Case Report

Nephron-sparing surgery in bilateral Wilms' tumor: A report of two cases

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Abstract

Nephron-sparing surgery (NSS) has been proposed by many as an alternative to bilateral nephrectomies and renal replacement therapy in bilateral Wilms' tumor (BWT). NSS is not without significant recurrence, morbidity, and mortality. Long-term follow-up, especially with regard to the renal function, remains lacking. Preoperative computed tomography angiogram can help prepare a roadmap for NSS but can underestimate the salvageable parenchyma due to compression of normal adjacent parenchyma. Intraoperative ultrasound can delineate the boundary of surgical margin and help achieve negative margins. We present two cases of BWT, aged 7 and 13 months, managed with neoadjuvant chemotherapy followed by bilateral NSS and adjuvant chemotherapy and report the follow-up of the same. We also explore the role of preoperative imaging and intraoperative ultrasound in the management. Both patients are alive without recurrence at a follow-up of 12 and 8 months.

Key Words: Neoadjuvant chemotherapy, nephron-sparing surgery, Wilms' tumor

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INTRODUCTION

Five to seven percent of all Wilms' tumors are bilateral. Treatment protocols developed by the National Wilms' Tumor Study (NWTS), Children's Oncology Group (COG), and European International Society of Pediatric Oncology have led to significantly improved survival.[1] Nephron-sparing surgery (NSS) has been proposed as an alternative to bilateral nephrectomies and renal replacement therapy in these cases. With NSS, 5-year survival rates are >90%.[2] However, it may be associated with renal insufficiency and/or need for dialysis in around 23% of the patients.[3] Recurrence is thrice more common in NSS than total nephrectomy, around 13%.[4] The use of intraoperative ultrasound may help in better identification of tumor margins; however, subsequent modification of the surgical management may not translate into improved survival.[5] NSS should be performed wherever possible but for tumors where it may not be possible to preserve adequate renal parenchyma oncological principles should be followed and total nephrectomy must be performed; NSS can be performed on the contralateral side. Since 25–33% of one kidney avoids the need for dialysis, unilateral NSS for bilateral disease may be sufficient.[6]

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Despite being effective, NSS is not without significant recurrence, morbidity, and mortality. Long-term follow-up, especially with regard to renal function, remains lacking. Whether to stage the bilateral procedure and which kidney to be operated first, both remain a subject of debate.[1] Literature on the amount of renal parenchyma to be left in NSS in children is lacking. We present two cases of bilateral Wilms' tumor (BWT) managed with neoadjuvant chemotherapy followed by bilateral NSS.

CASE REPORTS

Case 1

A 7-month-old male child presented with a right abdominal lump for 1 month. Ultrasonography revealed a hyperechoic space-occupying lesion (SOL) arising from the upper pole of the right kidney. Another SOL was seen in the left kidney. Serum creatinine was 0.4 mg%. Contrast-enhanced computed tomography scan (CECT) revealed a 7.8 cm × 7.2 cm × 8.0 cm heterogeneously enhancing mass in the upper pole of the right kidney with hypodense areas suggestive of necrosis. Another similar lesion was seen in the lower pole. The left kidney revealed multiple similar hypodense lesions in the upper pole, largest 2.5 cm × 1.5 cm [Figure 1a].

Right-sided biopsy revealed spindle cells with skeletal muscle differentiation suggestive of Wilms' tumor with rhabdomyomatous differentiation. Five cycles of neoadjuvant actinomycin D, vincristine (VCR), and doxorubicin (DOX) chemotherapy were given. Postchemotherapy CECT showed partial response [Figure 1b]. Glomerular filtration rate (GFR) was 54 mL/min for the left kidney and 46 mL/min for the right kidney.

