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Original Article

Wilm's Tumor-Collaborative Approach is needed to Prevent Tumor Upstaging and Radiotherapy Delays: A Single Institutional Study

Abstract

Context: Successful management of Wilm's tumor (WT) necessitates meticulous attention for proper staging and collaborative effort for its optimal management. **Aims:** The aim of the study was to observe the patterns of WT. **Settings and Design:** This study was a single-institutional retrospective study. **Subjects and Methods:** Twenty-three WT case records were analyzed over 6 years and the data collected were interpreted as number, percent, mean ± and standard deviation with regard to clinicodemographic aspects, staging, and diagnostic modality and treatment options. **Results:** Mean age was 3.97 ± 2.67 years with maximum number in the 2–5-year age group. Males slightly dominated the number, and majority cases were from the rural area. The major clinical presentation was abdominal mass followed by abdominal pain, fever, vomiting, hematuria, and urinary retention. Left laterality was common and single bilateral WT was seen. Majority of tumors were >10 cm in their largest dimensions. Most WT presented in Stage III followed by Stage I and IV. One was a recurrent tumor. **Conclusion:** WT was usually diagnosed at the locally advanced or metastatic stages; hence, the comprehensive collaborative approach will help to manage the patients optimally and avoid tumor upstaging and radiotherapy delays. Besides awareness at community level is needed to pick up the disease at the earlier stage to have a better outcome in the form of disease control and disease-free survival.

Keywords: *Abdominal mass, nephroblastoma, radiotherapy delays, tumor upstaging, Wilm's tumor*

Shaqul Qamar Wani, Talib Khan[1], Saiful Yamin Wani[2], Mohammad Maqbool Lone, Fir Afroz

Department of Radiation Oncology, State Cancer Institute, Sher I Kashmir Institute of Medical Sciences (SKIMS), [1]Department of Anaesthesia, Pain and Critical Care, Sher I Kashmir Institute of Medical Sciences (SKIMS), Srinagar, [2]Department of Health Services Kashmir (DHSK), District Hospital Pulwama, Jammu and Kashmir, India

Introduction

Wilm's tumor (WT) is the most common renal malignancy in children and the fourth most common childhood cancer.[1-3] WT is a paradigm for the multimodal treatment of pediatric solid tumors. Improvements in surgical techniques and postoperative care, recognition of the sensitivity of WT to irradiation, and the availability of active chemotherapeutic agents have led to dramatic change in the prognosis for this, once uniformly lethal, malignancy.[4]

The survival of children with WT has improved over the past two decades. It is expected that more than 80% of all children with WT have long-term relapse-free survival with this treatment modality.[5]

The incidence of WT is 7.1 cases/1 million children younger than 15 years. Approximately 500 cases of WT are diagnosed in the United States each year. The incidence is substantially lower in Asians. The male-to-female ratio in unilateral cases of WT is 0.92:1.00, but in bilateral cases, it is 0.60:1.00. The mean age at diagnosis is 44 months in unilateral cases of WT and 31 months in bilateral cases.[3]

WT accounts for 6% of all childhood tumors, but more than 90% of all renal cancers in patients under the age of 20 years. The risk for developing WT is higher in African Americans and lower among Asian populations. Although unilateral disease is more common, with males presenting at a slightly earlier age (37 months) than females (43 months), approximately 6% of patients harbor bilateral disease at diagnosis, with males presenting slightly earlier (24 months) than females (31 months).[6]

Most children with WT come to medical attention because of abdominal swelling or the presence of an abdominal mass that may be noted by the caregiver during bathing or dressing the child. Abdominal pain, gross hematuria, and fever may be present at diagnosis. Hypertension is present in approximately 20% of cases.[6]

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Address for correspondence:
Dr. Talib Khan, Department of Anaesthesia, Pain and Critical Care, Sher I Kashmir Institute of Medical Sciences, Srinagar - 190 011, Jammu and Kashmir, India.
E-mail: drsqamar1@gmail.com

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WT may arise as sporadic or hereditary tumors or in the setting of specific genetic disorders[7] and is diagnosed by radiological impression and clinical presentation.[6,7]

We undertook this study to analyze the WT patterns in this part of Indian subcontinent which is ethnically and sociodemographically different from rest of India and to decipher any message of importance for optimal patient care management.

Subjects and Methods

A total of 23 cases of WT registered from January 2010 to December 2015 (6 years) were included in the study. The records were analyzed with regard to clinicodemographic, diagnostic workup, stage of the disease, upstaging, and treatment received. This study being retrospective in nature is exempted from the Institutional Ethical Committee approval. The data collected were transferred to Microsoft Excel chart and was interpreted as number (n), percentage (%), and mean ± standard deviation (SD).

