

The Role of Imaging in the Management of Rare Bilateral Advanced Nephroblastoma in A Six- Year-Old Girl

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Abstract: *This is a case of a 6-year-old girl who presented with history of progressive abdominal enlargement, gross haematuria and palpable bilateral flank masses. She has had imaging evaluation using plain abdominal radiography, ultrasonography and CT scan from which the diagnosis of bilateral Wilm's tumor was made which was confirmed at histology following biopsy. The patient had surgery thereafter with no post-operative complications.*

I. Introduction

Nephroblastoma (Wilms' tumor) is the most common intra-abdominal tumour of childhood accounting for 10% of all childhood malignancies¹. It is an undifferentiated mesodermal tumour of the intermediate cell mass (primitive renal tubules and mesenchymal cells) which may be sporadic or familial².

It is primarily a disease of the kidney but occasionally, extra renal locations have been reported especially in the retroperitoneum, the sacrococcygeal region, testis, uterus, inguinal canal and mediastinum³. The disease is commoner in blacks (than in Caucasians) and affects children between 1- 8 years of age with an incidence of 1:10,000 in the general population and has equal sex distribution³.

The disease appears to arise from one or more of several genes. Two loci on chromosome 11 have been implicated in the genesis of a minority of Wilms' tumors. Locus 11p13 is known as the WT1 gene, and locus 11p15 is known as the WT2 gene³. However, the genetics of Wilms tumor appear to be multifactorial, and abnormalities at other sites, including chromosomes 1, 8, and 12, are also recognized⁴.

It is most commonly a unilateral disease but in 5% of the patients, both kidneys are affected⁴. Imaging plays an important role in the management of this tumor. The extent of the tumor, local, regional and distant spread, involvement of renal vessels and the status of contra-lateral kidney are well demonstrated by imaging studies⁵.

The rarity of bilateral nephroblastoma coupled with the unusual clinical management challenges it presents warranted the reporting of this case.

II. Case Report

A.H. is a 6-year-old girl who was admitted to the paediatric ward of Aminu Kano Teaching Hospital with history of sudden onset of progressively enlarging abdomen for one month, haematuria for two weeks and anorexia of one week duration. She had no history of trauma prior to onset of symptoms and there was no family history of similar complaints. Physical examination revealed an ill looking young girl in no obvious respiratory distress with large protuberant abdomen and conjunctival palor. Abdominal examination revealed firm fixed masses in both flanks which extended into the pelvis. Percussion notes were stony dull especially at the flanks. The absence of mobility of the masses suggested their retroperitoneal origin. No associated congenital abnormality was found.

Her blood pressure at presentation was high, measuring 130/98 mmHg. Laboratory investigations revealed low hemoglobin concentration (6g/dl) and gross haematuria on urinalysis which suggested renal involvement by the masses. Her white blood cell count (WBC), serum electrolytes, blood urea and creatinine were within normal limits. A 24-hour urinary Vanilmandelic acid (VMA) was normal.

Plain abdominal radiograph (Fig. 1.) revealed abdominal distension with bulging of the flanks. There were opacities of soft tissue density in both flanks which obscured the Psoas muscle margins. The masses also caused displacement of the bowel loops peripherally and inferiorly, but no calcification of these masses or bony lesion was detected. Her chest radiograph was essentially normal.

Abdominal sonography (Fig. 2.) showed bilaterally enlarged kidneys (beyond the sonographic field of view) with mixed parenchymal echogenicities. The scan also showed focal hypoechoic areas due to tissue necrosis and there was loss of renal corticomedullary differentiations. Ascites was demonstrated but no enlarged lymph nodes seen. Other intra abdominal organs appeared normal.

Intravenous urography showed delayed uptake and excretion of contrast medium bilaterally with the nephrograms seen at 5th and 10th minutes on the right and left side respectively. Both kidneys were enlarged with lobulated outline noted on the left due to a mass which occupied the upper pole. Their bipolar lengths measured

18cm and 23cm on the right and left sides respectively. There was bilateral calyceal distortion with compression of the calyces. The ureters and urinary bladder were however within normal limits.

Computed tomography (CT) of the abdomen (Fig.3.) showed heterogeneously enhancing solid-cystic renal masses with Hounsfield units which ranged between 19 and 42. The masses were seen displacing and compressing the adjacent liver and spleen. Bowel loops were also displaced anteriorly by the masses. The renal veins and inferior vena cava (IVC) were patent and were not encased. Areas of hypodensities with HU values ranging from 2-3 were seen within the renal substance bilaterally due to hydronephrosis with layering of contrast medium noted in these areas (fig.3). Moderate ascites was also noted.

No retroperitoneal lymphadenopathy or distant metastases seen. The renal vessels were within normal limits bilaterally.

