Case Report

WILMS' TUMOR IN A 5 YEAR OLD FEMALE – A CASE REPORT

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ABSTRACT

Wilms' tumor, also called nephroblastoma, is a malignant (cancerous) tumor originating in the cells of the kidney. As with any cancer, prognosis and long-term survival can vary greatly from child to child, but most children with Wilms' tumor can be cured of the disease. The tumor usually affects a single kidney, but approximately 5 to 10 percent of children with Wilms' tumor have both kidneys involved. Here we present a case of a 5 year old female with wilms tumor originating from right kidney.

Keywords: Wilm's Tumor, Pediatric Malignant Renal Tumor

INTRODUCTION

Wilms'tumor is the most common type of renal cancer and accounts for about 7 percent of all childhood cancers (Grovas *et al.,* 1997). Wilms' tumor is unrelated to adult kidney cancer. Wilms' tumor occurs in children up to about age 8. About 75 percent of cases occur before age 5, and the average age of children with Wilms' tumor is 2 - 3 years. For unknown reasons, Wilms' tumor affects more black children than white children.

Most cases of Wilms' tumor occur by chance (sporadic). They are the result of mutations in cells in the kidneys that usually occur after birth. In some cases, however, a genetic defect increases the risk of Wilms' tumor.

Wilms tumors are grouped into 2 major types based on how they look under a microscope (their histology):

Favorable histology: Although the cancer cells in these tumors don't look quite normal, there is no anaplasia. More than 9 of 10 Wilms tumors have a favorable histology. The chance of cure for children with these tumors is very good.

Unfavorable histology (anaplastic Wilms tumor): In these tumors, the look of the cancer cells varies widely, and the cells' nuclei tend to be very large and distorted. This is called anaplasia. The more anaplasia a tumor has, the harder it is to cure.

CASES

A 5 year old female patient came to our hospital with swelling in right side of abdomen for 1 month noticed by mother. Swelling was gradually progressive in nature and associated with hypertension. There was no history of fever, abdominal pain, vomiting, hematuria and constipation as per her mother, the historian.

Our patient's past medical history was unremarkable. There were no recurrent sinus, middle-ear, or urinary tract infections, nor were there any congenital problems noted. Birth history revealed an uncomplicated full-term vaginal delivery. This child had no allergies, daily medications, or herbal supplements. Her development was normal, immunizations were up-to-date, and her health had been good since the swelling had been noticed. Family-social history consisted of a working father labour by occupaton and mother was house-wife, living in a house in the suburbs outside of a major city. Neither were smokers. There was no family history of neoplasms, gastrointestinal problems, seizure, congenital heart problems, hemoglobinemias or other major illnesses.

On physical examination our patient appeared sick. She was fatigued and completely indifferent to this examiner as well as the uncomfortable aspects of the exam, unlike most children her age. Her temperature was 98.6 degrees Fahrenheit axillary, pulse regular 110 beats per minute, and respirations 28 breaths per

Case Report

minute. Blood pressure was 130/90 mmHg. On abdominal exam a mass of 4 cm length by 3 cm width with regularly shaped margins was palpated with light depth and verified with percussion in the right upper quadrant.

The mass was smooth, slightly firm, oval, nonmobile, and did not cross the midline.

The child denied pain during the exam, but guarded and panted during palpation. All other systemic examination was within normal limits.

Laboratory data consisted of a complete blood count and differential revealing a slightly low hematocrit and hemoglobin with microcytic, hypochromic red cells. Leucocytosis with neutrophilia was also noted. See Table 1 for complete results.

HB (gm%)	10.4
TLC (cell/cumm)	20500
DC (%) N-	77
L-	17
E-	03
M-	03
PLATELET (lacs/cumm)	5.32
PCV (%)	33.5
MCV (fl)	64.4
MCH (pg)	20
MCHC (%)	31
T.RBC (mil/ul)	5.20
RDW (%)	14.5

The ultrasound revealed a Heterogeneous echogenic mass of size 9.2x9.5 cm seen in right renal fossa with internal areas of cystic necrosis with internal vascularity, defined as wilms tumor stage II. See Table 2 for tumor staging criteria.

