

## WILMS' TUMOR: THE TAWAM HOSPITAL EXPERIENCE

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Over the past two decades, there have been significant improvements in the survival of children with cancer in general and those suffering from Wilms' tumor in particular. This is largely attributed to the multicenter prospective studies conducted by the National Wilms' Tumor Study group (NWTS)<sup>1,2</sup> and the International Society of Pediatric Oncology (SIOP).<sup>3,4</sup> However, this may not be the case in developing countries, where social as well as regional factors contribute to the outcome of the disease. This study is an analysis of the clinical features, results of treatment, outcome and factors pertinent to the management of patients with Wilms' tumor in this part of the world.

### Patients and Methods

Tawam Hospital is a tertiary care referral hospital in the United Arab Emirates, and the only hospital in the country with a dedicated pediatric oncology unit where both chemotherapy and radiotherapy are provided. A retrospective review was done of all children treated for Wilms' tumor at the hospital between January 1982 and December 1997. During this period, 528 children were treated at the hospital for various types of malignancies. The medical records of patients with Wilms' tumor were reviewed for age at diagnosis, sex, mode of presentation, investigations, associated anomalies, age at the initiation of treatment, preoperative treatment, type of surgery, stage, postoperative treatment and outcome.

The pathological diagnosis of Wilms' tumor was based on the presence of a tumor composed of blastema, stroma and epithelial cells, usually in combination, but could be biphasic, or in rare cases, consist of a single cell type. Unfavorable histology was based on the presence of anaplasia, which is defined by the presence of large nuclei which are hyperchromatic, and the presence of

TABLE 1. *Mode of presentation.*

Presentation	Number of patients
Abdominal mass and abdominal distension	30
Abdominal pain	6
Weight loss	7
Fever	2
Hematuria	4
Vomiting	2
High blood pressure	1
Accidentally discovered	4

hyperdiploid mitotic figures, a sarcomatous appearance or rhabdoid features.

All the patients with unilateral Wilms' tumor were treated surgically, followed by postoperative chemotherapy with or without radiotherapy, depending on the stage of the tumor, and according to the NWTS protocols.<sup>1,2</sup> In 1994, we adopted the SIOP protocol, giving all the patients with unilateral Wilms' tumor a course of preoperative chemotherapy (actinomycin D 15 µg/kg for three days in the first and third weeks of the course, vincristine 1.5 mg/m<sup>2</sup> once a week for four weeks). This course of preoperative chemotherapy was given prior to biopsy, and in an attempt to reduce tumor size, decrease the incidence of intraoperative rupture and downstage the tumor. In all patients, including the seven who received preoperative chemotherapy, the staging system we used was a surgical one and was based on the NWTS recommendations.<sup>5</sup> For those with bilateral Wilms' tumor, preoperative chemotherapy was given to all except one.

### Results

Thirty-six children diagnosed with Wilms' tumor were admitted to Tawam hospital during the study period. Of these, 12 were United Arab Emirates nationals, 12 were from other Arab countries, and the remaining 12 were non-Arabs. Of the tumors, 19 (52.8%) were located on the left side, 10 (27.8%) on the right side and 7 (19.4%) were synchronous bilateral.

There were 22 males and 14 females. The male to female ratio was 1.6:1, and males had more left-side tumors, while females had more right-side tumors. The ages ranged from 11 months to 9 years (mean 3.24 years).

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Accepted for publication 8 February 1999. Received 19 September 1998.

TABLE 2. Patients with synchronous bilateral Wilms' tumor.

Patient #	Age at treatment (yr)/sex	Comparative tumor size	Preoperative treatment	Stage of each side	Histology	Type of surgery	Postoperative treatment	Outcome
1	4.7/M	L>R	Actinomycin D, vincristine, epirubicin	Lt stage II	Lt Unfavorable	Lt nephrectomy, rt disappeared	Chemotherapy and radiotherapy	Died
2	2/F	(Multifocal) R>L	Actinomycin D, vincristine, doxorubicin	Both sides stage I	Both sides favorable	Excision of 13 tumors on rt side, and 3 on lt side	Chemotherapy	Survived
3	2.7/M	R>L	Actinomycin D, vincristine, doxorubicin	–	Both sides unfavorable	No surgery	–	Died
4	5/F	L>R	Actinomycin D, vincristine, doxorubicin	Lt stage II, rt stage I	Both sides favorable	Bilateral partrial nephrectomies, followed by lt nephrectomy	Chemotherapy	Survived
5	5/M	R>L	No preoperative treatment	Both sides stage I	Both sides favorable	Rt nephrectomy and lt partial nephrectomy	Chemotherapy	Survived
6	2/M	L>R	Parents refused treatment	–	–	–	–	–
7	5/M	R>L	Actinomycin D, vincristine, doxorubicin	Lt stage II, rt stage III	Lt favorable, rt unfavorable	Bilateral partial nephrectomies, followed by rt nephrectomy	Chemotherapy and radiotherapy	Died

