follow-up MRIs reveal a new mass in the left renal hilum and no evidence of tumor recurrence in the right kidney. Given the previous diagnosis of an anaplastic tumor in the left kidney and its lack of response to chemotherapy, patient 2 undergoes a left nephrectomy. Diffuse anaplasia is noted, and she undergoes further treatment with chemotherapy and radiation. At follow-up 4 years following her final surgery, she has no evidence of tumor recurrence in her remaining right kidney and has a serum creatinine level of 0.6 mg/dL.

Figure 7. Abdominal ultrasonogram from a 3-month-old infant demonstrating a left renal tumor consisting of multiple cystic spaces. Pathologic analysis revealed a cystic nephroma.

CASE 3 PRESENTATION

Patient 3 is a 3-day-old male neonate who is noted to have a palpable abdominal mass. The past medical history is significant for maternal polyhydramnios during the recent pregnancy. On physical examination, the infant is noted to have elevated systolic blood pressures to 140 mm Hg and a palpable left abdominal mass. No adenopathy or other significant physical findings are detected.

- What is the next step in evaluating a child with an abdominal mass?

Two-thirds of abdominal masses in infants and children are of renal origin. The majority of these masses are benign, with hydronephrosis the most frequent diagnosis. In addition to a careful history and physical examination, laboratory studies should be performed, including complete blood count, platelet count, blood urea nitrogen, creatinine, and urinalysis. Abdominal ultrasonography is useful in determining whether a mass is of renal origin, and whether its characteristics are consistent with hydronephrosis, a multicystic dysplastic kidney, or a solid tumor (Figure 7). If a solid tumor is identified, further evaluation with CT or MRI is warranted. Measurement of urinary catecholamines can help distinguish between Wilms’ tumor and neuroblastoma; catecholamines are elevated in 95% of cases of neuroblastoma, although primary renal neuroblastoma is rare.12

Figure 7. Abdominal ultrasonogram from a 3-month-old infant demonstrating a left renal tumor consisting of multiple cystic spaces. Pathologic analysis revealed a cystic nephroma.

CASE 3 EVALUATION AND MANAGEMENT

Laboratory studies of patient 3 reveal no abnormalities with the exception of an elevated renin level of 52 ng/mL (normal, 0.2 to 2.3 ng/mL). Ultrasonography revealed a large solid left renal mass. A CT was obtained and confirmed a left upper renal pole mass and a normal-appearing contralateral kidney.

- What is the most common solid renal tumor in the neonate?

The most common solid renal tumor of the neonate is the congenital mesoblastic nephroma. It is frequently associated with polyhydramnios and occurs most often in boys.42 Although Wilms’ tumor is the most common solid renal tumor in childhood, it is rare in infants younger than 1 year.

- How does congenital mesoblastic nephroma present?

Congenital mesoblastic nephroma most frequently presents in the neonatal period as a palpable flank mass. Other symptoms may include hematuria, hypertension, emesis, hypercalcemia, and jaundice.12,43,44

- What is the recommended treatment of a suspected congenital mesoblastic nephroma?

Treatment involves complete excision of this generally benign lesion by a nephrectomy. Survival rate with this tumor is 98%. The margins of the tumor often demonstrate local infiltration; partial nephrectomy thus is not an appropriate treatment for this nonencapsulated tumor because it would increase the risk of local recurrence.
On occasion, a hypercellular variant of the congenital mesoblastic nephroma occurs and proves difficult to distinguish from a clear cell sarcoma of the kidney.\(^4\) This variant may be more aggressive and, rarely, children may develop metastases to the brain, bones, lungs, and heart. Chemotherapy with a Wilms' tumor regimen may be considered for patients with incomplete resection or a cellular variant with a high mitotic index, as well for as any patient with metastatic disease.\(^2\)

- **What are the pathologic findings of a congenital mesoblastic nephroma?**

It is an unencapsulated firm tumor that grossly resembles a leiomyoma with local invasion (Figure 8). Histologic evaluation demonstrates sheets of spindle-shaped uniform cells with a fibroblastic appearance. Dysplastic tubules and glomeruli are also apparent within the tumor.

- **How should patient 3 be monitored following nephrectomy?**

Most local recurrences occur within 1 year, and it is recommended that close monitoring with ultrasonography of the local site be performed for 1 year following surgery.\(^1\)

### Angiomyolipoma

**CASE 4 PRESENTATION**

Patient 4 is a 7-year-old girl with a diagnosis of tuberous sclerosis who is referred for urologic evaluation. Her past medical history is significant for seizures and mild mental retardation. Her physical examination is remarkable for adenaoma sebaceum. She has no palpable abdominal mass. Results of urinalysis are chemically and microscopically unremarkable.

