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Original Research

Surgical Treatment Results in Unilateral Wilms Tumor: Experience from a High-Volume Pediatric Oncology Center in Turkey

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ABSTRACT

Objective: The aim of the present study was to evaluate the clinical characteristics, factors affecting treatment approach, and long-term outcome of patients with Wilms tumor.

Methods: We identified the demographic features, mode of presentation, applied treatments, and long-term outcomes of 88 patients treated between 1990 and 2011 at Hacettepe University İhsan Doğramacı Children's Hospital according to the Turkish Pediatric Oncology Group protocol. Data were analyzed using SPSS program, and chi-square test was used for statistical analysis.

Results: The study included 88 patients (50 females and 38 males) with a mean age at presentation of 3±2.48 years. Patients were classified as stage 1 (n=35, 39.8%), stage 2 (n=16, 18.2%), stage 3 (n=17, 19.3%), and stage 4 (n=20, 22.7%). Pathological examination of tumors revealed favorable histology in 76 (86.4%) patients and unfavorable histology in 10 (11.4%) patients. Forty-nine (55.6%) patients received preoperative chemotherapy, and patient's age at diagnosis and physical examination findings influenced the decision of the administration of preoperative chemotherapy ($p<0.05$). Of the 88 patients, 25% aged <1 year and 75% aged between 3 and 5 years received preoperative chemotherapy. The palpated mass was crossing the midline in 20.5% of patients who were subjected to primary surgery. Tumor ruptured in 5.6% of patients intraoperatively. Long-term prognosis of patients was as follows: 68 (83.9%) children were cured and 13 (16%) children died due to recurrences and metastases. Survival rates reached 100% in stage 1 and 2 patients but decreased to 75% and 50% in stage 3 and 4 patients, respectively.

Conclusion: Age at presentation and physical examination findings are significant in surgical planning. Stage is the most important prognostic factor. Patients with Wilms tumor are treated with low complication and high survival rates due to multidisciplinary treatment approach at our institution.

Keywords: Child, preoperative chemotherapy, survival, Wilms tumor

INTRODUCTION

Wilms tumor is the most common renal tumor of childhood (1). Prognosis is excellent among patients with localized disease and favorable histology by virtue of multicenter collaborative studies (2). Safer reduction of chemotherapeutic agents and radiotherapy doses with improved surgical technique leads to fewer short- and long-term complications and longer life expectancy in these patients. However, metastatic, recurrent disease, unfavorable histology, and patients with syndromes or genetic predispositions to Wilms tumor still stand as a therapeutic challenge (3). The aim of the present study was to identify the characteristics of patients treated with unilateral Wilms tumor and the factors affecting treatment approach and prognosis from a surgical standpoint.

METHODS

The study was approved by the Hacettepe University Senate Ethics committee at 02.07.2012 with the issue number 429. All patients who presented with a diagnosis of unilateral Wilms tumor between 1990 and 2011 were identified. Patients whose surgical treatments and chemotherapy and radiotherapy applications were performed entirely in Hacettepe University İhsan Doğramacı Children's Hospital were included in the study. Exclusion criteria comprised patients receiving a part of medical or surgical treatment in another medical center. Eighty-eight patients with unilateral Wilms tumor were eligible for the study. The treatment algorithm of each patient was discussed by the multidisciplinary pediatric oncology team and planned according to the Turkish

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Pediatric Oncology Group (TPOG) protocol (4). Parental consent was not necessary since this was a retrospective chart review.

Age, gender, associated syndromes, presenting signs and symptoms, details of surgical intervention, complications of surgery, pathology results, stage, histology, metastasis, chemotherapy and radiotherapy regimens, and prognosis of these patients were reviewed retrospectively. Patient-related factors affecting the treatment algorithm (upfront surgery vs. chemotherapy) and survival were identified.

Statistical Analysis

Statistical analysis was performed by Statistical Package for the Social Sciences version 16.0 (SPSS Inc.; Chicago, IL, USA). Variables were analyzed by chi-square test. A p value <0.05 was accepted as statistically significant.

RESULTS

The study included 88 patients consisting of 50 girls and 38 boys with a mean age of 3±2.48 years. The most common presenting symptoms were abdominal distention as noted by the caregivers (n=53, 60.2%), abdominal pain (n=17, 19.3%), blood in urine (n=12, 13.6%), fever (n=8, 9.1%), and vomiting (n=5, 5.7%). The mass extending over the midline was palpated in 35.2% (n=31) of children. Hypertension was detected in 9 (10.2%) patients. The incidence of inguinoscrotal pathology was 6.8%. Among the Wilms tumor predisposing syndromes, two patients were diagnosed with Beckwith-Wiedemann syndrome (BWS), one with WAGR and another with Silver Russel syndrome. Tumor thrombus in the renal vein or inferior vena cava was present in six patients at the time of diagnosis. Stage distribution according to the TPOG and aforementioned data is represented in Table 1.

