MEDWELL PUBLISHING
Research Journal of Biological Sciences 4 (1): 86-89, 2009
ISSN: 1815-8846

Wilm's Tumor: Epidemiology and Survival

[1]M. Faranoush, [2]G.R. Bahoush [3]A. Mehrvar, [4]S. Hejazi, [5]P. Vossough,
[6]A.A. Hedayatiasl, [7]M.S. Rahiminejad, [8]F. Seighali, [9]R. Ghorbani and [10]M.A. Ehsani
[1]Department of Pediatric Hematology and Oncology,
Semnan University of Medical Sciences, Amir Al Momenin Hospital, Iran
[2]Department of Pediatric Hematology and Oncology,
Iran University of Medical Sciences, Ali Asghar Children's Hospital, Iran
[3]Department of Pediatric Hematology and Oncology,
Army University of Medical Sciences, Mahak Children's Hospital, Iran
[4]Department of Pediatric Hematology and Oncology, Uremia University of Medical Sciences, Iran
[5]Department of Pediatric Hematology and Oncology,
Iran University of Medical Sciences, Mahak Children's Hospital, Iran
[6]Department of Pediatric Hematology and Oncology,
Baghiyatallah University of Medical Sciences, Mahak Children's Hospital, Iran
[7]Department of Pediatric Hematology and Oncology,
Tehran University of Medical Sciences, Markaz Tebi Children's Hospital, Iran
[8]Department of Pediatric Gastroenterology,
Iranian Blood Transfusion Organization (IBTO), Iran
[9]University of Medical Sciences, Iran
[10]Department of Pediatric Hematology and Oncology,
Tehran University of Medical Sciences, Bahrami Children's Hospital, Tehran, Iran

Abstract: Wilms tumor is the most common childhood renal tumor accounting for about 6% of pediatric malignant disease. Most patients with Wilms tumor can be cured with treatment and subsequently lead normal life. The multidisciplinary management of Wilms tumor has resulted striking improvement in survival of more than 85% nowadays and has become a paradigm for successful cancer therapy. We describe the results of patients treated according to National Wilms Tumor studies (NWTS) 3-5, with surgical staging, Central pathology review and multimodality treatment. This is a historical cohort study on the all patients who had Wilms tumor. We used the existing files of all patients who had admitted to Ali Asghar Children's hospital with Wilms tumor in the years of 1990-2003. The patients evaluated for age, sex, histologic type of cancer, metastasis, outlook of relapse and outcome after 5 years from diagnosis. We analyzed 175 files of Wilms tumor. They are 49.7% are male and 50.3% female. Mean age (±S.D.) of patients at diagnosis was 3.8±0.4 year. The 5-year survival rate of these patients was approximately 76±4%. History of cancer in first degree of relative was 11.5% and family marriage was 36.4%. Tumor involvement were 45.3% in right kidney, 51.5% in left kidney and both kidney involvement in 3.2%. Congenital anomalies in association with Wilms tumor were urologic problem (1.5%), hemihypertrophy (0.5%), sporadic aniridia (0.5%) and without abnormalities (97.5%). Histologic type of tumor were 32.6% favorable, 65.2% unfavorable and 2.2% intermediate. Stage II and III were the most common (35.4 and 32.4%, respectively). Tumor relapse were occurred in 25.4%.

Key words: Wilms tumor, hemihypertrophy, epidemiology, survival

INTRODUCTION

Wilms tumor (WT) is the second most common malignant retroperitoneal tumor. It is most common primary renal tumor of childhood (Reinhard *et al*., 2007). Wilms tumor consist 6% of all childhood cancer. Male to Female ratio in unilateral disease is 0.92 and 0.6 in bilateral disease (Petruzzi and Green, 1997). Seventy-eight percent of children are diagnosed at 1-5years of age, with a peak incidence occurring between 3 and 4 years of age. Median

