

Original Research Article

Long term outcome of Wilms' tumor in tertiary care hospital

Jeevarathi T.¹, Gomathi Vadivelu^{2*}

¹Department of Pediatric Surgery, Institute of Child Health Hospital, Egmore, Chennai, Tamil Nadu, India

²Department of Pediatric Surgery, Stanley Medical College, Rayapuram, Chennai, Tamil Nadu, India

Received: 22 August 2020

Accepted: 08 September 2020

***Correspondence:**

Dr. Gomathi Vadivelu,

E-mail: arvindr84@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Nephroblastoma, or Wilms' tumor, is an embryonal tumor that develops from remnants of the immature kidney. It is the most common renal tumor of childhood. The aim is to analyze the long term outcome in Wilms' tumor in perplex situations as double moiety and to correlate with multiple organ defects.

Methods: It is a combined perspective and retrospective study that pediatric urology outpatient department (OPD) at the Institute of Child Health and Hospital for Children, Madras Medical College, Chennai. The study included patients with Wilms, who attended the pediatric surgery during the ten years, from March 2008 to February 2011. The patients were subjected to detailed clinical examination and relevant investigations were performed.

Results: Among patients with stage I–II fumarate hydratase (FH) tumors, the relative risk (RR) of relapse and death were increased for loss of heterozygosity (LOH) 1p only (RR=2.2 for relapse; RR=4.0 for death), for LOH 16q only (RR=1.9 and RR=1.4), and LOH for both regions (RR=2.9 and RR=4.3) in comparison with patients lacking LOH at either locus.

Conclusions: Stage I and II have a good prognosis. Stage III and IV need close surveillance since they have a high rate of recurrence. Stage V has a bad prognosis. Stage IV Wilms need lung irradiation. Neoadjuvant chemotherapy reduces tumor spillage in stage III and IV.

Keywords: Wilms' tumor, Long term outcome, Chromosomal abnormality, Intravenous urography, Treatment

INTRODUCTION

Nephroblastoma, or Wilms' tumor, is an embryonal tumor that develops from remnants of the immature kidney. It is the most common renal tumor of childhood. Wilms' tumor has many causes, which can broadly be categorized as syndromic and non-syndromic. Syndromic causes of Wilms' tumor occur as a result of alterations to genes such as the Wilms' tumor 1 (WT1) or Wilms' tumor 2 (WT2) genes, and the tumor presents with a group of other signs and symptoms.¹ Non-syndromic Wilms' tumor is not associated with other symptoms or pathologies. In particular, cases of bilateral Wilms' tumor, as well as cases of Wilms' tumor derived from certain genetic syndromes such as Denys-Drash syndrome, are strongly associated with nephrogenic rests.² Most nephroblastomas are on one

side of the body only and are found on both sides in less than 5% of cases, although people with Denys-Drash syndrome mostly have bilateral or multiple tumors they tend to be encapsulated and vascularized tumors that do not cross the midline of the abdomen.³ In cases of metastasis, it is usually to the lung. A rupture of Wilms' tumor puts the patient at risk of bleeding and peritoneal dissemination of the tumor. In such cases, surgical intervention by a surgeon who is experienced in the removal of such a fragile tumor is imperative.

Stage I

The tumor is limited to the kidney and was completely excised. The renal capsule has an intact outer surface. The tumor was not ruptured or biopsied before removal (fine-

needle aspiration biopsies are excluded from this restriction). The vessels of the renal sinus are not involved. There is no evidence of tumor at or beyond the margins of resection.

Stage II

The tumor extends beyond the kidney, but was completely excised. There may be a regional extension of tumor (i.e. penetration of the renal capsule or extensive invasion of the renal sinus). The blood vessels outside the renal parenchyma, including those of the renal sinus, may contain tumor. The tumor was biopsied (except for fine-needle aspiration), or there was a spillage of the tumor before or during surgery that is confined to the flank and does not involve the peritoneal surface. There must be no evidence of tumor at or beyond the margins of resection.

Stage III

Residual non-hematogenous tumor is present, and confined to the abdomen. Anyone of the following may occur: Lymph nodes within the abdomen or pelvis are found to be involved by the tumor (renal hilar, para-aortic, or beyond) (lymph node involvement in the thorax or other extra-abdominal sites would be a criterion for stage IV).⁴ The tumor has penetrated through the peritoneal surface. Tumor implants are found on the peritoneal surface. Gross or microscopic tumor remains postoperatively (e.g. tumor cells are found at the margin of surgical resection on microscopic examination).⁵ The tumor is not completely resectable because of local infiltration into vital structures. Tumor spill not confined to the flank occurred either before or during surgery.

Stage IV

Hematogenous metastases (lung, liver, bone and brain), or lymph node metastases outside the abdominopelvic region are present.