Considering the patient's age, a working diagnosis of bilateral Wilms' tumor (BWT) was made, while lymphoma was considered as a possibility. Biopsy of the renal masses confirmed the diagnosis of BWT.

The patient was commenced on tumor debulking adjuvant chemotherapy (combination of vincristine and actinomycin D) which she received for 12 weeks. This resulted in some degree of tumor shrinkage bilaterally. She was subsequently optimized for surgery and later had bilateral partial nephrectomy. She had an uneventful postoperative course and continued on post-op chemotherapy. She was discharged home and has been on follow-up at the Out-Patient Clinic. She has done well over the past 6-months of follow-up.



Fig. 1. Plain abdominal radiograph showing bulging of the flanks due to intra abdominal masses of soft tissue density. Scanty bowel gases are seen at the left flank. The psoas muscles are not identified, raising suspicion of retroperitoneal masses. There is no abnormal calcification or bony destruction seen.

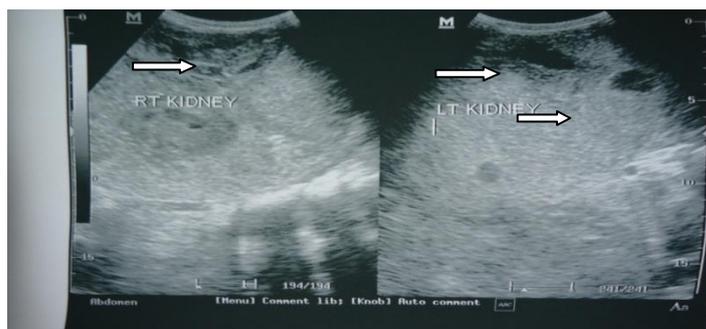


Fig.2. Bilateral renal sonogram (sagittal section); showing enlarged kidneys with mixed parenchymal echogenicities and necrotic foci (arrows). Both kidneys also show loss of corticomedullary differentiation.

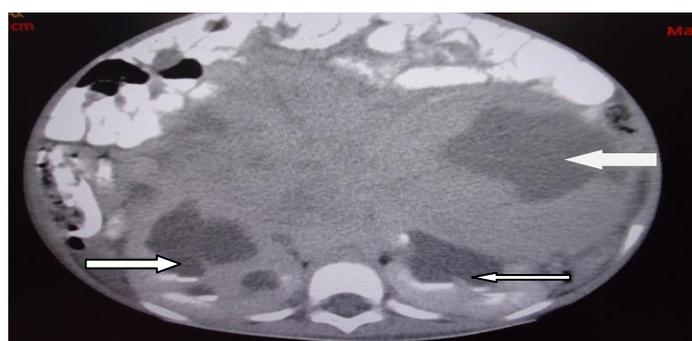


Fig. 3 Contrast-enhanced (oral and intravenous) axial computed tomographic image of the abdomen showing bilateral, heterogenous, moderately enhancing renal masses with renal architectural distortion. Areas of hypodensities due to hydronephrosis with contrast layering (white arrows) are seen bilaterally as well as a focal hypodense area in the left kidney due to tumor necrosis (black arrow).

III. Discussion

Wilms' tumour is the fifth most common paediatric malignancy overall (approximately 6% of all paediatric cancers)². Its peak incidence is at 3–4 years of age and 80% of patients present before 5 years of age⁴. This patient presented at the age of 6.

1-2% of patients have a positive family history³. Hereditary Wilms' tumour (either bilateral tumours or a family history of the neoplasm) is uncommon and are transmitted in an autosomal dominant manner³. The National Wilms' tumour study staging⁵ protocol employed in Europe and adopted for management of cases in our environment comprises: stage I, tumour limited to the kidney and is completely resectable; stage II, tumour extending beyond the kidney but still completely resectable; stage III, residual tumour confined to the abdomen without distant metastasis; stage IV, haematogeneous metastases to lung, liver, bone, brain; and finally stage V, bilateral renal involvement appearing initially or manifesting during treatment. Thus, BWTs are all considered stage-V disease like the presented patient.

Generally, both kidneys are asymmetrically involved; one kidney being more severely affected without any salvageable renal substance whereas the opposite side spares some part of the kidney⁵. Presentation of the disease may be in metachronous or synchronous fashion. Metachronous disease (two or more cancers appearing at different points in time) has an ominous prognosis⁵. In this patient, the tumours were synchronous, with left kidney being more severely affected than the right.

Though BWT accounts for about 5% of cases, it is associated with higher morbidity and mortality⁶. Discovery of Wilms tumor most commonly follows detection of a palpable abdominal mass, but it is discovered after coincidental trauma in up to 10% of cases⁷.

The patient may present with abdominal pain, haematuria and urinary tract infection¹. Other forms of presentations which include hypertension and gross haematuria are uncommon¹ but these were found in the index patient. They may also uncommonly present with fever and in advanced cases may present with respiratory symptoms due to lung metastases¹. There was no evidence to suggest such on the chest radiograph of this patient.