- **What is tuberous sclerosis?**

Tuberous sclerosis is a complex associated with an autosomal dominant genetic mutation with variable penetrance. This complex can include mental retardation, epilepsy, adenaoma sebaceum, glial nodules in the brain, subependymal giant cell astrocytomas, phakoma of the retina, lymphangiomyomatosis of the lungs, rhabdomyomas of the heart, facial angiofibromas, periungual fibromas of the skin, hamartomas of the liver or bone, and renal angiomyolipomas.\(^4\)\(^6\) The genes responsible for tuberous sclerosis complex are the tumor suppressor genes \(TSC1\) on band 9q34 and \(TSC2\) on band 16p13. Seventy-five percent of patients with tuberous sclerosis complex have spontaneous new mutations with no family history.\(^7\)

- **What are the renal manifestations of tuberous sclerosis?**

The renal manifestations of the tuberous sclerosis complex include angiomyolipoma, renal cysts, and renal cell carcinoma. Angiomyolipomas occur in up to 80% of patients with this disease, have no gender predominance, and are often multifocal and bilateral. These tumors are a significant cause of morbidity, including end-stage renal disease.

Children with angiomyolipomas almost always have the tuberous sclerosis complex, whereas adults may develop angiomyolipomas without the tuberous sclerosis complex. In fact, of all angiomyolipomas diagnosed in adults, fewer than 10% are thought to occur in individuals with tuberous sclerosis complex. Sporadic angiomyolipomas not associated with tuberous sclerosis complex occur more often in women and at an older age, and are usually solitary lesions.\(^7\) Angiomyolipomas also have been associated with von Recklinghausen’s neurofibromatosis and von Hippel-Lindau disease.\(^8\)

In a large series of patients with tuberous sclerosis, the mean age at which a patient with a previously normal renal ultrasonogram was noted to have an abnormality was 7.2 years. The most common lesion was an angiomyolipoma.\(^4\) The incidence of angiomyolipomas increased with age, and the size of the angiomyolipomas increased at variable rates over time. Angiomyolipomas greater than 4 cm in this series were only noted in the postpubertal age group.

Angiomyolipomas may present with abdominal discomfort, hematuria, hypertension, or renal insufficiency. Bleeding associated with the angiomyolipoma may cause acute onset of pain in the back, flank, or abdomen. Severe bleeding can cause hemorrhagic shock and death.\(^7\)

Renal cysts occur frequently in patients with tuberous sclerosis complex. These are usually located in the cortex and are highly variable in number and size. Some cysts may appear and then disappear spontaneously.\(^6\) The polycystic kidney disease 1 (\(PKD1\)) gene and the \(TSC2\) gene are both on band 16p13, and most patients with tuberous sclerosis complex and significant renal cystic disease have a mutation involving both of these genes.\(^7\)

Renal cell carcinoma also has been reported in some patients with tuberous sclerosis complex and, on
Pediatric Renal Tumors

average, occurs at 36 years of age; however, the incidence is unknown.

• How should a child with tuberous sclerosis be evaluated for renal manifestations?

Renal ultrasonography is a noninvasive, practical method of evaluating a child with tuberous sclerosis complex for angiomyolipomas, cysts, or other tumors (Figure 9). The fat component of the angiomyolipoma demonstrates bright echogenicity relative to the surrounding renal parenchyma; however, the amount of fat in an angiomyolipoma is highly variable. One surveillance regimen suggests a renal sonogram every 2 to 3 years for children before puberty, and yearly after puberty, when larger angiomyolipomas become more prevalent.46 CT scans of angiomyolipoma reveal dark areas in the tumor with Hounsfield units of –20 to –50, consistent with fatty tissue (Figure 10). The tumors are hyperintense on both T1- and T2-weighted MRI sequences. These tumors are often hypervascular and exhibit signal enhancement on both CT and MRI.

CASE 4 EVALUATION

A renal ultrasonogram is obtained of patient 4 and demonstrates a 2-cm right renal tumor with increased echogenicity, consistent with an angiomyolipoma.

• What are the histopathologic characteristics of angiomyolipomas?

These are benign tumors; however, they may extend into the renal vein, inferior vena cava, and right atrium.23 Angiomyolipoma also may be identified in local lymph nodes, although this is thought to represent hamartomatous development as opposed to true metastatic behavior. Angiomyolipomas are nonencapsulated tumors that contain variable amounts of abnormal blood vessels with thick walls, fat, and smooth muscle. The abnormal vessels may mimic neovascularization associated with a malignant tumor on angiogram. Angiomyolipomas may increase in size by as much as 4 cm within one year.46

• How should an angiomyolipoma be treated?