Sixteen of the patients were less than two years old at the time of diagnosis. Their mode of presentation is shown in Table 1. In four of the patients, the tumors were discovered accidentally. In one of these cases, it was discovered during evaluation of the urinary tract infection, in two cases during an attack of upper respiratory tract infection, and during routine physical examination in the fourth. Five of our patients had associated anomalies. One had bilateral undescended testis, while the other four had right hemihypertrophy. In those with right hemihypertrophy, two had left-sided Wilms' tumor, one had right-sided Wilms' tumor, and the fourth patient had bilateral synchronous tumors.

Of the 36 children we treated, one child with bilateral Wilms' tumor was excluded from analysis because the parents refused treatment. Twenty-two of the 29 children with unilateral Wilms' tumor did not receive preoperative chemotherapy, while the remaining seven had preoperative chemotherapy followed by surgery. Thirteen of our patients had stage I, five had stage II, six had stage III, five had stage IV and seven had stage V. Of the seven children who received preoperative chemotherapy, six were found to have stage I and one child had stage III. One of these patients had localized Wilms' tumor of favorable histology. This patient had preoperative chemotherapy followed by surgery, but did not have postoperative chemotherapy. He is now one year post treatment, with no evidence of recurrence.

Seven of our patients—five males and two females—had bilateral Wilms' tumor. Their ages at presentation ranged from 1.3-5 years (mean 3 years), and their ages at treatment ranged from 2-5 years (mean 3.8 years). Three of our patients (numbers 1, 3 and 7 in Table 2) presented early at the age of one year, 1.3 years and two weeks respectively, but the parents refused treatment initially, only to present later at the age of 4.7 years, 2.7 years and 5 years, respectively, with more advanced stages of the

TABLE 3. Outcome in relation to stage, histology and preoperative chemotherapy.

Stage	# Patients (%)	Sex M:F	Histology	Recurrence	Preoperative chemotherapy	Survival
I	13 (36)	6:7	F: 6; UNF: 7	– 3	6 –	100%
II	5 (14)	3:2	F: 3; UNF: 2	1 –	– –	100%
III	6 (16.6)	3:3	F: 3; UNF: 3	– 2	1 –	83%
IV	5 (1.4)	5:0	F: 3; UNF: 2	– –	– –	80%
V	7 (19.4)	5:2	F: 3; UNF: 3	1 1	2 3	50%

disease. Except for one patient who was treated in 1989, all patients received preoperative chemotherapy which led to decrease in the size of the tumor (Figures 1 and 2) and complete disappearance of the tumor on one side in one patient. Their demographic data, preoperative treatment, histology, stage, type of surgery and outcome are shown in Table 2. On follow-up, three patients survived following treatment and are now 2, 3.5 and 8.5 years post treatment and well. The remaining three patients with Wilms' tumor died, giving a two-year postoperative survival of 90.8% and an overall two-year survival rate of 82.6%.

It was difficult to define the long-term survival rate of each stage separately because the number of patients in each stage was small and our patients were from a highly mobile population. Some of them were expatriates, but in spite of this, the two-year survival rate for stages I and II was 100%, for stage III 83%, for stage IV 80% and for stage V 50%. Of the 13 patients who had stage I, six had a favorable histology, while the remaining seven had an unfavorable histology. Of the five patients with stage IV, three had a favorable histology and two had an unfavorable

histology. The outcome in relation to stage, histology, and preoperative chemotherapy is shown in Table 3.

### Discussion

Wilms' tumor is the most common renal tumor of infancy and childhood. It has an incidence rate of about 7.8 cases per one million children, and in the United States about 450-500 new cases occur annually.<sup>6,7</sup> The exact incidence of Wilms' tumor in the United Arab Emirates is not known. This is attributed to the lack of an informative tumor registry. In nearby Saudi Arabia, of the 600 cases of childhood cancers reported in 1982 by Sabbah from King Faisal Specialist Hospital in Riyadh, 5.2% were Wilms' tumor.<sup>8</sup> In 1996, Al Nasser et al. reported that of the 3291 children with cancer treated at King Faisal Specialist Hospital and Research Centre, 4.9% had a renal tumor.<sup>9</sup> Between January 1982 and December 1997, we saw 528 children with various types of malignancy, and 6.8% of them were Wilms' tumor.