Wilms' tumor often has varied imaging appearances depending on the choice of imaging modality and time of patients' presentation³. Ultrasound is the first imaging modality as for any child with abdominal mass. Chest radiograph is done at baseline as lung is the most common site for metastases³. On ultrasonography (US), WT is seen as a heteroechoic mass with variable foci of hemorrhage, necrosis and calcification. Renal vein/inferior vena cava/hepatic veins should be assessed for tumor thrombus. Caval extension of tumor thrombus is seen in about 4% of the cases, with the thrombus extending into the right atrium⁴. The contralateral kidney must always be inspected for its absence, synchronous tumor, nephrogenic rests and congenital abnormalities as it affects the management⁴.

Abdominal CT is more sensitive than US in identifying the tumor extent and nodal as well as liver involvement⁶. With the advent of multidetector CT, multiplanar reformatting (MPR) and maximum intensity projection (MIP) images allow viewing the mass in its entirety and one can clearly visualize regional invasion and the relationship of the vessels with the mass⁸. On non-contrast computed tomography (NCCT), it is seen as a well-circumscribed heterodense mass with areas of hypodensity due to necrosis, fat and old hemorrhage. Acute hemorrhage shows fluid–fluid level and calcification in ~9% of the cases⁸. On contrast-enhanced computed tomography (CECT), the tumor enhances less than normal renal parenchyma. A claw or beak sign is seen due to the normal renal tissue displaced by tumor⁸. CECT is essential for assessment of lymphadenopathy, vascular invasion, metastases to liver, peritoneal invasion and contralateral kidney for presence of synchronous small WT and nephrogenic rests⁸. CT examination of this patient revealed bilateral enlarged, moderately enhancing kidneys with cystic hypodense foci due to tumor necrosis. No evidence of tumor metastasis or vascular involvement was seen.

Magnetic resonance imaging (MRI) though not done for this patient, has been reported⁴ as the most sensitive modality for determination of caval patency. The disadvantage of CT is of course the radiation burden, which should be kept as low as possible in pediatric patients^{4,6}. The lung is the most common site for metastases in WT and, traditionally, chest radiography has been the means for assessing pulmonary metastases. CT chest has proved to be more sensitive for detection of pulmonary nodules⁶.

Intravenous urogram (IVU) may show distortion of the renal pelvis and loss of renal function¹. In this patient, IVU showed bilateral renal enlargement, delayed uptake and excretion of contrast medium in both kidneys. The calyces were distorted.

¹⁸F-fluorodeoxy glucose positron emission tomography (FDG-PET) plays an important role in the staging and surveillance of this tumour⁹ as uptake of the radiotracer by the tumor cells can help identify tumor spread to other regions of the body including metastatic chest disease.

Several congenital anomalies, none of which was found in the index patient are said to be associated with the disease including cardiac anomalies (septal defects), microcephalus and genitourinary abnormalities (double collecting system or fused kidneys)³, these could also be identified using the imaging modalities above.

Although the disease usually develops in otherwise healthy children, approximately 10% occur in children with recognised malformations; such as; 'Overgrowth syndromes' (Beckwith-Wiedemann syndrome) in which there is excessive prenatal and postnatal somatic growth resulting in macroglossia, nephromegaly, and hemihypertrophy¹. Others include Perlman syndrome, Sotos' syndrome, and Simpson-Golabi-Behmel syndrome¹.

No 'overgrowth' - associated with trisomy 18, Bloom's syndrome, Denys-Drash syndrome; or Wilms' with Aniridia, Gonadoblastoma (GU malformations), and Retardation (WAGR) syndrome¹.

Treatment of BWT aims at maximal conservation of uninvolved renal parenchyma, in order to salvage renal function. Preoperative chemotherapy is particularly important because each kidney is staged separately, and complete resolution of disease in one kidney may allow surgery on the contralateral kidney to achieve a definitive cure. A larger tumour is usually dealt with by radical nephrectomy, otherwise the surgical approach mainly entails tumour resection with sparing of normal parenchyma¹⁰. In contrast, unilateral Wilms' tumour is generally treated by total nephrectomy, followed by adjuvant chemotherapy. Pre-surgical treatment with chemotherapy may be used to promote shrinkage of the tumour, so as to improve outcome¹⁰.

The multidisciplinary management of Wilms' tumor has resulted in a striking improvement in survival as revealed by Hisham et al¹¹ whose findings were a 4-year overall survival rate of 70.1%, for Stages I and II, while stages III+IV+V with favorable histology had a 4-year overall survival of 82.3%, 56% and 41%, respectively. Stages I to IV with unfavorable histology had a 4-year survival of 65.7%.

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