کارکاه های آموزشی مرکز اطلاعات علمی جهاد دانشگاهی

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پروپوزال نویسی
Wilms’ Tumor: A 10 Year Retrospective Study

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Background: Wilms’ tumor (nephroblastoma) is the most common renal malignancy of childhood. The aim of the study was to evaluate the characteristics of Wilms’ tumor and the results of combined modality treatment obtained in our center in Tehran.

Methods: Fifty-five patients diagnosed as having Wilms’ tumor were studied in the period between February 1992 and March 2002. Demographic features, mode of presentation, associated anomalies, the stage of tumor, histopathologic results, and the survival rates were evaluated.

Results: Of these 55 patients, 31 were males and 24 were females (M/F = 1.2). The mean age at the time of diagnosis was 45.2 months. The distribution of 54 operated patients according to the surgical stage was: stage I 32.7%, stage II 16.36%, stage III 38.1%, stage IV 9%, and stage V 1.8% (one patient (1.8%) has not been operated). Favorable histology was diagnosed in 54.5% and unfavorable histology in 43.6% of the patients. The patients were treated according to National Wilms’ Tumor Study protocols. The relapse-free and overall 4 years survival rates were 71% and 86%, respectively.

Conclusion: As a developing country, with similar relapse free and overall survival rates to National Wilms’ Tumor Study, our institution showed an improvement in the treatment of patients with Wilms’ tumor in recent 10 years, but with more adaptation to the National Wilms’ Tumor Study treatment protocols better optimum results seem to be achievable.

Keywords: Relapse-free survival • nephroblastoma • Wilms’ tumor

Introduction

Wilms’ tumor (nephroblastoma), the most common genitourinary malignancy of childhood, is an embryonal tumor of renal origin.1 It affects approximately one child per 10,000 worldwide before the age of 15,2 and ranks fifth in incidence among the solid tumors of childhood, following central nervous system tumors, lymphoma, neuroblastoma, and soft tissue sarcomas. Its incidence appears to be slightly elevated for the U.S. and African blacks in comparison to the whites, but is only half as great among Asians.2 It is a curable disease in most of the affected children. The treatment of Wilms’ tumor has been improved in the past two decades, with the aid of multimodal therapy protocols.3, 5

Nowadays, the goal is to improve the outcomes by identifying the groups at risk and help them with more appropriate treatments. However, this may be the case in developing countries, where social as well as regional factors contribute to the outcome of the disease. The aim of this study was to evaluate the characteristics of Wilms’ tumor and report the results of treatments in patients admitted to Mofid Children’s Hospital in Tehran, Iran, from 1992 through 2002.

Patients and Methods

Mofid Children’s Hospital is a tertiary care referral hospital in Tehran, which has pediatric surgery and oncology departments. A retrospective review (existing data technique)
was done for all children treated for Wilms’ tumor at the hospital from 1992 through 2002.

All the patients with a pathologically proven diagnosis of Wilms’ tumor were included in our study.

The medical records of patients with Wilms’ tumor were reviewed for age at the diagnosis, sex, mode of presentation, investigations, involved kidney, associated anomalies, preoperative treatment, type of surgery, stage, postoperative treatment, and outcome.

Most of 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 National Wilms’ Tumor Study (NWTS) protocols.6, 8

For patients with bilateral Wilms’ tumor, preoperative chemotherapy and radiotherapy were given.

In all patients, histopathologic classification and clinical staging were done according to the Third and Fourth NWTS Group.7

Statistical methods

All the collected data were analyzed by SPSS software, version 11.5. The Kaplan-Meier method was used to assess the survival rates.

Results

Fifty-five children, diagnosed as having Wilms’ tumor, had been admitted at Mofid Children’s Hospital during the study period. Of them, 31 (56.3%) were males, and 24 (43.6%) were females (M/F = 1.29). The mean age at the time of diagnosis was 45.2 months [95% CI (36.63 – 51.72 months)] and ranged between 2 to 120 months.

Twenty-three point six percent of the patients were between 4 and 5 years, 20% under 1 year, and 14.5% between 3 and 4 years of age.

Fourteen associated anomalies were present in 6 patients (10.9%) as shown in Table 1. Some patients had more than one anomaly.

The most frequent presenting sign/symptom at the time of diagnosis was abdominal mass and distension found by the parents or physicians. The modes of presentation are shown in Table 2. Some patients had more than one presenting signs.