Our patient's computerized tomography scan (CT) helped determine the location and further staging of the Wilms' tumor using the same I-V criteria described in Table 2. Our patient was then admitted to the

Case Report

hospital and complete nephrectomy was done. Nephrectomy specimen was sent for histopathological examination and diagnosis of Wilms' tumor Stage I and favorable histology was given.

Stage	Criteria
I	Tumor limited to the kidney with intact capsule and completely excised.
II	Tumor grossly excised but penetrates through the capsule into peri-renal soft tissues. Microscopic spillage of tumor is confined to the flank.
III	Gross residual tumor confined to the abdomen (Tumor incompletely excised secondary to lymph node involvement, diffuse peritoneal contamination, or peritoneal implants.)
IV	Hematogenous metastases, beyond Stage III, to lung, noncontiguous liver, bone, or brain.
V	Bilateral renal involvement at diagnosis

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DISCUSSION
The risk of developing Wilms tumor varies among ethnic groups, with a greater risk in African-Americans and a lower risk in the Asian population (Grovas *et al.,* 1997; Goodman *et al.,* 1989; Stiller *et al.,* 1996). Epigenetic differences may contribute to the lower rate of disease in Asian children, as demonstrated by a study that reported infrequent loss of IGF2 imprinting in tumors from Asian patients (Fukuzawa, 2004).

The most common manifestation of Wilms tumor is an asymptomatic abdominal mass; an abdominal mass occurs in 80% of children at presentation. Abdominal pain or hematuria occurs in 25%. Urinary tract infection and varicocele are less common findings than these. Hypertension, gross hematuria, and fever are observed in 5-30% of patients. A few patients with hemorrhage into their tumor may present with hypotension, anemia, and fever. Rare patients with advanced disease may present with respiratory symptoms related to lung.

Wilms tumor is primarily a sporadic disease, and only 1 to 2 percent of individuals with Wilms tumor have a relative with the disease (Huff, 2011). In some children, Wilms tumor occurs as a part of a multiple malformation syndrome (Scott, 2006). These syndromes include WAGR, Denys-Drash, and Beckwith-Wiedemann syndromes.

Patients with associated congenital anomalies, such as aniridia or genitourinary abnormalities, are also diagnosed at an earlier age (Breslow *et al.,* 1988).

Wilms' tumor arises anywhere in the kidney as embryologic precursors to renal cells. These cells mimic normal development of the kidney and consist of three components: blastema, epithelium, and stroma (Anderson *et al.,* 2000). A favorable histology consists of well-differentiated cells, or cells that appear closely related to normal cell sources such as those mentioned (Marina *et al.,* 1995; Goodman *et al.,*

Case Report

1989). Unfavorable outcomes are typically related to the anaplastic cell with diffuse or focal involvement, making up 10% of Wilms' tumor cases (Lanzkowsky, 1995). The anaplastic cells are undifferentiated, which means they appear so abnormal, their origin cannot be determined (Marina 1995; Lanzkowsky, 1995). These cell types are more aggressive in their growth and behavior. Diffuse anaplasia bears the worst prognosis (Lanzkowsky, 1995). Our patient's histology was luckily favorable.

Wilms' tumor usually spreads past its pseudomembraneous capsule into renal sinuses, intrarenal lymphatics and blood vessels (Caty *et al.,* 1993). Intratumoral hemorrhaging in 8% of patients will seed and spread this fragile tumor (Caty *et al.,* 1993). Common sites for metastasis are the lungs, regional lymph nodes, and liver (Young *et al.,* 2000). This explains why microscopic hematuria occurs in 25% of patients (Young *et al.,* 2000). Our patient's urine happened to be heme-negative on microscopic analysis at the referral center. Wilms' tumor also produces renin causing hypertension in 25-75% of children (Kassabian, 1995). Our patient fell into this category with an admitting blood pressure of 130/90.