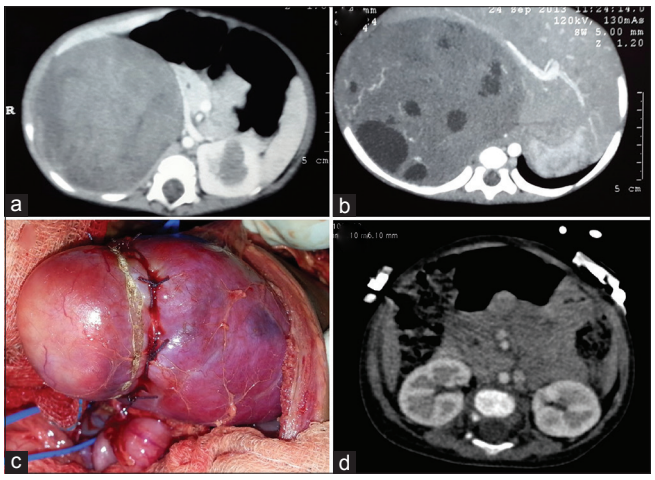

Figure 1: Case 1: (a) preoperative contrast-enhanced computed tomography scan showing bilateral renal masses, (b) postchemotherapy computed tomography scan showing necrosis within the lesions, (c) intraoperative image of nephron-sparing surgery, and (d) postoperative contrast-enhanced computed tomography scan image showing the residual renal parenchyma

The patient underwent open left partial nephrectomy [Figure 1c]. Histopathology revealed multicentric Wilms' tumor, favorable histology with stromal predominance, confined to the capsule. Open right partial nephrectomy was done after 1 month. Histopathology revealed Wilms' tumor with extensive rhabdomyomatous differentiation and negative surgical margins. Dimercaptosuccinic acid (DMSA) scan after bilateral partial nephrectomy showed a split function of 40% for the right and 60% for the left kidney. Postoperative GFR was 45 mL/min for the left kidney and 31 mL/min for the right kidney. The patient received 24 cycles of adjuvant chemotherapy and is on regular follow-up with no recurrence till date (24 months) [Figure 1d].

Case 2

A 13-month-old male child presented with a right-sided abdominal lump for 1 month. Ultrasound revealed a hyperechoic SOL in the right kidney measuring 6 cm × 6 cm replacing whole of the renal parenchyma and a left upper pole renal SOL of 2 cm × 2 cm. Serum creatinine was 0.4 mg%. CECT revealed multiple rounded well-defined lesions, replacing whole of upper and mid pole parenchyma on the right side, largest measuring 8 cm × 7 cm × 5 cm, with interspersed hypodense areas [Figure 2]. The left kidney had a solitary upper pole renal mass, 3 cm × 3 cm × 3 cm in size. GFR was 45 mL/min for the left kidney and 23 mL/min for the right kidney.

Right renal mass core biopsy revealed Wilms' tumor with predominantly epithelial component. Four cycles of neoadjuvant chemotherapy were given as per NWTS protocol.

Postchemotherapy computed tomography (CT) scan showed partial response with the largest mass of 6 cm × 6 cm × 5 cm at the upper pole of the right kidney and a 2.3 cm × 1.5 cm mass at the upper pole of the left kidney. Two additional cycles of neoadjuvant chemotherapy were given.

A left partial nephrectomy was done. Histopathology showed predominantly epithelial Wilms' tumor confined to the capsule. Postoperative serum creatinine was 0.6 mg%. Six additional cycles of chemotherapy were planned, but the patient had

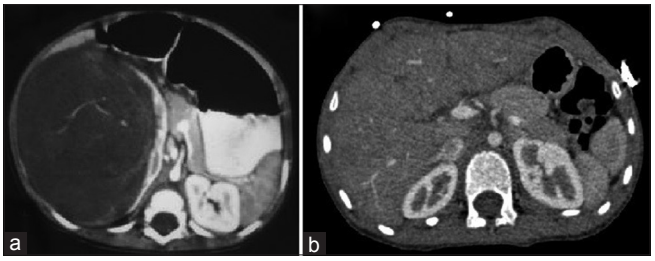

Figure 2: Case 2: (a) preoperative contrast-enhanced computed tomography scan showing the large right renal mass before chemotherapy and (b) postoperative contrast-enhanced computed tomography scan image showing the residual renal parenchyma. The right kidney is smaller and atrophic

chemotherapy intolerance with severe neutropenia which was managed conservatively. A right partial nephrectomy was done 1 month later, revealing epithelial predominant Wilms' tumor with positive margins. DMSA scan after bilateral partial nephrectomy showed a nonvisualized right kidney and a small left kidney. Twenty-four cycles of adjuvant chemotherapy in addition to adjuvant radiotherapy were given. At 20 months of follow-up, the serum creatinine remains at 0.6 mg% without any recurrence. Postoperative GFR was 35 mL/min for the left kidney whereas the right kidney was nonfunctioning.

Both patients have completed chemotherapy and are beyond 20 months of follow-up. They are followed with 3 monthly serum creatinine, blood pressure monitoring, and urine protein measurement. CECT is done at 6-month intervals for up to 5 years and annually thereafter.