Of the 88 children, 49 (55.7%) were administered preoperative chemotherapy and 39 (44.3%) underwent upfront nephrectomy. Partial nephrectomy was performed in one patient with BWS and solitary kidney. Cavatomy and thrombectomy were performed in four patients with tumor thrombus. Lymph nodes were sampled from the paracaval and paraaortic region in 28 (31.8%) and from the renal hilum in 25 (28.4%) patients. Tumor ruptured during surgery in five (5.6%) patients, and two of them were operated without preoperative chemotherapy. Pathology results revealed favorable histology in 86.4% and unfavorable histology in 11.4% of cases.

Table 1. Clinical characteristics of patients with Wilms tumor

Characteristics	Patients	n (%)
Gender	Male	38 (43.2)
	Female	50 (56.8)
Presenting symptom	Abdominal distention	53 (60.2)
	Abdominal pain	17 (19.3)
	Blood in urine	12 (13.6)
	Fever	8 (9.1)
	Vomiting	5 (5.7)
Physical examination findings	Mass limited to one side of the abdomen	57 (64.8)
	Mass extending over the midline	31 (35.2)
	Hypertension	9 (10.2)
	Inguinoscrotal pathologies	6 (6.8)
Stage distribution	Stage 1	35 (39.8)
	Stage 2	16 (18.2)
	Stage 3	17 (19.3)
	Stage 4	20 (22.7)
Presence of tumor thrombus in the inferior vena cava or renal vein		6 (6.8)
Associated syndromes	BWS	2 (2.3)
	WAGR	1 (1.1)
	Silver Russel syndrome	1 (1.1)

BWS: Beckwith–Wiedemann syndrome; WAGR: Wilms tumor, aniridia, growth retardation

Table 2. Distribution of upfront surgery versus chemotherapy with respect to age

	<1 year n (%)	1–2 years n (%)	3–5 years n (%)	≥6 years n (%)	Total n (%)
Upfront chemotherapy	2 (25)	16 (45.7)	24 (75)	7 (53.8)	49 (55.7)
Upfront surgery	6 (75)	19 (54.3)	8 (25)	6 (46.2)	39 (44.3)
Total	8 (100)	35 (100)	32 (100)	13 (100)	88 (100)

p=0.022

Table 3. Distribution of upfront surgery versus chemotherapy with respect to physical examination findings

	Mass extending over the midline n (%)	Mass limited to one side of the abdomen n (%)	Total n (%)
Upfront chemotherapy	23 (46.9)	26 (53.1)	49 (100)
Upfront surgery	8 (20.5)	31 (79.5)	39 (100)
Total	31 (35.2)	57 (64.8)	88 (100)

p=0.01

Table 4. Prognosis according to stage of patients

Stage	Cure n (%)	Exitus n (%)	Total n (%)
1	33 (100)	0 (0)	33 (100)
2	14 (100)	0 (0)	14 (100)
3	12 (75)	4 (25)	16 (100)
4	9 (50)	9 (50)	18 (100)
Total	68 (83.9)	13 (16)	81 (100)

Seven patients were lost to follow–up
p=0.01

The administration of preoperative chemotherapy was more common among older patients than among infants aged <12 months (Table 2). Upfront surgery was preferred over chemotherapy more commonly in patients when the palpated mass is limited to one side of the abdomen (Table 3).

Local recurrence in the tumor bed was seen in 10 patients. Pathological examination revealed unfavorable histology in one of them. Metastatic involvement of the lymph nodes was present in 2 of 3 children who had lymph node sampling. Among the possible causes of recurrence, capsule invasion was noted in four, and tumor rupture during surgery was seen in two patients. Recurrent tumor was resected in four children.

Among the 81 patients with long-term follow-up, 83.9% survived the disease, and 16% died due to the disease and complications of treatment. Seven patients were lost to follow-up. Survival was not affected by gender or administration of preoperative chemotherapy (p=0.587 and p=0.086, respectively). Survival rates were not different across age groups (p=0.562), but all infants aged <1 year survived the disease. All patients with syndromes predisposing to Wilms tumor had complete remission of disease. Stage was the only statistically significant parameter affecting prognosis (p=0.01). All of the children with disease stages 1 and 2 were cured. Cure rates decreased to 75% and 50% in patients with stage 3 and 4 diseases, respectively (Table 4).