The study of the epidemiology and pattern of cancer is of the utmost importance for the establishment of both preventive and therapeutic measures. This calls for the setting up of a National Cancer Registry in the United Arab Emirates. The incidence of synchronous bilateral Wilms' tumor is estimated at 5% to 10%.<sup>10,11</sup> Of the 36 patients with Wilms' tumor we examined, seven (19.4%) had bilateral synchronous tumor. The exact reason for this high frequency of bilaterality in our series is not known. In our series as well as others, boys outnumbered girls. This male preponderance, as well as the high frequency of bilateral tumors in our series, may only reflect regional variations of Wilms' tumor.

In the management of patients with Wilms' tumor, the timing of surgery in relation to chemotherapy is still controversial. According to the NWTS protocol, these children are to be treated by surgery first, followed by chemotherapy with or without radiotherapy, depending on the stage.<sup>1,2</sup> This approach is thought to enable accurate assessment of the stage of the disease and histology, and thus make it easier to plan subsequent treatment accordingly. The SIOP group, on the other hand, advocate preoperative chemotherapy followed by surgery.<sup>3,4</sup> This approach is an attempt to decrease the size of the tumor and so reduce the risk of intraoperative rupture. The survival in both groups, however, is similar. The number of patients who received preoperative chemotherapy in our series is too small to draw any meaningful conclusions, but it was interesting to note from our findings that six of the seven patients who received preoperative chemotherapy were stage I at the time of the surgery, and the histology was favorable in all.

Compared with other reports from Western countries, our patients presented with more advanced stages of the disease. Other reports from nearby countries such as Saudi Arabia indicate a similar trend.<sup>8,12</sup> We also found a higher



FIGURE 1. CT scan showing large bilateral Wilms' tumor.

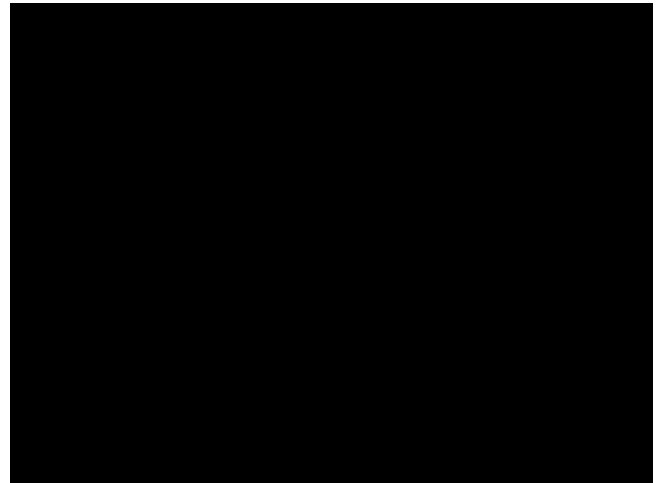


FIGURE 2. CT scan after preoperative chemotherapy showing a marked reduction in the size of both tumors.

than expected proportion of tumors with unfavorable histology.<sup>2</sup> This may suggest the existence of a more aggressive form of the disease in this part of the world, or it may be due to delay in presentation by some of our patients and delay in initiation of the treatment because of initial parental refusal. This calls for the formation of a Wilms' tumor study group in this part of the world. This will lead to centralization of patients, as well as a more systematic approach to the treatment and the initiation of protocols that will benefit outpatients. A recent proposal in the management of localized stage I Wilms' tumor and of favorable histology is to omit postoperative adjuvant chemotherapy.<sup>13</sup> This was adopted in one of our patients recently. He is now one year post treatment with no recurrence. Such an approach, however, needs further evaluation.

The management of children with bilateral synchronous Wilms' tumor has changed over the years. A

more conservative approach aiming at preservation of as much renal tissue as possible is now advocated. Although our patients with bilateral synchronous Wilms' tumor were detected preoperatively, intraoperative inspection and palpation of the contralateral kidney to exclude bilateral Wilms' tumor is strongly recommended. This is in spite of the recent advances in preoperative imaging techniques which should accurately assess the contralateral kidney, obviating the need for contralateral exploration.<sup>14,15</sup> We routinely explore and inspect the contralateral kidney. The importance of this cannot be overemphasized, as the NWTs found that preoperative CT scan failed to detect the contralateral Wilms' tumor in 15% of those with bilateral