Abdominal ultrasonography, computerized tomography (CT), chest radiography, and intravenous pyelography (in earlier cases) were the modalities used to investigate the patients. CT scan was the performed method to define the origin of the tumor within the kidney, evaluate the possible presence of a second Wilms’ tumor in the opposite kidney, assess caval extension, and depict hepatic metastases. The combination of CT scan and ultrasonography was the most useful and accurate method for the diagnosis and assessment of the patients before operation.

The left kidney was affected in 30 (54.5%), and the right one in 24 (43.6%) cases. One of the cases, a boy (1.8%), had bilateral Wilms’ tumor at presentation.

Nephrectomy was performed in 52 cases. One child was excluded because the parents refused treatment. The tumor was inoperable in two other cases, one with Budd-Chiari syndrome and the other with metastasis to the skull at the time of presentation. Preoperative chemotherapy was done in two cases after obtaining biopsies. One patient with bilateral Wilms’ tumor was treated with total nephrectomy on one site and partial nephrectomy on the opposite kidney.

Inferior vena cava (IVC) was involved in 2 (3.6%) and renal vein in 3 (5.5%) a cases.

Surgical stage

The distribution of stages in all patients is shown in Figure 1 and the distribution of stages among both sexes in Table 3. There were seven recorded complications, which required hospitalization. In 2 children the complications were directly attributable to myelosuppression (one

<table>
<thead>
<tr>
<th>Table 1. Associated anomalies in the 6 patients with Wilms’ tumor in this study.</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated anomalies</td>
<td></td>
</tr>
<tr>
<td>Hypospadias</td>
<td>3</td>
</tr>
<tr>
<td>Cryptorchidism</td>
<td>3</td>
</tr>
<tr>
<td>Congenital cataracts</td>
<td>2</td>
</tr>
<tr>
<td>Aniridia</td>
<td>1</td>
</tr>
<tr>
<td>Ambiguous genitalia</td>
<td>1</td>
</tr>
<tr>
<td>Duplicated ureter</td>
<td>1</td>
</tr>
<tr>
<td>Clift lip</td>
<td>1</td>
</tr>
<tr>
<td>Bilateral ingunal hernia</td>
<td>1</td>
</tr>
<tr>
<td>Down’s syndrome with ASD* and VSD**</td>
<td>1</td>
</tr>
</tbody>
</table>

*ASD = atrial septal defect; VSD = ventricular septal defect.

<table>
<thead>
<tr>
<th>Table 2. Mode of presentation of Wilms’ tumor in this study.</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presenting sign/symptom</td>
<td></td>
</tr>
<tr>
<td>Abdominal mass and abdominal distension</td>
<td>90.9</td>
</tr>
<tr>
<td>Hematuria</td>
<td>14.5</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>10.9</td>
</tr>
<tr>
<td>Fever</td>
<td>5.5</td>
</tr>
<tr>
<td>Weight loss</td>
<td>1.8</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1.8</td>
</tr>
</tbody>
</table>
episode of pancytopenia with petechia and epistaxis and one episode of sepsis due to neutropenia). There were two cases of convulsions following chemotherapy. One of the patients developed peripheral neuropathy after receiving vincristine. Renal failure was observed in one of the patients with unilateral Wilms’ tumor. Drug-induced hepatitis occurred in one patient, but cardiotoxicity was not detected in any of the patients receiving doxorubicin (Adriamycin).

Favorable histologic finding was diagnosed in 30 (54.5%) and unfavorable histology in 24 (43.6%) patients; one patient (1.8%) has not been operated (Figure 2). The distribution of 20% of cases with unfavorable histology that was reported in the pathology reports was as follows: anaplasia (focal or diffuse) in 7.3% and clear cell sarcoma in 12.7% of the cases. In 23.6% of unfavorable cases, the type of histology has not been reported and also in this study the rhabdoid sarcoma was not reported.

Tumor relapse was seen in four patients (7%), three in stage III and one in stage IV. Of these four patients, three had unfavorable histology (75%) and one had favorable histology (25%). Sites of relapse were abdomen (3 cases) and lungs (1 case). One case of abdominal recurrence occurred following surgical rupture of the tumor. The mean time for relapse after surgery was 13 months. Metachronous bilateral Wilms’ tumor was seen in one of the patients. The sites of metastases were lungs (3 cases), liver (3 cases), and brain (1 case).

