Wilms' Tumor in Children (Clinical Features & Management) An Experience in Child Central Teaching Hospital

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ABSTRACT:

BACKGROUND:

Wilms tumor is one of the most common nephrologic paediatric tumors, a retrospective study of 24 patients had wilms tumor were reviewed from clinical and epidemiological point in the oncology unit of Child Central Teaching Hospital for the period (June 1st 2004 to June 1st 2010).

OBJECTIVE:

To find out the main clinical features, diagnosis,treatment modalities and outcome of children with wilms tumor admitted to central teaching hospital.

PATIENTS AND METHODS:

Records of 24 cases were collected and analyzed as aretrospective study done in oncology unit in central teaching hospital over 6 year period from June 1st2004 to June 1st 2010

RESULTS:

Patients included 13 males and 11 females; the mean age at presentation for males was 3.7 years and 2.5years for females,male to female ratio was 1.18:1 .

Asymptomatic abdominal mass was the most common presenting feature in 24 patients (100%) followed by haematuria in 7patients (29.2%), hypertension in 3 patients (12.5%), congenital anomaly(which was hemihypertrophy of the Lt. side) in 1patient (4.2%) & other presenting features including: fever, weight loss, nausea, vomiting, abdominal pain in 15 patients (62.5%).

The tumor was left sided in 14 (58.3%) patients, right sided in 8 (33.4%) patients & bilateral in 2 patients (8.4%).

Stage III wilms tumor was the commonest histopathological type in 7 patients (29.2%).

The overall survival was (41.6%); the overall mortality rate was (16.7%); infection and sepsis were the main causes of death in 2 patient (8.3%).We had 4 patients died ,2 of them due to infection &sepsis , other 2 patients cause of death not reported.

CONCLUSION:

The study showed the clinicodemographic fates of patient with wilms tumor were similar to other studies but still infection &sepsis were common causes of death in advanced stages because of delayed referral in most cases.

KEY WORDS: wilms' tumor ,clinical features &management.

INTRODUCTION:

Wilms' tumor (nephroblastoma) is the most common primary malignant renal tumor of childhood[1], it is the second most common malignant retroperitoneal tumor[2] ,and it was first described by MAX WILMS in his classic 1899 monograph

Epidemiology:

Wilms' tumor represented 6 % of childhood cancer, with an incidence of 9 new cases in 1 million children diagnosed annually[2]

Central Teaching Hospital of Paediatric.

Etiology:

Wilms' tumor is thought to arise from abnormal renal development, with proliferation of metanephric blastema without normal differentiation into tubules & glomeruli. Alterations in genes controlling growth & differentiation have been associated with Wilms' tumor

Wilms' tumor appears to result from the loss of function of certain tumor suppressor genes as opposed to the activation of oncogens

Staging of wilms' tumor:

as recommended by the national wilms' tumor study group (nwtsg)

Clinical presentation:

Most children with wilms' tumor are brought to medical attention because of abdominal swelling or the presence of abdominal mass[12]. aabdominal pain; gross haematuria and fever are other frequent finding at diagnosis. Regarding haematuria is not common but is more often seen microscopically than on gross examination[2].hypertension presents in approximately 25%of cases, has been attributed to an increase in rennin activity[(13)] .

or less commonly due to compression of renal vasculature.[(2)]

During the physical examination it is important to note the location and size of the abdominal mass. A wilms' tumor is usually a large flank mass that does not particularly move with respiration. These finding help to differentiate wilms' tumor from splenomegally and neuroblastoma, the latter often arising in the celiac axis or extending across the midline because of lymph node involvement. A varicocele secondary to obstruction of spermatic vein may be associated with the presence of tumor thrombus in the renal vein or inferior vena cava.[1]other findings may include polycythemia which is occasionally present in association with male, older age, and low clinical stage, the erythropoietin levels are usually increased but can also be normal[(2)]. So any child with unexplained polycythemia should be investigated for wilms' tumor.[(2)] Also Bleeding diathesis might occur and it is due to the presence of acquired von willebrands' disease(reduced von willebrand's factor antigen level ,prolonged bleeding time, decreased factor eight level and factor eight ristocetin cofactor activity)[(2)].