Results

The mean age was 3.97 ± 2.67 years ranged from 0.58 years to maximum of 10 years. Males were 52.17% (n = 12/23) and females were 47.82% (n = 11/23). Most of the patients (69.56% [n = 16/23]) were from rural area and urban were 30.43% (n = 7/23). All 100% (n = 23/23) WT cases were Muslims. With regard to the mode of delivery, 43.47% (n = 10/23) children were born by vaginal route and 17.39% (n = 4/23) children were born by cesarean section. Mode of delivery was not known in 39.13% (n = 9/23) WT cases. With regard to birth order, 4.34% (n = 1/23) were first order, 34.78% (n = 8/23) were 2nd in birth order, and 13.04% (n = 3/23) were 3rd in birth order. Birth order was not known in 47.82% (n = 11/23) of children. Majority of patients (56.52% [n = 13/23]) were in the age group of 2–5 years, followed by equal distribution of 21.74% (n = 5/23) each in below 2- and above 5-year groups, respectively [Table 1].

With regard to clinical presentation, abdominal mass was an initial presentation in 73.91% (n = 17/23), followed by pain in 39.13% (n = 9/23) and fever in 26.08% (n = 6/23). Left-sided WT was present in 65.21% (n = 15/23), while right-sided WTs were in 30.43% (n = 7/23) and bilateral WT was in single 5-year-old male child, i.e., 4.35% (n = 1/23) [Table 2].

Ultrasonography (USG) abdomen was done in 82.60% (n = 19/23) and contrast enhanced computed tomography (CECT) chest and abdomen was done in 100% (n = 23/23) as diagnostic modality for WT. Tumor diameter in centimeters (cm) its largest dimensions was more than 10 cm in 65.21% (n = 15/23) WT cases, 5–10 cm in 21.74% (n = 5/23) cases, and <5 cm in largest dimension in 13.04% (n = 3/23) WT cases [Table 2].

Among 23 patients, a maximum number of patients (43.47% [n = 10/23]) had Stage III disease, followed

Table 1: Demographic features in Wilm's tumor

	***n* (%)**
Cases registered yearly	
2010	1 (4.34)
2011	4 (17.39)
2012	5 (21.74)
2013	4 (17.39)
2014	4 (17.39)
2015	5 (21.74)
Age (years)	
<2	5 (21.74)
2-5	13 (56.52)
>5	5 (21.74)
Total	23 (100)
Mean±SD	3.97±2.67
Minimum	0.58
Maximum	10
Gender, *n* (%)	
Male	12 (52.17)
Female	11 (47.82)
Male: Female	1.09:1
Dwelling, *n* (%)	
Rural	16 (47.82)
Urban	7 (30.43)
Religion, *n* (%)	
Muslims	23 (100)
Other	0
Mode of delivery, *n* (%)	
Vaginal delivery	10 (43.47)
CS	4 (17.39)
Not known	9 (39.13)
Birth order, *n* (%)	
1	1 (4.34)
2	8 (34.78)
3	3 (13.04)
Not known	11 (47.82)

CS – Cesarean section; SD – Standard deviation

Table 2: Clinical presentation, laterality, and size in larger dimension

	***n* (%)**
Clinical presentation	
Swelling	17 (73.91)
Pain	9 (39.13)
Fever	6 (26.08)
Hematuria	1 (4.34)
Retention of urine	1 (4.34)
Vomiting	2 (8.69) 1
Laterality	
Right	7 (30.43)
left	15 (65.21)
Bilateral	1 (4.35)
Size in larger diameter (cm)	
<5	3 (13.04)
5-10	5 (21.74)
>10	15 (65.21)

by Stage I and IV each in 21.73% (n = 5/23) WT cases, respectively. A single case of recurrence was observed who was treated a few years back with upfront surgery and reported to us as Stage I recurrence [Table 3].

With regard to treatment modalities, upfront surgery was done in 65.22% (n = 15/23) WT cases and 34.78% (n = 8/23) had preoperative chemotherapy. Nearly 34.78% (n = 8/23) had received radiotherapy (RT), of which 7 had received RT to the primary site and one had received to metastatic bony sites. No treatment was received by 8.70% (n = 2/23) patients, of which one had bilateral disease [Table 4].

A total of 47.82% (n = 11/23) patients were subjected to upfront biopsy [Table 4], which lead to disease upstaging in 21.73% *(n* = 5/23*)* patients to Stage III, out of which Stage I were 13.04% (n = 3/23) and Stage II were 8.69% (n = 2/23) [Table 5].

