Nephron Sparing Surgery for Unilateral Non-Syndromic Wilms Tumor

R. B. Nerli · V. C. Pujar · M. B. Hiremath · S. M. Jali ·
S. S. Joshi · S. C. Hiremath · A. K. Guntaka

Received: 9 April 2013 / Accepted: 30 December 2013 / Published online: 22 January 2014
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Abstract The initial therapy for most children with Wilms tumor is radical nephrectomy. Several centers, have explored the role of Nephron-sparing procedures in children with unilateral non-syndromic Wilms tumors. The primary motivation for this approach is concern about late occurrence of renal dysfunction after unilateral nephrectomy. We report our experience with NSS for unilateral non-syndromic Wilms tumor. We reviewed the records of nine children who underwent nephron sparing surgery for unilateral, nonsyndromic Wilms tumors at our Hospital **between Jan 2000 through Jan 2012**. All patients received preoperative chemotherapy with two drugs (vincristine, and dactinomycin) following which patients underwent tumor resection. Subsequent renal function was assessed by estimating the glomerular filtration rate using creatinine clearance and other measures of long-term renal function assessment included blood pressure evaluation and the need for antihypertensive medications. During the study period nine children with a mean age 19.66 ± 14.37 months at diagnosis and presenting with unilateral non-syndromic Wilms tumor underwent nephron sparing surgery. In all the nine children, the renal plane of resection showed a tumor-free margin. Post-operative serum creatinine repeated at the end of 3 months revealed maintenance of good renal function in all children. Nephron sparing surgery is a safe and effective option in the management of **early stage**

unilateral non-syndromic Wilms tumor. It is oncologically safe and does not lead to decreased local tumor control. The function of the kidney remnant remains rather well.

Keywords Wilms tumor · Nephrectomy · Nephron sparing surgery · Child

Introduction

Wilms tumor is the most common primary malignant renal tumor of childhood. This embryonal tumor develops from remnants of immature kidney. Although an excellent outcome is now expected for most children, there are subgroups of high-risk patients for whom more effective treatment is needed [1]. There are a number of syndromes with overgrowth features at risk for the development of Wilms tumor, including hemihypertrophy, which may occur alone or as part of the Beckwith-Wiedemann syndrome (BWS), Perlman, Sotos, and the Simpson-Golabi-Beckwith syndromes [1]. The risk of nephroblastoma in children with BWS and hemihypertrophy is estimated to be 4 % to 10 %, with 21 % of children presenting with bilateral disease [1].

The initial therapy for most children with Wilms tumor is radical nephrectomy. However this approach of initial radical nephrectomy is not followed in children with bilateral tumors. These children receive preoperative chemotherapy with the goal of tumor shrinkage and then undergo nephron (renal) sparing surgery (NSS) [2]. Preservation of renal tissue is important to decrease the incidence of renal failure, which approaches 15 % at 15 years post-treatment in patients with bilateral Wilms tumor [3,4]. Currently unilateral Wilms tumor associated with predisposing syndromes are treated with a strategy that mirrors the approach followed for children with bilateral tumors or neoplasms arising in a solitary kidney [2–4]. However several centers, have also explored the role of Nephron-sparing procedures in children with unilateral

R. B. Nerli (✉) · V. C. Pujar · S. M. Jali · S. S. Joshi ·
S. C. Hiremath · A. K. Guntaka
KLES Kidney Foundation, KLES Dr Prabhakar Kore Hospital &
MRC, Belgaum, Karnataka, India
e-mail: director@kleskf.org
URL: <http://www.kleskf.org>

M. B. Hiremath
Department of Studies in Biotechnology & Microbiology,
Karnatak University, Dharwad, India

R. B. Nerli
Department of Urology, KLE University's JN Medical College,
Belgaum 590010, India

non-syndromic Wilms tumors [5–7]. The primary motivation for this approach is concern about late occurrence of renal dysfunction after unilateral nephrectomy. We report our initial experience with NSS for unilateral non-syndromic Wilms tumor (Figs. 1, 2 and 3).