DISCUSSION

Wilms tumor is the most common renal malignancy of childhood. Currently, survival reaches 90% in localized disease and 70% in metastatic cases. This success is attributed to the work of multicenter collaborative studies conducted by international consortiums (2). This effort leads to a reduction in chemotherapy and radiotherapy regimens and standardization of surgical treatment. In the present study, we reviewed our 20-year experience in treating patients with Wilms tumor from a surgical perspective.

Wilms tumor can be seen at any age, but it is most common in the third year of life. In our study, the mean age of the patients was similar to other studies (5, 6). The major complaints are nonspecific symptoms, such as abdominal pain, distention, vomiting, and hematuria (7). Hypertension and genitourinary anomalies can be observed during physical examination (8). We observed that the frequency of presenting symptoms was not different from the ones stated above in our patients.

There are two large clinical groups conducting trials for Wilms tumor: Children's Oncology Group (formerly NWTSG), which advices upfront surgery, and Société Internationale d'Oncologie Pédiatrique (SIOP), which supports upfront chemotherapy. Tumors are staged before chemotherapy in the former and after chemotherapy in the latter group. Upfront surgery carries the risk of tumor rupture, relapse, and advancement of stage. On the other hand, chemotherapy before tissue diagnosis carries the risk of unnecessary treatment for benign tumors, inadequate regimen for renal tumors other than nephroblastoma, downstaging, and therefore inadequate chemotherapy afterwards (2, 7, 9). TPOG established a national protocol, and patients are evaluated individually for upfront surgery or chemotherapy by the local multidisciplinary pediatric oncology team (4). Upfront surgery and chemotherapy approaches were almost equally distributed among our patients. Given the fact that our institution is a referral center for pediatric oncology patients in Turkey, we encounter more patients with advanced tumor stage, associated syndromes, and surgically challenging tumors. Patients with

these features are directed to upfront chemotherapy to prevent surgical complications. Attitude toward upfront surgery among infants aged <12 months can be justified by the fact that congenital mesoblastic nephroma is frequent in this age group (10). Physical examination finding of a mass at the time of diagnosis was an important determinant of upfront surgery or chemotherapy decision in our study. Chemotherapy decreases tumor size and risk of rupture (11). Tumor rupture rate was 5.6% among all patients in our study. This rate increases to 15.3% in NWTSG and decreases to 2.2% in SIOP (12, 13). From the perspective of surgical complications, our approach is reasonable.

Documentation of surgical details has utmost importance. Tumor rupture; spill; extension to adjacent organs; palpation of tumor thrombus in the renal vein or vena cava, perihilar, paraaortic, and paracaval lymph node sampling; and exploration of contralateral kidney and solid organs for metastasis if performed should be written in detail (1). These facts can change the stage and treatment algorithm of the patient toward a more or less aggressive way. Ehrlich et al. (12) found that many deviations from the guidelines are observed during surgery including failure to sample lymph nodes and tumor spill in the NWTS-5 surgical quality assessment. In our series, lymph node sampling was performed in 31.8% of our patients. This rate is much lower than NWTSG results and accepted as a self-criticism. Recurrent tumor in patients with stage 2 tumor was higher than expected among children without lymph node sampling in NWTS-5 (14). Fortunately, none of our patients with stage 2 disease had recurrent tumor.

Anaplasia, stage, lymph node status, and chromosomal abnormalities are the most important prognostic parameters in children with Wilms tumor (7). Age and gender did not appear to affect survival, but many studies including ours found an increased survival trend in infants diagnosed before the age of 1 year. Small abdominal cavity and apparent mass result in early diagnosis and localized disease. Anaplasia is also rare in this age group (1, 10). Cure rates were not different in patients with upfront surgery or chemotherapy. Although overall prognosis is excellent, it is much lower in stage 3 and 4 diseases. In our study, stage was the only significant parameter on survival. The small number of patients appears to be the reason of statistical insignificance in other parameters. Our finding is supported with other studies (15). We argue that survival is not affected by the mode of treatment but particular characteristics of the patient and disease itself.

CONCLUSION

Preference over upfront surgery or chemotherapy should be done in a case-based manner. Although this approach does not have an effect on prognosis, it can reduce surgical complications in patients with Wilms tumor. Further prospective studies are necessary to compare results.

Ethics Committee Approval: Ethics committee approval was received for this study from the Hacettepe University Senate ethics committee at 02.07.2012 with the issue number 429.

Informed Consent: Due to the retrospective design of the study, informed consent was not taken.

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