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Original Research

Uncorrected

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 this study is to evaluate the clinical characteristics, factors effecting treatment approach and long-term outcome of patients with Wilms tumor.

Methods: We identified demographic features, mode of presentation, applied treatments and long term outcomes of 88 patients treated between 1990-2011 at Clinical Ethics Committee of Hacettepe University Faculty of Medicine.according to Turkish Pediatric Oncology Group protocol. Data were processed with SPSS programme and chi-square test was used for statistical analysis.

Results: Study included 88 patients consisting of 50 females and 38 males and the mean age at presentation was 3±2.48 years. Patients are 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%). Pathologic examination of tumors revealed favorable histology in 76 patients (86.4%) and unfavorable histology in 10 patients (11.4%). Forty nine patients (55.6%) received preoperative chemotherapy and patient's age at diagnosis and the physical examination findings influence the decision of administration of preoperative chemotherapy ($p<0.05$). 25% of patients under 1 year of age and 75% of patients between 3-5 years old received preoperative chemotherapy. The palpated mass were 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 were as follows: 68 (83.9%) children were cured, 13 (16%) children died due to recurrences and metastasis. 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. Wilms tumor patients are treated with low complication and high survival rates due to multidisciplinary treatment approach at our institution.

Keywords: Wilms tumor, survival, child, preoperative chemotherapy

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 lead 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). In this study, we aim to identify the characteristics of patients treated with unilateral Wilms tumor and the factors effecting treatment approach and prognosis from a surgical standpoint.

METHODS

Following approval from Clinical Ethics Committee of Hacettepe University Faculty of Medicine ethics committee, all patients who presented with the diagnosis of unilateral Wilms tumor between 1990 and 2011 were identified. Patients whose surgical treatments, chemotherapy and radiotherapy applications performed entirely in Hacettepe University were included in the study. Exclusion criteria was receiving a part of medical or surgical treatment in another medical center. Eighty-eight patients with unilateral Wilms tumor were eligible for the study. Treatment algorithm of each patient was discussed by multi-disciplinary pediatric oncology team and planned according to Turkish Pediatric Oncology Group (TPOG) protocol (4). Parental consent was not necessary since this is 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 effecting

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the treatment algorithm (upfront surgery vs chemotherapy) and survival were identified. Statistics were done by SPSS ver 16.0. Variables were analysed with chi-square test. $p<0.05$ was accepted as statistically significant.

RESULTS

Study included 88 patients consisting of 50 girls and 38 boys with the mean age of 3±2.48 years. Most common presenting symptoms were abdominal distention 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%). Mass extending over midline was palpated in 35.2% (n=31) of children. Hypertension was detected in 9 patients (10.2%). Inguinoscrotal pathology incidence was 6.8%. Among the Wilms tumor predisposing syndromes; two patients were diagnosed with Beckwith–Wiedemann syndrome (BWS), one with WAGR and another one with Silver Russel syndrome. Tumor thrombus in renal vein or inferior vena cava was present in 6 patients at the time of diagnosis. Stage distribution according to TPOG and aforementioned data are represented in Table 1.

Preoperative chemotherapy was administered in 49 (55.7%) children and 39 (44.3%) had upfront nephrectomy. Partial nephrectomy was performed in one patient with BWS and solitary kidney. Cavatomy and thrombectomy was performed in four patients with tumor thrombus. Lymph nodes were sampled from paracaval and para-aortic region in 28 (31.8%) and from renal hilum in 25 (28.4%) patients. Tumor ruptured during surgery in 5 (5.6) patients and 2 of them were operated without preoperative chemotherapy. Pathology results revealed favorable histology in 86.4% and unfavorable histology in 11.4% of cases.

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

Local recurrence in tumor bed was seen in 10 patients. Pathologic examination revealed unfavorable histology in one of them.

Table 1. Clinical characteristics of patients with Wilms Tumor

		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 abdomen	57 (64.8%)
	Mass extending over midline	31 (35.2%)
	Hypertension	9 (10.2%)
	Inguino-scrotal 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 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

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

	<1 year, n (%)	1–2 years, n (%)	3–5 years, n (%)	≥6 year, 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 vs chemotherapy with respect to physical examination findings

	Mass extending over midline, n (%)	Mass limited to one side of 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	Exitus	Total
1	33 (100%)	0	33 (100%)
2	14 (100%)	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

Metastatic involvement of 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 4 and tumor rupture during surgery in 2 patients. Recurrent tumor was resected in 4 children.

Among the 81 patients with long-term follow-up, 83.9% of them survived the disease and 16% died due to disease and complications of treatment. Seven patients were lost to follow-up. Survival was not effected by gender or administration of preoperative chemotherapy (p=0.587, p=0.086 respectively). Survival rates were not different across age groups (p=0.562) but all infants under 1 year of age survived the disease. All patients with syndromes predisposing to Wilms tumor had complete remission of disease. Stage was the only statistically significant parameter effecting 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 disease respectively (Table 4).

DISCUSSION

Wilms tumor is the most common renal malignancy of childhood. Today, 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 this study, we reviewed our 20-year experience in treating Wilms tumor patients from a surgical perspective.

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

There are two large clinical groups conducting trials for Wilms tumor: COG (Children's Oncology Group, formerly NWTSG) which advices upfront surgery and SIOP (Société Internationale d'Oncologie Pédiatrique) 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, down-staging and therefore inadequate chemotherapy afterwards (2,7,9). Turkish Pediatric Oncology Group established a national protocol and patients are evaluated individually for upfront surgery or chemotherapy by the local multi-disciplinary 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 challing tumors. Patients with these features are directed to upfront chemotherapy to prevent surgical complications. Attitude towards upfront surgery among infants younger than 12 months old can be justified by the fact that congenital mesoblastic nephroma frequency in this age group (10). Physical examination finding of 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 carries utmost importance. Tumor rupture, spill, extension to adjacent organs, palpation of tumor thrombus in renal vein or vena cava, perihilar, paraaortic and paracaval lymph node sampling, 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 towards to a more or less aggressive way. Ehrlich et al found out that numerous deviations from guidelines were observed during surgery including failure to sample lymph nodes and tumor spill in the NWTS-5 surgical quality assessment (12). In our series, lymph node sampling was performed in 31.8% of our patients. This rate is much lower compared to 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 seem to effect survival but many studies including ours found an increased survival trend in infants diagnosed before 1 year of age. 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 was not different in patients with upfront surgery or chemotherapy group. Although overall prognosis is excellent, it is much lower in stage 3 and 4 disease. In our study, stage was the only significant parameter on survival. Small number of patients seems to be the reason of statistical insignificance in other parameters. Our finding is supported with other studies (15). We argue that, survival is not effected by mode of treatment but particular characteristics of patient and disease itself.

CONCLUSION

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

Ethics Committee Approval: Ethics committee approval was received for this study from the Clinical Ethics Committee of Hacettepe University Faculty of Medicine.

Informed Consent: Consent was not taken from parents since this is a retrospective chart review study. Ethic approval from committee is adequate for chart reviews.

Peer-review: Externally peer-reviewed.

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