investigations in wilms' tumor

Complete blood count: presence or absence of polycythemia.
Urinalysis.
Blood chemistries: BUN, creatinine, uric acid, S.ALT, SAST, LDH, ALP.
Assessment of coagulation factors:PT,PTT,fibrinogen level, bleeding time(if abnormal, factor eight level,von willbrand 's factor antigen level, factor eight ristocetin cofactor activity)[a]
Assessment of cardiac status: ECG, ECHO, in all patients who receive Adriamycin, ECHO may be useful in detecting the presence of tumor in the right atrium.
Abdominal ultrasound
Abdominal CTscan :with special attention to
Presence and function of the opposite kidney
Evidence of bilateral involvement
Evidence of involvement of blood vessels with tumor
Lymph node involvement
Liver infiltration
Chest radiograph (PA,LAT)
Chest CT scan: helps recognize small metastases that may be hidden behind ribs, diaphragm, and heart and may be missed on chest radiograph.
Skeletal scintogram: only in cases of clear cell sarcoma –bone metastasizing renal tumor of childhood.
Magnetic resonance imaging and(MRI) /or CT scan of brain: only in cases of rhabdoid tumors, which are frequently associated with CNS tumors and clear cell sarcoma of kidney, which may metastasize to the brain.
Peripheral blood for chromosomal analysis: in cases of congenital anomalies, such as aniridia, beckwith-wiedmann syndrome,hemihypertrophy[2].

[a]to exclude associated acquired von willebrand's disease

Treatment:

Controversial issues in the management of wilms' tumor include the use of preoperative chemotherapy and radiation therapy, and also the composition of chemotherapeutic agents the intent is to reduce the incidence and nature of late effect while providing optimum therapy[15].More than 90%of wilms' tumor cases are cured. For the majority of cases, therapy consists of surgery, followed by chemotherapy, and in some patient's radiotherapy[15]. Treatment of wilms' tumor is based on the conclusions of the NWTS program.

- Prognosis:

About 85 – 90 % of children with Wilms' tumors who receive treatment are cured

AIM OF STUDY:

1. To find out the clinico-pathological features&outcome of wilms' tumor in children admitted to central teaching hospital in Iraq.
2. To compare the result of our study with the result of other studies done inside and outside Iraq.

PATIENTS &METHODS:

A retrospective study was done in the oncology unit in the Child's Central Teaching Hospital in Baghdad on the records of (25) patients who were diagnosed and treated as cases of Wilms' tumor over 6 years period from June 1st 2004 to June 1st 2010.

Information regarding (age, sex, residency, clinical presentation & congenital anomalies, family history, staging of tumor, laboratory investigations, imaging, diagnostic method, treatment modalities and outcome) was recorded. These informations were collected from the oncology outpatient clinic files where the patients have been treated and followed up.The diagnosis of Wilms' tumor was made in most of the cases (79.1%) by surgical exploration (excision biopsy or incision biopsy), FNA in (20.9%) of case.

The protocols used in treating patients were randomized according to stage,histopathology was SIOP AND CTHC PROTOCOLS(modifiedfrom NWTS) depending on the site, resectablity, blood vessels, capsule involvement as shown below[1]:

Stage	description
I.	Tumor confined to the kidney and completely resected. No penetration of the renal capsule or involvement of renal sinus vessels. (43% of cases).
II.	tumor extends beyond the kidney but is completely resected(negative margins and lymph nodes).at least one of the following has occurred:(a)penetration of the renal capsule,(b)invasion of the renal sinus vessels,(c)biopsy of tumor before removal(d) spillage of tumor locally during removal.(it represents 23%of cases).
III.	gross or microscopic residual tumor remains postoperatively, including inoperable tumor ,positive surgical margins, tumor spillage involving peritoneal surfaces , regional lymph node metastases, or transected tumor thrombus .(23%).
IV.	Hematogenous metastases or lymph node metastases outside the abdomen (e.g., lung, bone, brain). (10%).
V.	Bilateral renal wilms' tumors at onset. (5%).