Stage V

Bilateral renal involvement is present at diagnosis. An attempt should be made to stage each side according to the above criteria based on the extent of disease before biopsy or treatment.⁶

METHODS

It is a combined perspective and retrospective study that pediatric urology OPD at the Institute of Child Health and Hospital for Children, Madras Medical College, Chennai. The study included patients with Wilms, who attended the pediatric surgery during the ten years, from March 2008 to February 2011. The patients were subjected to detailed clinical examination and relevant investigations were performed, namely, ultrasound examination, an intravenous urogram (IVU), \pm contrast-enhanced computed tomography (CECT). The treatment modalities

were studied and patients were followed up to screen for residual lesion size, recurrences, and liver and lung secondaries.

Selection criteria

All patients with renal mass, hematuria, fever, abdominal pain.

Inclusion criteria

All patients with Wilms' tumor were proven radiologically, sonographically and histopathological examination (HPE) wise.

Exclusion criteria

Stromal tumors as clear cell sarcoma, congenital mesonephric hamartoma, rhabdoid tumor, and angiomyolipoma of the kidney. The patients were subjected to detailed clinical examination and relevant investigations were performed, namely, ultrasound examination, IVU, and/or CECT. The treatment modalities were studied and patients were followed up to screen for residual lesion size, recurrences, and liver and lung secondaries.

Statistical analysis

The software used was Statistical Package for the Social Sciences (SPSS) software version 20. Mean, median and standard deviation (SD) was calculated for descriptive analysis. Chi-square test can be used to compare data @5% level of significance.

RESULTS

Demographics of Wilms' tumour

Gender distribution showed slight male predominance i.e. male-99 and female-57. Age at diagnosis was found to be: most of the children were between 1-5 years, number of children under 1 year - 14 (8 male and 6 female), number of children between 1-5 years - 117 (70 male and 47 female), number of children between 6-10 years - 23 (20 male and 3 female) and number of children more than 10 years - 2 (1 male and 1 female) (Figure 1).

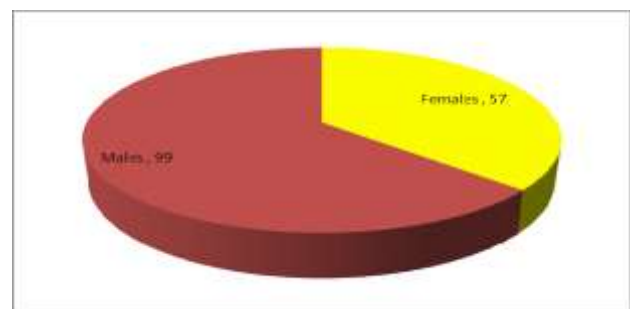


Figure 1: Demographics.

Histopathology

Histopathology of 156 patients showed unfavorable histology in 2 patients and 154 patients showed favorable histology (FH), which includes 145 triphasic histology and 9 monophasic variety. Only 2 out of 156 cases were of unfavorable histology. Both cases were in stage III.

On gross specimen, Wilms’ tumor had a varied appearance of smooth to cystic and variegated on cut section. There was no distinct capsule, but the surrounding mesenchyme condensed to form a pseudocapsule. Occasionally, hemorrhage and necrosis were noted on gross specimen

examination. The whole specimen was handled very carefully, and gross specimen examination, microscopic study, and further biological studies were performed according to the protocols by International Society of paediatric oncology (SIOP) 2002 in Europe and the American College of Pathologists in the United States.

For microscopic examination, the tumor should be sent to the pathology department intact without formalin preservative. The examination includes specimen weight, tumor location, capsule invasion, renal vein, and sinus invasion, ureter, and cut surface of the kidney if a heminephrectomy was performed (Figure 2).

Table 1: Histopathology.

Stage-I	Stage-II	Stage-III	Stage-IV	Stage-V
30	61	46	10	9
27-triphasic	57-triphasic	44-FH	8-triphasic	9-favorable histology
3-monophasic	4-monophasic	2-unfavorable histology	2-monophasic	



Figure 2: Gross specimen of Wilms’ tumour.



Figure 3: A 3 year male child presented with lung secondaries and right kidney involved with Wilms’ tumour.

A computed tomography scan of a 3.5-year-old girl who presented with a large abdominal mass demonstrating the characteristic findings of Wilms' tumor. The tumor mass can be seen protruding from the right kidney with a margin of renal parenchyma along the periphery. Management consists of surgery for removal of the primary tumor with the kidney (radical nephrectomy), with chemotherapy and

radiotherapy in some cases. The management is guided by the national Wilms’ tumor study (NWTS) protocol in International council for harmonisation of technical requirements for pharmaceuticals for human use (ICH), Chennai and the United States and the SIOP protocol in Europe according to the stage of the tumor. Radical nephrectomy for removal of the primary tumor with the kidney is the mainstay of treatment. This procedure allows the removal of the primary tumor and accurate staging of the tumor. The usual approach is transperitoneal through a transverse abdominal incision, which gives good access to the tumor and vasculature (Figure 4).