Corresponding Author: Mohammad Ali Ehsani, Bahrami Children Hospital, Shahid Kiaee (Ghasem-Abad) Street, Damavand Avenue, Imam Hossein Square, Tehran, Iran

age of presentation is 44 months in unilateral disease, 32 months in bilateral disease (Zugor *et al*., 2007). The median age of presentation is 36.5 months for boys and 42.5 months for girls. WT is rare in adults (>16 years of age) (Seyed-Ahadi *et al*., 2007). Wilms tumor is usually sporadic. Congenital anomalies occur in 12-15% of cases (Abu-Gosh *et al*., 2002). Children with renal tumor most of which are favorable histology Wilms tumor, have an excellent 5 year survival rate (Petruzzi and Green, 1997; Zugor *et al*., 2007; Seyed-Ahadi *et al*., 2007; Abu-Gosh *et al*., 2002; Pastore *et al*., 2006). Modern therapy includes nephrectomy and combination chemo-therapy and for some, radiation therapy to the abdomen and/or lungs (Pastore *et al*., 2006; Mitchell *et al*., 2006; Dome and Coppes, 2002; Beckwith *et al*., 1996; Balaguer *et al*., 2006). The most frequent site of relapse is the lungs, while recurrence in the original tumor bed, at other intra-abdominal sites, brain and bone are less frequent. The percentage of event-free survival and overall survival at diagnosis are in relationship to the stage of disease and histology (Mitchell *et al*., 2006). Positive prognostic factors include the following: Stages I and II, Negative Para-aortic nodes, Absence of anaplastic or sarcomatous histology, Absence of tumor rupture, Site of metastases at relapse: lung better than liver, Time of relapse: Late better than early (>15 months from diagnosis). Initial treatment of children with Wilms tumor has been so successful (Dome and Coppes, 2002). We describe the results of patients treated according to National Wilms Tumor studies (NWTS) 3-4, with surgical staging, Central pathology review and multimodality treatment.

MATERIALS AND METHODS

Clinical characteristics: One hundred and seventy five patients with diagnosis of wilm's tumor registered in this study. The clinical data, including treatment details and follow-up information, were gathered from retrospective review of patient charts. This is a historical cohort study on the all patients who had Wilms tumor. We used the existing files of all patients <14 years who had admitted to Ali Asghar Children's hospital with Wilms tumor in the years of 1990-2000. All patients underwent an initial nephrectomy after completing a pre-operative assessment, which was to include radiographic imaging of the kidneys (abdominal CT scan), inferior vena cava and lungs, CBC, blood chemistries, coagulation factor and assessment of cardiac status. The surgical procedure was to performed through a transabdominal incision. The contalateral kidney was to be mobilized, all surface inspected and any lesion suspicious for Wilms tumor biopsied. A stage was according to surgical-pathological staging system (NWTSG).

Treatment protocol: Children received chemotherapy protocol according their stage of disease. We used NWTS 3-4 chemotherapy protocol. Radiation therapy was usually begun for stage III and IV shortly after chemotherapy to the tumor bed at a dose 1080 cGy.

Statistical analysis: Five year survival and Overall Survival (OS) were calculated from the time of diagnosis to the time of last followup. OS were estimated using the Kaplan-Meier and Log rank test by SPSS 11.5.

The patients evaluated for age, sex, histologic type of cancer, metastasis, outlook of relapse and outcome after 5 years from diagnosis.