RESULTS:

Patient characteristics:

A total no. of 25 cases were reviewed in this study, one case were excluded (died before starting chemotherapy).Among (24) patients with Wilms' tumor there were 13(54.2%) males &11(45.8%) females, male to female ratio was 1.18:1 as shown in Table1.Age range, between 6 months - 8 years, most of patients(19)(79.2%) were between 1-5 years as shown in Table2.The mean age of presentation was 3.20±1.98 years.The duration between onset of symptoms and time of diagnosis was ranged between 1 week- 16 weeks, mean duration was 5 weeks.

The most common presentation was asymptomatic abdominal mass in all patients(24)(100%)with left side predominance(14 patients)(58.3%),right sided mass present in 8 patients(33.4%),whereas the remaining present as bilateral masses(2 patients)(8.3%), gross hematuria in (7)patients(29.1%), hypertension in (3) patients(12.5%), congenital anomalies(which was hemihypertrophy of the left side) in (1) patient(4.2%) and other presentation (nausea, vomiting, abdominal pain, pleural effusion,

dyspnea , ascitis) in [15] patients (62.5%)as shown in Table3. Positive family history for malignancy was found to be present in 4patients (16.6%) including sister with osteosarcoma, brother with acute lymphoblastic leukemia, grandmother with lung carcinoma, and for one patient having aunt with breast carcinoma, cousin with leukemia.table3.

Initial radiological & laboratory investigations:

As an initial investigations U/S & CXR done to all patients routinely, results showed an abdominal mass that is left sided in 14 patients(58.3%), right sided in 8 patients(33.4%) & bilateral in 2 patients(8.3%). CXR done to 20 patients, 19patients (79.2%) had normal x-ray findings and only one case (4.2%) had pleural effusion the other 4 patients (16.6%) were not reported. IVU was performed in 2 patients (8.3%), both of them had abnormal findings (non-functioning kidney, distorted PCS, hydronephrosis) the other 22 patients (91.7%) no IVU were done.Abdominal CT done to 10 (41.7%) patients and the abnormal findings included (contra lateral kidney involvement, renal vein(either compression or thrombus) & retroperitoneal masses) while 14(58.3%) patients no CT reported. Chest CT done to one patient only (4.2%) which showed small localized metastases in the lung. Complete blood count done to all patients and 5 patients (20.9%) found to be anemic as shown in Table4.

Diagnosis: Majority of cases were diagnosed by biopsy (19patients) 79.1% (excision or incision biopsy),the remaining cases diagnosed by FNA(5 patients)20.9% as shown in Table5.

Staging and histopathology: Clinically stage III is the common stage (29.1%) table 6

Treatment:

Most of cases(18 patients)(75%) were treated by immediate nephrectomy, followed by chemotherapy, the time between the diagnosis and initiation of chemotherapy ranged from 1week – 16 weeks, over all survivors was(15 patients)(83%) of those who underwent immediate nephrectomy.No reported cases were treated by presurgical chemotherapy (to reduce tumor bulk) and then delayed surgery. The remaining group of patients was inoperable at time of diagnosis& were managed by chemotherapy with 33.3% overall mortality, because of late presentation and in advanced stage as shown in Table7.

Radiotherapy:

Radiotherapy was given in only one case which was stage II and relapsed after treatment.

Summary of treatment result:

Disease free survival (DFS) (the patient who is alive with complete remission with no recurrence) is45.9%, death occurs in 4 patients 16.6%, the most common cause behind was infection & sepsis, bleeding , in 2 patients were the cause of death was not reported. Relapse (patient who have recurrence of the disease after 3months of completing the course of treatment) occurs in 3 patients (all those patients off treatment), progressive disease (in which the patient having localized tumor or in distant site for < 3months after finishing treatment) present in 3 patients (12.5%), the remaining 3patients(12.5%) discontinued treatment and we lost the follow up,as shown in Table8.