Table 3: Stage at disease presentation

	***n* (%)**
I	5 (21.73)
II	1 (4.34)
III	10 (43.47)
IV	5 (21.73)
V	1 (4.34)
R*	1 (4.34)
Total	23 (100)

*Recurrence in the registered year had been treated few years back with upfront surgery only reported to us as Stage I recurrence and treated by surgery and chemotherapy

Table 4: Management patterns in Wilm's tumor

	***n* (%)**
Upfront biopsy	11/23 (47.82)
Upfront surgery	15/23 (65.22)
Upfront chemotherapy	8/23 (34.78)
RT	8/23 (34.78)
No treatment	2/23 (8.70)

RT – Radiotherapy

Table 5: Total upfront biopsies

Initial staging	**Upfront FNA/biopsy, *n* (%)**	**Upstaging**
I	3/23 (13.04)	III
II	2/23 (8.69)	III
III	1/23 (4.34)	Total WT upstaged=5/23 (21.73%)
IV	4/23 (17.40)	
V	1/23 (4.34)	
Total	11/23 (47.82)	

FNA – Fine-needle aspiration; WT – Wilm's tumor

Discussion

WT is one of the most common renal tumors of childhood. The mean age at diagnosis is 44 months in unilateral cases and 31 months in bilateral cases of WT [3,6-9] which correlates with our study where majority of the patients were in the age group of 2–5 years with overall mean of 3.97 ± 2.67 years; however, there was single case of male bilateral WT aged 5-year age contrary to most of the literature. Left-sided tumors were significantly high in our study (65.21% [n = 15]). There is a slight female preponderance in the Western data with male: female ratio of 0.92:1 in the unilateral case and 0.6:1 bilateral case;[3] however, our study showed the male preponderance with male: female ratio of 1.09:1. Male preponderance was also seen in the study of Rais *et al.* and Mishra *et al.,*[2,9] while equal gender distribution was seen in the study of Naguib *et al.,*[10] majority of the patients were from rural dwelling due to the fact that most population in this northern belt of Indian subcontinent Kashmir lives in rural area.[11,12] None of our patients had physically obvious genetic abnormality and were likely sporadic. None of the patients had undergone genetic analysis due to economic constraints.

Most children with WT present with abdominal swelling/mass. Abdominal pain, gross hematuria, and fever may be present at diagnosis[3,6,7] similar to our study.

Some patients (10%) may present with hypertension and some other with constitutional symptoms such as malaise and metastatic symptoms such as hemoptysis, pulmonary embolism,[3,6] and bony pains.[13]

Clinical representation may reflect the stage at presentation in WT; however, most of the literature has shown the disease presentation at Stage III from Asian continent.[1,2] However Western data suggest earlier presentation of the tumor,[14] where the presentation is mainly Stage I and II. In our study of 23 patients, 11 (47.82%) had upfront biopsies, which lead to the disease upstaging in 21.73% (n = 5/23) WT cases, of which 13.04% (n = 3/23) were upstaged from Stage I and 8.69% (n = 2/23) were upstaged from stage II. Rest of six patients in whom upfront biopsy was done had already Stage III and above. Upfront biopsy leads to disease upstaging to Stage III.[7,8,15] However, upfront biopsy may be done in cases of diagnostic dilemma like, if age of the patient does not fit in the provisional diagnosis of WT.

The management of WT is either upfront surgery as per children oncology group (COG) guidelines or upfront chemotherapy as per the International Society of Pediatric Oncology (SIOP) guidelines. The patients can be started on either protocol except if the age of child is <6 months and should be subjected to upfront surgery as per the COG protocol, also if the tumor is large enough and the surgeon finds it difficult to remove tumor in toto and anticipates tumor spillage to prevent tumor upstaging, and bilateral disease presentation can undergo neoadjuvant chemotherapy.[6,14,15] In our study, upfront surgery was done in 65.22% (n = 15) cases and one patient with stage III disease had tumor spillage during the surgical procedure, while 34.78% (n = 8)

had preoperative chemotherapy. Almost 34.78% (n = 8) had received RT, of which 7 had received RT to primary site and one had received to metastatic bony sites. No treatment was received by two patients (8.70%), of which one had bilateral disease. Out of the seven patients who received RT to primary site, none of the patients received RT within 14 days postsurgery considering 0 day as the operative day, all of them had received RT beyond 1 month because of the delay of the referral within the specified time period and lack of communication and multidisciplinary treatment approach. As per the majority of the literature supporting the evidence that the RT should be received within 14 days of surgery to have its optimum effect and thereby avoiding the tumor recurrences and metastasis,[3,6,7,14,15] the same was delayed in our study.

Conclusions

The study stresses on the fact that majority of the patients with WT are diagnosed at the locally advanced or metastatic stages. By means of comprehensive collaborative approach, children will be managed optimally and prevent tumor upstaging and the radiation treatment delays (wherever RT is indicated).

Besides the awareness at community level is needed to pick up the disease at the earlier stage so that the children suffering from the disease will have a better outcome in the form of disease control and disease-free survival besides lesser treatment-induced morbidity.

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Conflicts of interest

There are no conflicts of interest.

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