In the past, patients with bilateral Wilms' tumor were treated with nephrectomy of the more advanced side and partial excision of the contralateral side. This approach, however, was associated with a high incidence of renal failure.<sup>11</sup> The role of preoperative chemotherapy in such patients is now well established and has proved to be effective in debulking the tumor and downstaging it.<sup>10,16,17</sup> With preoperative chemotherapy, there was total disappearance of the tumor on one side in one of our patients. Total disappearance of Wilms' tumor, as well as converting enlarged tumors into resectable ones, has been reported before.<sup>18</sup>

Several factors should be taken into consideration in the surgical management of children with synchronous bilateral Wilms' tumor. These include the stage of each separate tumor, the side of the tumor in each kidney, and the histology and response to preoperative chemotherapy. The extent of surgical resection is to be individualized for each case.

### References

1. D'Angio GJ, Evans A, Breslow N, et al. The treatment of Wilms' tumor. Results of the Second National Wilms' Tumor Study. *Cancer* 1981;47:2302-11.
2. D'Angio GJ, Breslow N, Beckwith JB, et al. The treatment of Wilms' tumor. Results of the Third National Wilms' Tumor Study. *Cancer* 1989;64:349-60.
3. Lemerle J, Voute PA, Tournade MF, et al. Effectiveness of pre-operative chemotherapy in Wilms' tumor. Results of an International Society of Pediatric Oncology (SIOP) trial. *J Clin Oncol* 1983;1:604-9.
4. Tournade MF, Com-Nougué C, Voûte PA, Lemerle J, de Kraker J, Delemarre JFM, et al. Results of the Sixth International Society of Pediatric Oncology Wilms' Tumor Trial and Study: a risk-adapted therapeutic approach in Wilms' tumor. *J Clin Oncol* 1993;11:1014-23.
5. Farewell VT, D'Angio GJ, Breslow N, Norhool P. Retrospective validation of a new staging system for Wilms' tumor. *Cancer Clin Trials* 1981;4:167-71.
6. Young JL Jr, Miller RW. Incidence of malignant tumors in US children. *J Pediatr* 1975;86:254-8.
7. Mesrobian H-GJ. Wilms' tumor: past, present, future. *J Urol* 1988;140:231-8.
8. Sabbah RS. Childhood cancer in Saudi Arabia: current problems and suggested solutions. *King Faisal Spec Hosp J* 1982;2:273-6.
9. Al-Nasser AA, Al-Sedairy RM, Solh H, et al. Pediatric cancer. The King Faisal Specialist Hospital and Research Centre experience. *Ann Saudi Med* 1996;16:530-3.
10. Blute ML, Kelalia PP, Oxford KP, et al. Bilateral Wilms' tumor. *J Urol* 1987;138:968-73.
11. Montgomery BT, Kelasis PP, Blute ML, et al. Extended follow-up of bilateral Wilms' tumor: results of the National Wilms' Tumor Study. *J Urol* 1991;146:514-8.
12. Farsi HMA, Mosli HA, Rawas MM, Jan MY, Ghafori HM. Wilms' tumor: King Abdulaziz University experience. *Ann Saudi Med* 1989;9:576-87.
13. Green DM, Breslow NE, Beckwith JB, et al. Treatment outcomes in patients less than two years of age with small, stage I/favorable histology Wilms' tumor. A report from the National Wilms' Tumor Study. *J Clin Oncol* 1993;11:91-5.
14. Goleta-Dy A, Shaw PJ, Stevens MM. The necessity of contralateral surgical explorations in Wilms' tumor with modern noninvasive imaging technique: a reassessment (letter). *J Urol* 1992;17:171.
15. Koo AS, Koyle MA, Hurwitz RS, Weese D, Applebaum H, Fonkelsrud EW, et al. The necessity of contralateral surgical exploration in Wilms' tumor with modern noninvasive imaging technique: a reassessment. *J Urol* 1990;144:416-7.
16. Coppes MH, de Kraker J, van Kijken PJ, et al. Bilateral Wilms' tumor: long-term survival and some epidemiological features. *J Clin Oncol* 1989;7:310-5.
17. Shaul DB, Srikanth MM, Ortega JA, Mahour GH. Treatment of bilateral Wilms' tumor: comparison of initial biopsy and chemotherapy to initial surgical resection in the preservation of renal mass and function. *J Pediatr Surg* 1992;27:1009-15.
18. Bracken RB, Sutons WW, Jaffe N, et al. Preoperative chemotherapy for Wilms' tumor. *Urology* 1982;19:55-60.