RESULTS

The mean (±S.D.) age at diagnosis was 3.8±0.4 year (range 8 months -13 years). There is 49.7% (87 patients) male and 50.3% (88 patients) female. Positive family history of cancer in first degree of relative was 11.5%. History of family marriage was positive in 36.4%. Initial signs and symptoms, in order of frequency, are listed in Table 1. Tumor involvements were 45.3% in right kidney, 51.5% in left kidney and both kidney involvement in 3.2%. Congenital anomalies in association with wilm's tumor were urologic problem (1.5%), hemihypertrophy (0.5%), sporadic aniridia (0.5%) and without abnormalities (97.5%). Histologic type of tumor were 32.6% favorable, 65.2% unfavorable and 2.2% intermediate. A stage frequency according to surgical-pathological staging

Table 1: Initial signs and symptoms of Wilm's Tumor in order of frequency

Sign/symptom	Frequency (%)
Palpable mass in abdomen	65.0
Obstipation	6.0
Hematuria	5.0
Abdominal pain	3.5
Vomiting	3.0
Respiratory discomfort	2.0
Weight loss	1.5
Others	14.0

Table 2: Relation of 5-year survival with age, stage and sex

	5-year survival (%)	p-value
Age		
<1year	90±9	ns
1-5 year	79±5	
5-10year	66±9	
>10 year	65±8	
Stage		
I	100±0	0.03
II	85±6	
III	82±3	
IV	45±6	
V	30±8	
Sex		
Male	85±4	0.01
Female	64±7	

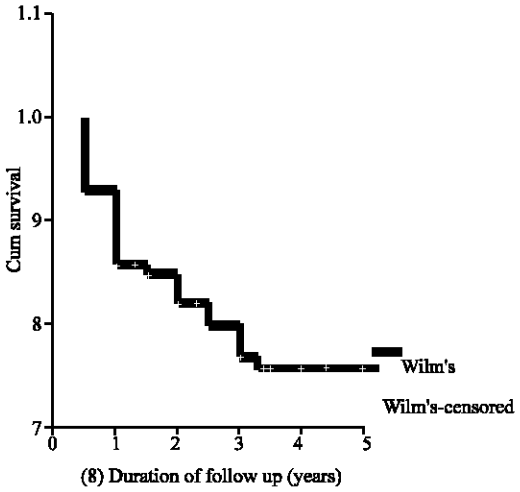

Fig. 1: Survival analysis of Wilm's tumor

system (NWTSG) was I (23.3%), II(35.4%), III(32.4%), IV(5.1%) and V (3.8%) (Table 2). The overall relative 5 year survival rate for children with wilm's tumor was approximately 76±4% (Fig. 1). Males with wilm's tumor had better survival rate than females with significant difference (85±4 vs. 64±7% P = 0.01) (Table 2). The 5-year survival rate was better in for patients under 1 years compare to others, respectively (90±9% vs. 73±4%, P = 0.85) (Table 2). Renal function test in all patients was normal except in 2 patients with bilateral wilm's tumor report increase BUN. Relapse had occurred in 25.4% of patients. The most common site of relapse is primary site (52.7%), lung (33.3%) and mixed (14%). The tumor relapse rate among patients with stage I, II, III and IV disease was 0, 15, 18 and 55%, respectively. The time of relapse is 56.2% during treatment (1-9 months) and 43.7% after treatment (1 month -1 years).