Table1: Sex distribution.

Sex	No.	%
Male	13	54.2
Female	11	45.8
M:F 1.18:1		

Table 2:Age distribution.

Age (years)	Total	%
< 1	2	8.3
1-5	19	79.2
>5-8	3	12.5
Total	24	100

Table 3: Clinical presentation.

Clinical presentation	No.	%
(nausea, vomiting, dyspnea Pleural effusion, ascitis)and other presentations	15	62.5
Abdominal mass	24	100
Left sided mass	14/24	58.3
Right sided mass	8/24	33.4
Bilateral mass	2/24	8.3
Haematuria	7	29.1
Hypertension	3	12.5
Minor congenital anomalies(hemihypertrophy of Lt. side)	1	4.2
Positive family history osteosarcoma acute lymphoblastic leukemia lung carcinoma breast carcinoma&leukemia	4 1/4 1/4 1/4 1/4	16.6

Table 4: Initial Radiological& Laboratory results of 24 patients.

	No.	Percent (%)
U/S Finding		
Lt. sided mass	14	58.3
Rt. sided mass	8	33.4
Bilateral mass	2	8.3
CXR finding		
Normal	19	79.2
Abnormal findings(pleural effusion)	1	4.2
Not recorded/not done	4	16.6
I.V.P		
Normal	0	0
Abnormal findings(non_functioning kidney ,distorted PCS, hydronephrosis)	2	8.3
Not recorded/not done	22	91.7
CT abdomen		
Abnormal findings(cotralateral kidney,renal vein compression or thrombus ,retroperitoneal masses)	10	41.7
Not recorded/not done	14	58.3
CT chest		
Abnormal findings(small localized metastases in lung)	1	4.2
Not recorded/not done	23	95.8
Complete blood count		
Anemia	5	20.9

Table 5: Method of diagnosis.

Method	No.	%
excisional biopsy	17	70.8
Incision biopsy	2	8.3
FNA	5	20.9
Total	24	100

Table 6: Staging system proportion in the current study.

Stage	No. of patients	%
I	4	16.6
II	6	25
III	7	29.1
IV	5	20.9
V	1	4.2
Unknown	1	4.2
Total	24	100

Table 7: Summary of treatment results.

Treatment results	No.	Percentage
Relapse	3	12.5
Died	4	16.6
Discontinued(lost to follow up)	3	12.5
PD (progressive disease)	3	12.5
DFS(Disease free survival)	11	45.9
Total	24	100

Table 8: Outcome of 24 patients .

Type of treatment	No.	%
Immediate surgery followed by chemotherapy	18/24	75%
Alive*	15/18	83
lost to follow up	1/18	6
Death	2/18	11
Inoperable	6/24	25%
Alive*	2/6	33.3
Death	2/6	33.3
Loss follow up	2/6	33.3

*Alive patients include those who have disease free survival (DFS), progressive disease (PD) and those with relapse.

DISCUSSION:

Wilms' tumor is the most common primary malignant renal tumor of childhood. [12]

Evaluation of cases referred to our oncology unit over a period of 6 years was done depending on the following parameters (age, sex, clinical presentation, investigations, treatment & outcome).

Mean age at presentation was (38.4 months) which is below that mentioned in Lanzkowsky et al study [2] (44 months), Hung IJ et al study[14] (44.4 months), & Amel et al study [15] in Tunisia (45 months), but higher than that that mentioned in S. AL-Haddad study [16] (33 months), Madani et al study[17] in Morocco (36 months) & of Pianezza ML et al study [18] in Canada (28.5 months).

Most of the cases presented between (1-5) years of age (79.2%) which is higher than that mentioned in Lanzkowsky et al study [2] (75%) and higher than other Iraqi study[19] (72.6%), with nearly equal (M/F) ratio (1.18:1) similar to that mentioned in Lanzkowsky textbook [2], but different from that mentioned in Yildiz I et al study[20] in Turkey (1. 35).