Hemorrhage is the most common complication of an angiomyolipoma. Lesions over 3.5 cm have an increasingly greater risk of bleeding with increased size. For this reason, some have advocated removal of angiomyolipomas exceeding 4 cm in diameter, although the true risk of bleeding is unknown.57,46 Given the multifocal and recurrent nature of this disease, treatment of the tumor(s) with renal-sparing methods are advocated. This may employ embolization or partial nephrectomy and a large lesion is not considered a contraindication for tumor enucleation.48

CASE 4 TREATMENT AND FOLLOW-UP

Owing to its size, patient 4’s angiomyolipoma is not removed. The patient is followed with renal ultrasonography every 2 years. At age 11, a solid 3.5-cm renal mass is detected and confirmed to be a signal-enhancing tumor on CT scan. This tumor has no fat component. The patient undergoes a left radical nephrectomy, and pathologic examination reveals a renal cell carcinoma.

• How often does renal cell carcinoma occur in children?

Renal cell carcinoma accounts for 2% to 6% of primary pediatric renal tumors, making it the second most common malignant pediatric renal tumor after Wilms’ tumor. Although it may occur in infants, it most often occurs between the ages of 9 and 15 years. In patients between the ages of 10 and 20 years, a primary renal tumor has an equal chance of being Wilms’ tumor or renal cell carcinoma.

• How does the evaluation and management of renal cell carcinoma in children differ from that of adults?

Unlike adults, in whom renal cell carcinoma is frequently detected incidentally, children often present with Figure 8. Gross specimen of congenital mesoblastic nephroma. Dense interlacing bundles of tissue are visible. (Reprinted with permission from Cooper CS, Snyder HN III. Pediatric neoplasia. In: Weiss RM, George NJ, O’Reilly PH, editors. Comprehensive urology. London: Mosby International Ltd; 2001:222.)
1 or more of the “classic triad,” consisting of flank or abdominal pain, a palpable mass, and gross hematuria. On occasion, a child with renal cell carcinoma also may have hypertension, polycythemia, or other paraneoplastic syndromes. In addition to its association with tuberous sclerosis, renal cell carcinoma in childhood has been reported in children with a multicystic dysplastic kidney and is associated with Beckwith-Wiedemann and von Hippel-Lindau syndromes.

Other than radiographic imaging, preoperative evaluation of a renal mass presumed to be renal cell carcinoma includes a chest radiograph and bone scan. There is an increased incidence of calcification noted on CT with renal cell carcinoma compared with Wilms’ tumor, although this finding is not diagnostic.

The overall 5-year survival rate in children with renal cell carcinoma is between 56% and 64%. Disease-free survival decreases with increasing stage, and is 94%, 74%, 69%, and 8% for stages I, II, III, and IV, respectively. As with adult renal cell carcinoma, no effective chemotherapy or radiotherapy exists, making complete surgical removal essential for survival.

MULTICYSTIC DYSPLASTIC KIDNEY

CASE 5 PRESENTATION

Patient 5 is a 6-week-old male infant referred for management following hospitalization for a urinary tract infection. His past medical history is significant for a left multicystic dysplastic kidney (MCDK) initially detected on prenatal ultrasonography at 23 weeks. An ultrasound examination performed after birth confirmed the diagnosis. His pediatrician discharged the infant with plans for a follow-up ultrasound examination in 2 months.
At 4 weeks of age, the infant developed high fevers and emesis. Subsequent evaluation revealed an elevated leukocyte count and *Escherichia coli* urosepsis. He was admitted to the hospital and given 7 days of intravenous antibiotics. He was subsequently placed on amoxicillin prophylaxis and referred for further urologic management.

- **How often is an MCDK diagnosed by prenatal ultrasonography?**

  With the routine use of prenatal ultrasonography, MCDK is now most often identified antenatally. The fetal bladder and kidneys are evaluated routinely as part of every second- and third-trimester ultrasound examination. A unilateral MCDK is the second most common antenatally detected urinary tract abnormality, thought to occur in approximately 1 in 3500 births. Antenatal hydronephrosis constitutes the most common urinary tract abnormality detected by prenatal ultrasonography. It occurs in up to 1% of pregnancies using a certain set of criteria; using a different set of criteria for mild hydronephrosis, the incidence is 3% to 5%. An MCDK is sometimes misdiagnosed on prenatal ultrasonography as a severely hydronephrotic kidney.

- **What is the clinical presentation of an MCDK when it is discovered postnatally?**

An MCDK may present as an abdominal mass in infants or with pain, hypertension, or a urinary tract infection. It occurs slightly more often in boys and on the left side.