Figure 4: Intravenous urography shows calyceal distortion in right kidney in Wilms’ tumour.

DISCUSSION

Wilms’ tumor (also called Wilms’ tumor or nephroblastoma) is a type of childhood cancer that starts in the kidneys. It is the most common type of kidney cancer in children. About 9 of 10 kidney cancers in children are Wilms’ tumors. Cancer starts when cells in the body begin to grow out of control.⁷ Cells in nearly any part of the body can become cancer and can spread to other

areas of the body. The presence of thrombus is picked up with high-resolution ultrasound in IVC and atrium. They were serially screened for its disappearance with radiotherapy and chemotherapy. It takes 24 weeks to two years for the tumor thrombus to resolve as reported by Flentje et al.⁸ We had six cases of tumor thrombus. 4 cases of IVC thrombus were resolved with chemotherapy. One out of 2 atrial thrombi underwent cardiac bypass and atrial thrombectomy atrial thrombus resolved with chemotherapy.⁹ The other cases of. The computed tomography (CT)-contrast study was done in all bilateral tumors after chemotherapy and radiotherapy (RT) to look for the residual lesion. 5 year survival is 98% in stage 1 and 2. Long term disease-free survival over 10 years is seen in 10 of our Wilms' tumor patients. Hypertension was present at 1% after ten years. We have had no second malignant neoplasm in our series.¹⁰ Microalbuminuria was present in 1% of long term survivors. Their skeletal growth was affected by two children in our series. Ionizing radiation affects epiphyseal growth, soft tissue hypoplasia and diminished bone growth are followed by scoliosis our series of patients had stunted growth but no scoliosis. They did not show any delay in sexual maturity. Damage to the reproductive systems may represent one of the main late sequelae of both, gonadal radiation or chemotherapeutic agents.¹¹ Prognosis in Wilms' tumor is directly dependent on the stage of the disease. This emphasizes the need for accurate staging before chemotherapy and radiotherapy. Quality of life was well preserved in stages 1, 2 and 3 diseases. Recurrences are more common in tumor spillage and recurrent tumors have uniformly failed to respond to salvage regimen.¹² Those children with advanced-stage disease who responded favorably to chemotherapy and radiotherapy regime have survived beyond five years. The non- responders of this group deteriorated over the next five years. We have had follow-up stage I and II children till 20 years of life and observed 97% disease-free survival status. We have followed stage III children up to 10 years of their lives and observed 70% of disease-free survival status. We have followed stage IV Wilms' tumor children for 5 years and observed 50% mortality in our series. Stage V has shown 2 years of survival from the onset of disease. Stages I and II have a good prognosis. 97% of the cases show a disease-free survival status.¹³ Mortality is nil in our study from 1998 to date in stages I and II. We have had 10 recurrences in stage III. Salvage chemotherapy was not effective in these children. In stage IV, 50% of mortality was seen. Syndromic variety tumors do well with surgery, postoperative chemotherapy and RT.¹⁴ Bilateral Wilms have a bad prognosis. Life expectancy in bilateral Wilms' is two years from the time of onset of disease. We had given neoadjuvant chemotherapy for 14 cases, 9 bilateral cases 5 large tumors and 1 ascites patient.¹⁵ All bilateral Wilms patients were under 7 years of age. Stages I and II have a good prognosis. 97% of the cases show a disease-free survival status. Mortality is nil in our study from 1998 to date in stages I and II.¹⁶ We have had 10 recurrences in stage III. Heminephrectomy was done in one of double moiety and the child was not given radiotherapy as a child was understated. Salvage chemotherapy was not effective

in these children.¹⁷ Tumour spillage and defaulting chemotherapy or radiotherapy results in recurrences. In stage IV, 50% of mortality was seen. Syndromic variety tumors do well with surgery, postoperative chemotherapy and RT. Bilateral Wilms have a bad prognosis.¹⁸