Materials and Methods

We reviewed the records of nine children who underwent nephron sparing surgery for unilateral, nonsyndromic Wilms tumors at our Hospital during the 12-year period from Jan 2000 through Jan 2012. Patient demographics, including congenital anomalies, tumor histology, surgical procedure and outcomes (including surgical complications, long-term renal function, tumor recurrence, and survival), were determined from a review of each patient's medical record. This retrospective review and study was approved by the Institutional Review Board of our Hospital.

All patients received preoperative chemotherapy with two drugs (vincristine, and dactinomycin) following confirmation of diagnosis on needle biopsy. This approach was within the scope of the recommended **SIOP** guidelines. After an initial treatment with preoperative chemotherapy for 4 to 6 weeks, patients underwent tumor resection. Subsequent renal function was assessed by estimating the glomerular filtration rate using the Schwartz formula: $\text{creatinine clearance} = (k \times \text{height in cm}) / \text{serum creatinine}$, in which $k = 0.55$ for children aged > 18 months, and $k = 0.45$ for children aged < 18 months. Other measures of long-term renal function included blood pressure evaluation and the need for antihypertensive medications, the presence of proteinuria, and the need for dialysis and/or kidney transplantation. Post-operatively all children received chemotherapy as per protocol.

Our operative approach was similar to the ones reported in literature [5–7]. The peritoneal cavity was entered through a chevron or transverse upper abdominal incision. The colon was released and the kidney was mobilized completely and elevated on its vascular pedicle with vessel loops. Hypothermia with surface cooling was created using ice slush in all cases. Perirenal fat lying directly on top of the tumor was left intact as much as possible to ensure negative margins and decrease chances of tumor surface disruption. The lesion was identified by palpation. Resection proceeded in a plane of normal appearing parenchyma (including the dissection plane commonly seen after chemotherapy with development of a pseudocapsule) to ensure negative surgical margins, which were verified by frozen section of the renal bed and specimen margins. If the collecting system was entered, it was closed with absorbable sutures and a double J stent was inserted. The resulting defect was approximated by interrupted absorbable sutures through the renal capsule, using Surgicel®.

Results

During the study period children underwent treatment for Wilms tumor at our center. Of these nine children with a mean age of 19.66 ± 14.37 months at diagnosis and presenting with unilateral non-syndromic Wilms tumor underwent nephron sparing surgery. All these children had stage I tumors and histology was confirmed on histopathological examination of the needle biopsy specimen. All these children had favourable histology Wilms tumor (Table 1).

Following pre-operative chemotherapy, all the tumors showed massive shrinkage of the tumor ($> 50\%$). There were no serious complications noted during the pre-operative chemotherapy period. All children underwent a post-chemotherapy CT imaging. A total of seven patients underwent partial nephrectomy (PN) and the remaining two underwent hemi-nephrectomy (HN) after Chemotherapy. Of the seven PN cases, two had a lower pole tumor and five had an upper pole tumor. Both the cases of hemi-nephrectomy had well defined lower polar tumors. In all nine children, the renal plane of resection showed a tumor-free margin. No major intra/post-operative complications were noted. Three children received intra-operative blood transfusions, whereas two other children received post-operative blood transfusions.

All the nine children had stage I disease and tumor recurrence in the same kidney was found in none of the patients in the follow-up period. A metachronous tumor in the contralateral kidney was similarly not seen during the follow-up period. The mean follow-up period was 22.33 ± 11.12 months. Post-operatively all received chemotherapy as per the protocol and underwent evaluation and imaging as needed. Post-operative serum creatinine repeated at the end of 3 months revealed maintenance of good renal function in all children.

In the follow-up period all children were assessed for blood pressure. None of the children have been advised use of anti hypertensive medications.