DISCUSSION

Childhood Wilm's tumor or nephroblastoma represents one of the challenges for pediatric oncologists in developing countries (Beckwith *et al*., 1996; Balaguer *et al*., 2006; Green *et al*., 1997; Metzger and Dome, 2005; Hartman and Maclennan, 2005; Zils *et al*., 2008; Pession *et al*., 2008). Wilms tumor is one of the commonest childhood solid tumors which has an excellent outlook in the developed world with 5 year overall survival exceeding 90% (Balaguer *et al*., 2006; D'Angio, 2003; Uba and Chirdan, 2007; Abuidris *et al*., 2008). We review the clinical characteristics and outcome of management of childhood nephroblastoma. In our study overall relative 5 year survival rate for children with wilm's tumor was approximately 76±4% (Green *et al*., 1997). A highly significant improved 5 year overall survival rate was found for relapsed patients with consultation (65 vs. 10%) in SIOP 2001 trial (Van den Heuvel-Eibrink *et al*., 2008). In another were 32 children (M: F=1.9:1) with histologically confirmed nephroblastoma seen over the 7 year period. Their median (range) age was 4 (3-15) years. The patients invariably presented with a palpable abdominal mass, but hematuria was exceptional (Metzger and Dome, 2005; Hartman and Maclennan, 2005; Zils *et al*., 2008; Pession *et al*., 2008). At presentation, 1 (3.1%) patient was in stage I, 8 (25%) stage II, 11 (34.4%) stage III and 12 (37.5%) stage IV. About 72% of the patients presented with stage III-IV disease same as our study (Pession *et al*., 2008; D'Angio, 2003). Overall, only 43.8% were alive between 1 and 9 months (median: 6 months) of follow-up period, but there was no survivor at 2 years after treatment. Childhood nephroblastoma has a high mortality rate in poor developing country because of late clinical presentation with advanced disease, poor availability of cytotoxic drugs and frequent interruptions in treatment and inadequate follow-up but in Iran we had good result (Uba and Chirdan, 2007; Abuidris *et al*., 2008). In another study 5 years event-free survival (EFS) was 80% and overall survival (OS) 86% (Zils *et al*., 2008; Pession *et al*., 2008). Renal tumors diagnosed in the first 7 months of life generally have an excellent prognosis though histology is an important prognostic factor same as our study. In the SIOP 93-01/GPOH trial and study 1 020 patients with a newly diagnosed renal tumor, the stage distribution of the tumors was stage I in 315 (61%), stage II N- in 126 (24%), stage II N+ in 25 (5%) and stage III in 36 (7%) patients against our study (D'Angio, 2003). The event free survival (EFS) after 5 years was 91% for all patients with unilateral Wilms tumor without distant metastasis (Uba and Chirdan, 2007). Today the results of the treatment of Wilms tumors are very good. In the NWTS-3 the 4 year relapse-free survival rate in stage 1 with favorable and with anaplastic histology was 92%, in stage 2 with favorable histology 88%, in stage 3 with favorable histology 79%, in stage 4 and in stage 2, 3 and 4 with unfavorable histology 71% (Abuidris *et al*., 2008; Van den Heuvel-Eibrink *et al*., 2008). The Italian group has obtained less impressive results in the 80%, but similar results in the first stage with the 92% (Merguerian, 2003; Slovis, 2008). Finally wilm's tumor are good prognosis, today we know the optimal treatment for most children diagnosed with wilm's tumor. Work continues on trying to identify effective treatment for children with unfavorable histologies.

CONCLUSION

Although, excellent survival has been maintained, many patients receive less therapy today than patients

with similar characteristic did a decade ago. Today we know the optimal treatment for most children diagnosed with Wilms tumor. Work continues on trying to identify effective treatment for children with unfavorable histology. Better understanding of biological processes that leads to this childhood cancer will allow further improvements in its management.

REFERENCES

Abu-Gosh, A.M., M.D. Krailo, S.C. Goldman, R.S. Slack, V. Davenport, E. Morris, J.H. Laver, G.H. Reaman and W Cairo, 2002. Ifosfamide, Carboplatin and etoposide in children with poor risk relapsed Wilms tumor: A Children's Cancer Group report. Ann. Oncol., 13: 460-469.

Abuidris, D.O., M.E. Elimam, F.M. Nugud, E.M. Elgaili, M.E. Ahmed and R.S. Arora, 2008. Wilms tumour in Sudan. Pediatr. Blood Cancer, 50 (6): 1135-1137.

Balaguer, G.J., J.M. Fernández Navarro, A. Cañete Nieto, M.D. Muro Velilla, Hernández M. Martí and V. Castel Sánchez, 2006. Renal tumors in infants aged <1 year. Ann. Pediatr. (Barc), 64 (5): 433-438.

Beckwith, J.B., C.E. Zuppan, N.G. Browning, J. Moksness and N.E. Breslow, 1996. Histologicalanalysis of aggressiveness and responsiveness in Wilm's tumor. Med. Pediatr. Oncol., 27: 422-428.