- **What is an MCDK?**

An MCDK consists of a nonfunctioning kidney characterized by multiple cysts of variable size. Several authors have reported communication between some of the cysts. The MCDK is thought to be the result of either abnormal interactions between the ureteric bud and metanephric blastema, or of severe atresia and/or obstruction of the ureter during nephrogenesis. Because the ureteral bud arises from the wolffian duct, males with MCDK have an associated increase in ipsilateral absence or ectopia of the vas deferens, as well as cystic dysplasia of the testis. Bilateral MCDK is not compatible with extrauterine life and is associated with severe oligohydramnios as well as pulmonary hypoplasia and Potter’s syndrome.

- **What are the histopathologic characteristics of an MCDK?**

On gross examination, the MCDK often appears as a collection of variable-sized cysts without typical renal configuration (Figure 11). The renal vessels and ureter are often atretic. Occasionally, a hydronephrotic renal pelvis exists. Primitive ducts noted on histologic examination confirm the presence of dysplasia. The cysts arise from all portions of the nephron.

- **What is the standard evaluation of a child with an MCDK?**

The diagnosis of MCDK is made based on ultrasonography and nuclear renal scan. A postnatal ultrasound examination is obtained to confirm the prenatal findings. An ultrasonogram (as well as a CT or MRI) of a patient with MCDK demonstrates complete replacement of the kidney with multiple cysts separated by a small amount of nonfunctioning parenchyma (Figure 1). It may be difficult on imaging to distinguish MCDK from severe hydronephrosis; however, in an MCDK, the largest “cyst” (which in severe hydronephrosis would be the renal pelvis) is not usually in a medial location; furthermore, with MCDK, there is a loss of the renal sinus as well as renal parenchyma (Figure 1). A nuclear renal scan should also be obtained. An MCDK will exhibit a complete lack of function, whereas a severely hydronephrotic kidney usually exhibits some uptake of radiotracer (Figure 12).
Contralateral renal anomalies, including ureteropelvic junction obstruction and reflux, are frequently associated with dysplastic kidneys. Ureteropelvic junction obstruction occurs in 3% to 12% of patients with MCDK. In addition, ureterovesical junction obstruction occurs in approximately 5% of patients with MCDK. A nuclear renal scan helps rule out ureteropelvic or ureterovesical junction obstruction in the contralateral kidney.

Children with MCDK also should undergo a voiding cystourethrogram to rule out reflux, which occurs in 11% to 37% of patients. Reflux occurs most commonly on the contralateral side (15% to 28%). Until this study is obtained, children are often placed on prophylactic antibiotics to decrease the chance of urinary tract infections and pyelonephritis, which could injure the solitary functioning kidney.

**CASE 5 EVALUATION**

Patient 5’s postnatal ultrasonogram is reviewed and reveals a 5-cm MCDK. A nuclear renal scan is performed, which demonstrates a complete lack of function in this kidney. A voiding cystourethrogram demonstrates contralateral grade 2 reflux.

- **How should patient 5’s MCDK be managed?**

The treatment of a child with MCDK is not uniform among pediatric urologists. The size of the cysts usually diminishes with time, and the kidney involutes to the point where it is no longer detectable on ultrasonography. Unfortunately, complete disappearance on ultrasonography does not eliminate the risk of developing hypertension or malignant degeneration. Complete disappearance may occur in more than 40% of children by the end of a 5-year follow-up period and in fact, many adults with a solitary kidney may have had a unilateral MCDK at birth. In some children (4% to 18%), the MCDK increases in size.

Indications for surgical removal of the kidney include pain, pulmonary compromise from a large MCDK (this rare condition may be managed with percutaneous decompression), suspicion of tumor development, or suspected renovascular hypertension. The incidence of hypertension or tumor development appears sufficiently low that prophylactic nephrectomy is not warranted in all children with an MCDK; however, surgical consideration also should reflect parental wishes secondary to anxiety regarding the MCDK—nephrectomy offers immediate cure and elimination of extended follow-up. Surgery also may be warranted in a child in whom compliance with recommended follow-up is unlikely. A nephrectomy in these children is usually straightforward with rapid recovery, and may even be performed on an outpatient basis.

**CASE 5 CONCLUSION**

Patient 5’s MCDK is retained, and the child is maintained on prophylactic antibiotics because of the vesicoureteral reflux.

- **What follow-up should patient 5 receive?**

As with treatment, no uniform recommendations exist on the frequency of follow-up for a child with MCDK. Rarely, children with MCDK develop hypertension, infection, or malignancy. Therefore, children should be assessed for these complications with periodic blood pressure measurement, urinalysis, and renal imaging. Follow-up imaging by serial ultrasonography constitutes the standard management of a child with MCDK; however, the optimal frequency of imaging is unknown. Many physicians follow the child with ultrasound imaging every 3 to 4 months during the first several years of life, whereas others suggest an ultrasound examination at 2, 5, and 10 years of age is sufficient. Because patient 5 has reflux, a yearly nuclear cystogram should be obtained to assess for resolution of his reflux.

**REFERENCES**


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