Wilms' tumor grows rapidly. Zoubek and colleagues estimated it's doubling time, the time required for cell numbers to double in size, to be approximately 11-13 days (Craft, 1999). It usually takes approximately 30 doublings to make up a 1 cubic centimeter mass or 1 gram of tumor, which takes up to a year, would more than likely be unpalpable, but detectable by ultrasound at that point in growth (Craft, 1999; Shakney, 1978). Tumor growth is not completely linear with a rapid acceleration of growth that eventually slows with increasing size and cell death (Shakney, 1978; Fleming *et al.,* 1995). After the tumor reaches 1 cubic centimeter, it takes only approximately 7 doublings to increase in size to approximately 500 cubic centimeters using an eleven day doubling time, which may continue to be difficult to palpate (Craft, 1999). In our patient's case, the tumor's retroperitoneal location made it difficult to palpate the mass until it had become very large, displacing the kidney.

Figure 1: A large well-defined soft tissue density lesion with multiple necrotic areas within noted involving right kidney (Scout image and axial images)
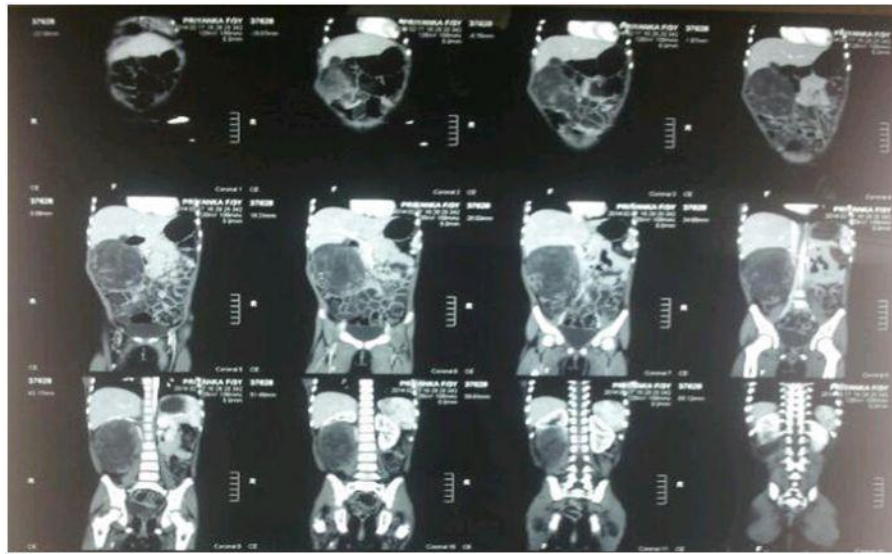
Case Report

Figure 2: A large well-defined soft tissue density lesion with multiple necrotic areas within noted involving right kidney (Coronal images)

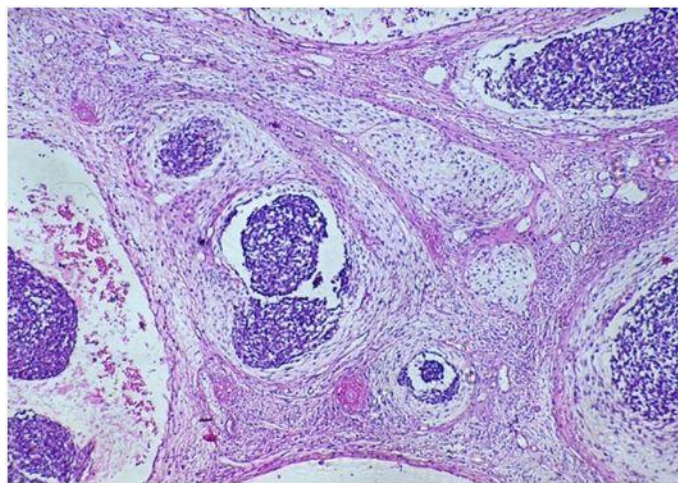**Figure 3: Gross specimen showing tumor mass and compressed renal tissue**