CONCLUSION

We have had 10 recurrences in stage III. Heminephrectomy was done in one of double moiety and the child was not given radiotherapy as the child was understated Salvage chemotherapy was not effective in these children. Tumour spillage and defaulting chemotherapy or radiotherapy results in recurrences. In stage IV, 50% of mortality was seen. Syndromic variety tumors do well with surgery, postoperative chemotherapy and RT. Bilateral Wilms have a bad prognosis. Life expectancy in bilateral Wilms' is two years from the time of onset of disease. Stage I and II have a good prognosis. Stage III and IV need close surveillance since they have a high rate of recurrence. Recurrent tumors are not amenable to salvage chemotherapy. Stage V has a bad prognosis. Stage IV Wilms need lung irradiation. Neoadjuvant chemotherapy reduces tumor spillage in stage III and IV. Survival is poor in patients with Wilms' tumor and coexisting renal anomalies like horseshoe kidney. Recurrent tumors are treated based on their histology. Wilms' tumor usually does not recur, if treated adequately with chemotherapy and proper follow-up.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Green DM, Beckwith JB, Breslow NE, Faria P, Moksness J, Finklestein JZ, et al. Treatment of children with stages II to IV anaplastic Wilms' tumor: a report from the National Wilms' Tumor Study Group. *J Clin Oncol.* 1994;12:2126-31.
2. Coppes MJ, de Kraker J, Van Dykes HJM, Perry HJ, Delemarre JF, Tournade MF, et al. Bilateral Wilms' tumor; long-term survival and some epidemiological features. *J Clin Oncol.* 1989;7:310-5.
3. D'Angio GJ, Evans A, Breslow N, Beckwith B, Bishop H, Feigl P, et al. The treatment of Wilms' tumor: results of the Second National Wilms' Tumor Study. *Cancer.* 1981;47:2302-11.
4. D'Angio GJ, Evans AE, Breslow N, Beckwith B, Bishop H, Feigl P, et al. The treatment of Wilms' tumor: results of the National Wilms' tumor study. *Cancer.* 1976;38:633-46.
5. Ehrlich PF, Ritchey ML, Hamilton TE, Haase GM, Ou S, Breslow N, et al. Quality assessment for Wilms' tumor: a report from the National Wilms tumor study group. *J Pediatr Surg.* 2005;40:208-13.
6. Farber S. Chemotherapy is the treatment of leukemia and Wilms' tumor. *JAMA.* 1966;198:826-36.

7. Farewell VT, D'Angio GJ, Breslow N, Norkool P. Retrospective validation of a new staging system for Wilms' tumor. *Cancer Clin Trials.* 1981;4:167-71.
8. Flentje M, Weirich A, Potter R, Ludwig R. Hepatotoxicity in irradiated nephroblastoma patients during postoperative treatment according to SIOP0/GPOH. *Radiotherapy Oncol: J Eur Society Therapeutic Radiol Oncol.* 1994;31:222-8.
9. Green DM, Breslow NE, Beckwith JB, Finklestein JZ, Grundy PE, Thomas PR, et al. Comparison between single-dose and divided-dose administration of dactinomycin and doxorubicin for patients with Wilms' tumor: a report from the National Wilms' Tumor Study group. *J Clin Oncol.* 1998;16:237-45.
10. Green DM, Breslow NE, Beckwith JB, Finklestein JZ, Grundy P, Thomas PR, et al. Effect of duration of treatment on treatment outcomes and cost of treatment for Wilms' tumor: a report from the National Wilms' Tumor Study Group. *J Clin Oncol.* 1998;16:3744-51.
11. Kumar R, Breatriach F, Fitzgerald R. Is Contralateral exploration in Wilms' tumor necessary? A result of UKCCSG Bilateral Wilms' Tumour study (abstract). 27th SIOP Meeting. 1996;218:1-30.
12. Lipshitz HI, Cohen MA. Radiation-induced osteochondromas. *Radiology.* 1982;142:643-7.
13. Ritchey ML, Green DM, Breslow NE, Monksness J, Norkool P. Accuracy of current imaging modalities in the diagnosis of synchronous bilateral Wilms' tumor. A report from the National Wilms' Tumor Study Group. *Cancer* 1995;75:600-4.
14. Ritchey ML, Shamberger RC, Hamilton T, Haase G, Argani P, Peterson S. Fate of bilateral lesions missed on preoperative imaging: a report from the National Wilms' Tumor Study Group. *J Urol.* 2005;174:1519-21.
15. Ritchey ML, Shamberger RC, Haase G, Horwitz J, Bergemann T, Breslow NE. Surgical complications after nephrectomy for Wilms' tumor: a report from the National Wilms' Tumor Study Group. *J Am Coll Surg.* 2001;192:63-8.
16. Shamberger RC, Guthrie KA, Ritchey ML, Haase GM, Takashima J, Beckwith JB, et al. Surgery related factors and local recurrence of Wilms' tumor in National Wilms' Tumor Study 4. *Ann Surg.* 1999;229:292-7.
17. Steckler RE, Riehle RA Jr, Vaughan ED Jr. Hyperfiltration- induced renal injury in normal myth or reality. *J Urol.* 1990;144(6):1323-7.
18. Wallace WHB, Shalet SM, Crowne EC, Morris-Jones PH, Gattamaneni HR. Ovarian Failure following abdominal irradiation in children; natural history and prognosis. *Clin Oncol.* 1989;1:75-9.

Cite this article as: Jeevarathi T, Vadivelu G. Long term outcome of Wilms' tumor in tertiary care hospital. *Int Surg J* 2020;7:3234-8.