The relative relapse-free and overall survival rates at 4 years were 71% and 86%, respectively (Figures 3 and 4). It was difficult to define the long-term survival rate of each stage separately, because there were few patients in each stage.

Drug-induced hepatitis, IVC involvement and pulmonary emboli, Down’s syndrome associated cardiac anomalies (VSD and ASD), and surgery of skull metastases, were some of the causes of mortality.

Discussion

Wilms’ tumor is the most common renal tumor of infancy and childhood. It affects one child per 10,000 worldwide before the age of 15.1,2

The exact incidence of Wilms’ tumor in Iran is unknown. That is attributed to the lack of an informative tumor registry. Setting up of a National Cancer Registry in Iran will be of demand.

The gender ratio (M/F) in our series was 1.2:1 that was similar to Europe but different from the USA, where there is female predominance.3, 4 The median age of the patients in our study was similar to most of other countries, but slightly higher than some of them (38 months).2,10

In our study, the most frequent presenting sign was abdominal mass (90.9%). The United Kingdom Children’s Cancer Study Group(UKCCSG) in their

<table>
<thead>
<tr>
<th>Sex</th>
<th>No.</th>
<th>Surgical stage (%)</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>5</td>
<td>27.7</td>
<td>8</td>
<td>9</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>13</td>
<td>72.2</td>
<td>1</td>
<td>11</td>
<td>57.1</td>
<td>60.0</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>100.0</td>
<td>9</td>
<td>21</td>
<td>5</td>
<td>1</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 3. The distribution of surgical stages among both sexes.
Wilms' tumor trial reported this rate to be 74%. The reason that the abdominal mass had been the most frequent sign in our study may be because of the advanced stages of the disease in our patients at the presentation time.

Having compared the surgical stages of our patients with NWTS3 results, we found that in NWTS3, stage I patients constituted 42% of all patients, while it was 32.7% in our study. Stage III patients constituted 38% of our study population compared with 23% in NWTS3 patients. So, we may conclude that in Iran, patients still refer to specialized centers with much delay.

Associated anomalies were seen in 10.9% of our cases, which was higher than the rate of NWTS group (7.3%). Hemihypertrophy was the most common congenital malformation in NWTS group, whereas, there was not such anomaly in our study.

In our series, the left kidney was mostly affected (54.5%). It was compatible with the report of Lemerle et al but in contrast to the results reported by Mott who reported the similar right and left kidney involvement.

Fifty-four point five percent of our patients had favorable and 43.6% had unfavorable histology. The rate of unfavorable histology in NWTS3 was 11.12%. This may suggest the existence of a more aggressive form of the disease in our region, or it may be due to the delay in the presentation by some of our patients. This fact calls for the formation of a Wilms' tumor study group in this part of the world. Formation of this group will lead to centralization of patients, as well as a more systematic approach to the treatment and initiation of protocols that will be more suitable for the patients.

In this study, the lungs were the most frequent site of distant metastases (43%), and the second most frequent site was liver. The most frequent site of relapse was the abdomen in contrast to Second and Third NWTS, in which lungs accounted for 58% of all relapses.

Relative relapse-free survival rate and overall survival rate at 4 years were 71% and 86%, respectively (Figures 3 and 4). The similar rates in NWTS3 were 81% and 89%, respectively. In comparison with NWTS3 and United Kingdom Wilms' tumor Study 1(UKWS1) results (overall survival rate of 83% at 6 years), we had lower rates of relapse-free and overall survival. Lower percentage of stage I patients and higher percentage of stage III cases seem to be one of the reasons of this difference.

In the literature, there are only a few reports about the protocols and treatment results from Iran. Avoiding surgical rupture of the tumor and emphasizing the role of lymph node sampling will reduce the risk of local recurrences. With more adaptation to the NWTS treatment protocols, early diagnosis facilitated by ultrasonography, CT scan and magnetic resonance imaging, and reducing the percentage of patients lost to follow-up, the optimum results seem to be achievable. Lack of cytogenetic investigation was one of the weak points of our study. A larger sample size would provide greater confidence with respect to the
general finding of these results. We recommend a more comprehensive investigation with special attention to cytogenetic events, parental occupation, maternal hormonal exposures, and a long-term follow-up of patients for studying the late effects of treatment and the rates of survival for each stage and histopathologic group.

References

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