Figure 4: Photomicrograph showing primitive components (stromal, blastimal and epithelial) (10x view)
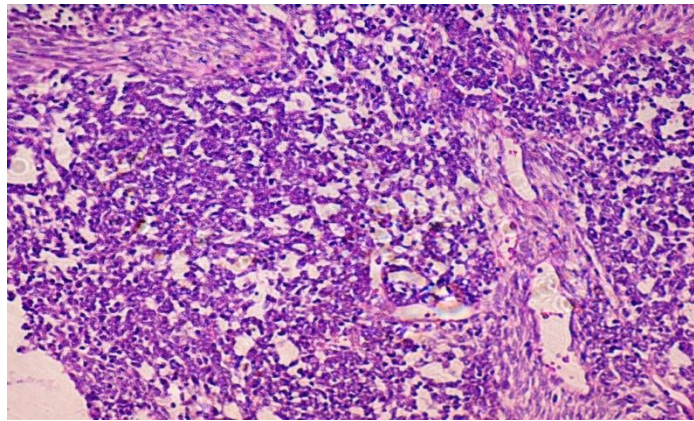
Case Report

Figure 5: Photomicrograph showing primitive tubule formation with stromal component (40x view)
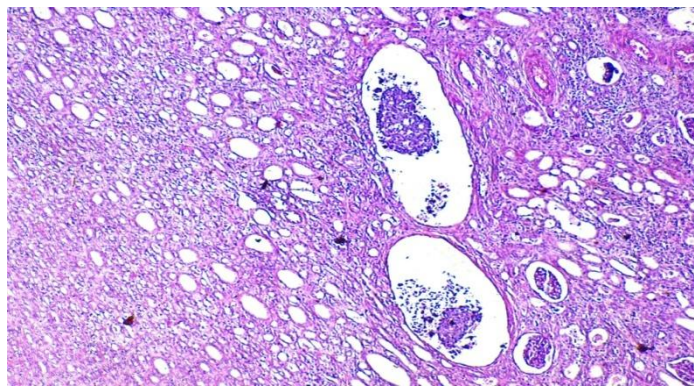

Figure 6: Photomicrograph showing tumor cell metastasis in vessels (10x view)

Wilms' tumor's short doubling time is what most likely makes this tumor susceptible to chemotherapy and accounts for its low mortality rate (Shakney *et al.,* 1978; Fleming *et al.,* 1995). Most cases of bilateral renal involvement have a 3-year survival of 75%-81% using combined chemotherapy and radiation (Marina *et al.,* 1995; Geller *et al.,* 1997; Paul *et al.,* 2000). For patients having single kidney involvement, long-term survival is usually 80-90% (Rostad *et al.,* 1997).

Treatment is chemotherapy and nephrectomy for single kidney involvement with excision of tumor cells and preservation of normal cell functioning for bilateral kidney involvement (Rostad *et al.,* 1997). Combination chemotherapy and radiation are given as a pretreatment in high-risk cases such as the bilateral renal involvement, diffuse anaplasia, or metastases (Rostad *et al.,* 1997). This is done to possibly shrink the size of the tumor (Rostad *et al.,* 1997).

Conclusion

Findings from current literature recommend an abdominal ultrasound by a radiologist with pediatric experience within 24 hours if there is no known origin of an abdominal mass (Anderson *et al.,* 2000; Caty *et al.,* 1993; Rostad *et al.,* 1997). As the differential diagnosis is slim for right upper quadrant masses with other possibilities being potentially very serious, it is key to identify the mass as quickly as possible. The abdominal ultrasound revealed the location and the nature of this tumor as well as ruling out a host of differential diagnoses. It is also important to gather as much history and laboratory data as possible. Nephrectomy is preferred in cases of single kidney involvement. Patient with favorable histology have better prognosis as in our case.

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Case Report

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