13 cases were males account54.2% of cases,11 cases were females account for45.8% of cases which is nearly equal to that mentioned to Yildiz I et al study[20] (57% male,43% female) but different from that mentioned inS.AL-Haddad study [16](49%male,51% female) and from other Iraqi study[19] (49.3% male,50.7%female) .

All cases (100%) presented with asymptomatic abdominal mass which is higher than that mentioned in S.AL-Haddad study [16](76.4%), Pianezza ML et al study[18] (85%) & nearly equal to that of Madani et al study [17] (97.7%) .

Hematuria presented in (29.2%) of cases, which is higher than that mentioned in Lanzkowsky textbook [2] (15%) &S. AL-Haddad study [16] (10.9%) and other Iraqi study [19] (21.9%),Hypertension detected in(12.5%)of cases which is lower than that mentioned in Lanzkowsky textbook[2] (25%) &in other Iraqi study [19](37%) and higher than that mentioned in S. AL-Haddad study[16] (5.45%) this may be due to improved concept about measurement of blood pressure in patients with Wilms' tumor.

History of fever, weight loss,nausea,vomiting,&abdominal pain were recorded in (45.8%) of cases, which is higher than that mentioned in Lanzkowsky textbook [2](4%) and in AL-Haddad study [16] (25%) this is due to progressive disease

Congenital abnormalities(Lt. side hemihypertrophy) was found in (4.2%) of cases that is lower than that mentioned in S. AL-Haddad study [16](7.2%) and to that mentioned in the Lanzkowsky textbook [2](12-15%)**,** Hung IJ et al stud [14] (17.3%) and to that done in other Iraqi tudy [19] (13.7%).

Ultra sound were done for all cases (100%), CXR were done in83.4% of cases. I.V.P. was recorded in (8.3%) of cases either due to lack in initial registrations or shortage of dye(contrast) required for the test. CT of abdomen was done only in 41.7% of cases either due to the long waiting appointment given to the patients for doing CT or availability of this test in limited number of hospitals, chest CT done for one patient only (4.2%) .

overall Mortality was (16.6%), which is slightly higher than that mentioned in S. AL-Haddad study [16] (14.6%), this is a relatively high rate due to lack of proper supportive care in our center and referral of case in advanced stages of disease, but still lower than that mentioned in Sen S et al study[23] in India (44.8%).

Relapsed patients were (12.5%) which is lower to that mentioned in AL-Haddad study [16] (21.7%), and nearly equal to that Madani et al study [17] (15%) & Pianezza ML et al study[18] (10%).

Lost to follow up was reported in (12.5%) of cases which is lower than that mentioned in S. AL-Haddad study [16] (50%), in Sen S et al study[23] in India (18.4%).

The difference in study results from other studies that was done in Iraq in other centers might be explained with the difference in the number of cases referred to our centre and the delay in referral, also during the time of recorded patients, our hospital have been worked with the minimum capacity due to reconstruction of the old building done during that time

CONCLUSION:

1. High frequency of stage III, IV due to delay in diagnosis and referral.
2. Delayed referral of cases post nephrectomy because of Ethical issues of some surgeons about the need for chemotherapy post surgery.
3. Low survival rate due to high percentage of advanced stages of disease.
4. Limited use of radiotherapy in the treatment for patients with unfavorable histopathology due to old generation machines and poor physics, long waiting list with delay the proper timing of radiotherapy with management protocols.

Recommendation

1. Immediate referral after surgery to start early treatment (chemotherapy and / or radiotherapy).
2. The need for trained multidisciplinary care team including pediatric oncologist, surgical oncologist, radiotherapist, pathologist and well-equipped cancer center.
3. The need for accurate and complete recording of the patient's presentation, investigation, complications will help us to get good source of information for doing studies and follow up our patients.

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