D'Angio, G.J., 2003. Pre or post operative treatment for Wilms tumor? Who, what, when,where, how, why and which. Med. Pediatr. Oncol., 41: 545-549.

Dome, J.S. and M.J. Coppes, 2002. Recent advances in Wilm's tumor genetics. Curr. Opin. Pediatr., 14: 5-11.

Green, D.M., 1997. Wilm's tumor. Eur. J. Cancer, 33: 409-418.

Hartman, D.J. and G.T. MacLennan, 2005. Wilms tumor. J. Urol., 173 (6): 2147.

Merguerian, P.A., 2003. Pediatric genitourinary tumors. Curr. Opin. Oncol., 15: 222-226.

Metzger, M.L. and J.S. Dome, 2005. Current therapy for Wilm's tumor. Oncologist, 10 (10): 815-826.

Mitchell, C., K. Pritchard-Jones, R. Shannon, C. Hutton and S. Stevens *et al.*, 2006. For the United Kingdom Cancer Study Group. Immediate nephrectomy versus preoperative chemotherapy in the management of non-metastatic Wilm's tumour: Results of a randomised trial (UKW3) by the UK Children's Cancer Study Group. Eur. J. Cancer, 42 (15): 2554-2562.

Pastore, G., A. Znaor, F. Spreafico, N. Graf, K. Pritchard-Jones and E. Steliarova-Foucher, 2006. Malignant renal tumours incidence and survival in European children report from the Automated Childhood Cancer Information System Project. Eur. J. Cancer, 42 (13): 2103-2114.

Pession, A., E. Dama, R. Rondelli, C. Magnani, M.D. Rosa, F. Locatelli, F. Fagioli, R. Haupt, M. Jankovic, B. Terracini, F. Merletti and G. Pastore, 2008. Italian Association of Paediatric Haematology and Oncology. Survival of children with cancer in Italy, A report from the hospital based registry of the Italian Association of Paediatric Haematology and Oncology (AIEOP). Eur. J. Cancer, 44 (9): 1282-1289.

Petruzzi, M.J. and D.M. Green, 1997. Wilm's tumor. Pediatr. Clin. North Am., 44: 939-951.

Reinhard, H., R. Furtwängler and N. Graf, 2007. Wilm's tumor-update. Urologe A, 46 (2): 143-145.

Seyed-Ahadi, M.M., A. Khaleghnejad-Tabari, A. Mirshemirani, N. Sadeghian and O. Amonollahi, 2007. Wilm's tumor: A 10 year retrospective study. Arch. Iran Med., 10 (1): 65-69.

Slovis, T.L., 2008. Wilms tumour minisymposium. Pediatr. Radiol., 38 (1): 1.

Uba, A.F., L.B.Chirdan, 2007. Childhood Wilm's tumour: Prognostic factors in North Central Nigeria. West Afr. J. Med., 26 (3): 222-225.

Van den Heuvel-Eibrink, M.M., P. Grundy, N. Graf, K. Pritchard-Jones, C. Bergeron, C. Patte, H. Van Tinteren, A. Rey, C. Langford, J.R. Anderson, J. De Kraker, 2008. Characteristics and survival of 750 children diagnosed with a renal tumor in the first seven months of life: A collaborative study by the SIOP/GPOH/SFOP, NWTSG and UKCCSG Wilms tumor study groups. Pediatr. Blood Cancer, 50 (6): 1130-1134.

Zils, K., R. Furtwängler, H. Reinhard, M. Alkassar and N. Graf, 2008. Consultation within the nephroblastoma trial SIOP/GPOH as part of the workload in the trial office. Klin. Padiatr., 220 (3): 183-188.

Zugor, V. and D. Krot, 2007. Schott GE.Risk factors for intra and postoperative complications in Wilm's tumor surgery. Urologe A, 46 (3): 274.