Discussion

Wilms tumor accounts for 6 % to 7 % of all childhood cancers. In children less than 15 years of age, the annual incidence rate is about 7 to 10 cases per million [1]. More than 80 % of cases are diagnosed before 5 years of age, with a median age of 3.5 years. Nevertheless, older children and, occasionally, even adults can be affected [8]. The median age at diagnosis is lower in children with bilateral Wilms tumor [1]. Wilms tumor presents at an earlier age among males with both unilateral and bilateral tumors [1]. Approximately 5 % to 7 % of these patients will have disease in both kidneys [9]. Several studies have demonstrated that patients with bilateral Wilms tumor are at risk for developing renal failure [10–12]. A review from the National Wilms Tumor Study Group (NWTSG) indicated

Fig. 1 Twelve month old female child presented with left renal mass. **a** CT scan showing left renal mass (pre chemotherapy). **b** CT scan showing shrinkage of left renal mass following preoperative chemotherapy. **c** CT scan following post left partial nephrectomy

Fig. 2 Operative photographs. **a** Left kidney with Wilms tumour. **b** Left kidney following partial nephrectomy. **c** Approximation of remanent renal parenchyma. **d** Specimen of partial nephrectomy

Fig. 3 Eight months female child presented with left renal mass. **a** Prechemotherapy CT scan revealing a huge mass. **b** Specimen of partial nephrectomy

that, among patients who had unilateral Wilms tumor without genitourinary abnormalities, Denys-Drash syndrome, or Wilms tumor-aniridia-genitourinary abnormality- mental retardation (WAGR) syndrome, the cumulative incidence of renal failure was only 0.6 %. However, in patients who had bilateral disease, the incidence of renal failure was 11.5 %, and patients with Denys-Drash and WAGR syndromes had an incidence > 50 % [4]. This is probably due to mutation of WT1, which is necessary for normal development [1]. The exact etiology of renal failure is not always clear and is likely to be multifactorial, with contributing factors including intrinsic, progressive renal disease related to a genetic predisposition, inadequate renal parenchyma after one or more tumor resections, the nephrotoxic effects of chemotherapy and radiation, and the potential for hyperfiltration injury to the remaining renal parenchyma [4,11].

The management of synchronous, bilateral Wilms tumors has evolved from primary kidney resection to renal-preserving surgical approaches facilitated by the use of preoperative chemotherapy. In 1979, the NWTSG formally recommended

initial biopsy and chemotherapy before surgical resection of bilateral tumors [13]. Since then, several studies have confirmed the beneficial effects of preoperative chemotherapy followed by conservative surgical resection in patients with amenable, favorable histology, bilateral Wilms tumors [14–16]. In the NWTSG-4, 36 of 186 patients (19.4 %) with synchronous, bilateral Wilms tumors underwent bilateral nephron-sparing procedures [17]. Other smaller series have reported performing bilateral nephron-sparing procedures in from 30 to 70 % of patients with bilateral Wilms tumors [2,14,18]. Davidoff et al [19] reported on the feasibility and outcome of nephron sparing surgery (NSS) in ten children with bilateral Wilms tumor. The complications were minimal and long term renal function and survival were excellent. Similarly Millar et al [19] reported on their experience of 23 children with bilateral Wilms tumor who underwent initial biopsy, neoadjuvant chemotherapy and tumorectomy. Twelve children were alive and free of disease one to 15 years after treatment, with well preserved renal function (lowest GFR 65 ml/min per 1.73 m²). They concluded that children

Table 1 Patient characteristics

No	Age at presentation (months)	size of tumor at presentation on CT (cms)	Post-chemotherapy size of tumor on CT (cms)	Nature of surgery	Intra operative blood loss (cc)	Post-op chemotherapy (weeks)	Sr. Creatinine at 3 months follow-up (mg%)	Creatinine clearance at 12 months follow-up ml/min	Follow-up (months)
1	8	11×7	6×3	Partial Nephrectomy (PN)	40	12	0.4	77.2	49
2	11	12×8	5×3	(PN)	50	32	0.6	54.6	24
3	6	11×7	5×3	(PN)	40	32	0.5	72.2	24
4	23	10.8×6	4×5	(PN)	50	32	0.5	76.9	24
5	25	8×5	3×2	Hemi-nephrectomy (HN)	50	12	0.4	97.4	23
6	18	6×4	3×2	(HN)	40	12	0.4	90.7	16
7	18	12.5×8	7.5×6.8	(PN)	40	32	0.4	90.7	15
8	54	10×6	4.5×4	(PN)	60	32	0.5	95.5	14
9	14	7.8×6.5	3×2	(PN)	40	32	0.4	85.9	12

undergoing nephron sparing surgery could achieve good results with preservation of adequate renal function, unfavourable histology did not have a reduced survival and that metastatic spread outside the kidney carried a poor prognosis.

Romao et al [20] described their experience with nephron sparing surgery for unilateral Wilms tumor in children with predisposing syndromes, who are at risk for metachronous lesions. Eight of the 13 children with predisposing syndromes had unilateral tumors. Of these eight children, six underwent nephron sparing surgery and all had favorable histology Wilms tumor. No recurrences were noted after a mean follow-up of 36 months and all children had normal creatinine. They opined that nephron sparing surgery was safe, with preservation of renal function and good oncologic outcome in children with unilateral Wilms tumor associated with predisposing syndromes. Nephron sparing surgery in patients with Wilms tumor and predisposing syndromes remains largely unreported. It makes sense to consider this approach in children who have a longer life expectancy and cumulative risk of renal insufficiency [21].

Several publications have also addressed the role of nephron sparing surgery for non-syndromic Wilms tumor, performed in the setting of SIOP (Societe Internationale d'Oncologie Pediatrique) protocols [5,6,16], with the conclusion that NSS is an option for carefully selected patients with Wilms tumor, ie stage I tumors with low or intermediate risk histology, no local invasion to vessels or collecting system and good response to chemotherapy [5]. The COG (Children's oncological group) has proposed a renal-sparing protocol for select patients with unilateral Wilms tumors. These include patients known to be at risk for bilateral disease or those at increased risk for renal failure. These patients will be managed with a strict surgical protocol to minimize risk for residual disease [16]. The lesion should be completely excised with a margin of normal renal parenchyma. These patients should not undergo partial nephrectomy if the tumor cannot be removed as a stage I entity. Patients with high-risk histologic patterns, such as anaplasia or persistent blastema-predominant tumor after chemotherapy, should be treated with complete nephrectomy because these tumors have resistance to chemotherapy. Haecker et al [5] evaluated results and long-term outcome after partial nephrectomy (PN) for unilateral Wilms tumor in relation to different histological features, performed as initial surgery or after induction chemotherapy. A total of 770 patients underwent TN and 37 underwent PN. Tumor stage, overall survival of 93 % and relapse-free survival of 88 % were equal after PN and Total Nephrectomy in analysis of the whole group. **Our study too revealed that NSS is safe and effective option in the management of unilateral non syndromic Wilms tumor. However, long term results in relation to oncological safety and preservation of renal function needs to be assessed. The small number of**

patients in our study remains the main drawback. Moorman-Voestermans et al [22] retrospectively analyzed 90 consecutive cases of histologically verified Wilms Tumors who were treated at their center and concluded that Partial nephrectomy was safe in approximately 10 % of Wilms' tumor patients and that the function of the kidney remnant remains well, and even permits contralateral nephrectomy.

Conclusions

Nephron sparing surgery is a safe and effective option in the management of **early stage** unilateral non-syndromic Wilms tumor. It is oncologically safe and does not lead to decreased local tumor control **during short term follow-up. The residual function of the kidney is adequately maintained as determined by creatinine clearance.**

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