DISCUSSION

Current COG protocol for patients with BWT recommends neoadjuvant chemotherapy with VCR, DOX, and dactinomycin followed by repeat imaging at 6 weeks.[7] If the tumor reduces by 50% or more, an NSS is done otherwise bilateral open biopsy followed by additional chemotherapy is given till a maximum of 12 weeks.[1] The objective of NSS is to preserve maximum functional renal tissue with complete tumor removal.

Radiologic assessment has a sensitivity, specificity, and accuracy of 87%, 97%, and 93%, respectively,[8] but has the potential to underestimate the salvageable renal parenchyma due to the volume effect of large masses.

Many have operated the kidney with a larger tumor burden first[8] while others have operated the less involved kidney first in anticipation of a possible radical nephrectomy on the other side.[9] Most, however, prefer NSS bilaterally during a single stage.[8,9] In both cases, we did a partial nephrectomy on the less involved kidney first.

Positive margins are associated with an increased risk of local recurrence.[10] In a study by Davidoff *et al*., positive margins were present in 14% of tumors after enucleation.[8] Intraoperative frozen sections also help in obtaining negative margins. Local recurrence after NSS ranges from 0% to 6% with overall survival of 50–100%.[7] Both of our cases are alive, without any recurrence till date. A recurrent tumor is usually manageable with adjuvant chemotherapy, especially if it is a favorable histology tumor. In the presence of anaplasia, positive surgical margins and subsequent recurrence (local or distant) would be associated with decreased survival. User *et al*. have shown that all the patients who developed metastasis and recurrence died from the disease while none of the survivors had a metastasis or recurrence.[11] This may indirectly suggest that recurrence is associated with poor survival. Intraoperative ultrasound can delineate the hilar anatomy and surgical margins as well.[12] It was used in one of our cases to obtain negative margins. Renal mass must be excised completely with a margin of normal renal parenchyma.[9] For massive tumors, sometimes it may not be possible to preserve adequate renal parenchyma if a conventional partial nephrectomy is one. Instead, tumorectomy can be performed preserving a thin peripheral rim of renal parenchyma although the rate of recurrence in such an endeavor may be up to 50%.[13] The positive margins after NSS may require re-resection in up to 22% of the patients and a third procedure may be needed in 5% of the patients.[14] Adjuvant radiotherapy is the standard treatment for patients with positive surgical margins.

The complications of NSS include pyelonephritis, urinary leak, bleeding, hypertension, renal insufficiency, and disease recurrence. Pyelonephritis responds to conservative management with broad spectrum antibiotics. A urinary leak is generally small and responds to observation alone or placement of a double J stent. Bleeding and hematoma may warrant exploration while hypertension which is multifactorial in most instances requires medical management. Loss of renal mass from surgery is a significant factor in the development of end-stage renal disease (ESRD) in these cases, though other factors such as nephrotoxicity from chemoradiation and intrinsic renal disease also contribute.[7] NWTS data show the incidence of ESRD of 10% in BWT compared to 0.7% in unilateral Wilms' tumor.[15] For renal insufficiency, the patient is managed with dialysis as per the standard indications. With NSS for bilateral tumors as large as 10 cm on each side, the postoperative GFR is usually well preserved in most patients, being >60 mL/1.73 m^2/min.[13] The overall survival is also around 90% for adequately resected tumors.[3] In our patients, the renal function is normal in both patients till date. Although NSS is now commonly attempted for bilateral disease, one may not be able to save the nondiseased parenchyma in all cases. The loss of uptake by the right kidney on DMSA in the second case represents nonsalvageability of the kidney. It requires conservative treatment and observation alone is sufficient. If the remaining parenchyma needs removal, such as for a local recurrence, then a standard exploration is needed. Adult data recommend a functioning renal remnant of at least 20% of one kidney to avoid ESRD.[16] This approximately corresponds to one major calyx or the area supplied by one segmental artery. Long-term studies with NSS in adults have suggested improved long-term renal function, cardiovascular health, decreased osteoporosis, and increased overall survival while maintaining equivalent oncological outcomes.[16,17] More data in the pediatric population are needed to see if the results

in adults can be replicated in this group as well. Vanden Berg *et al.* performed a review of 66 studies on surgery for BWT. Only 33 studies where NSS was performed reported tumor recurrences and the mean was 12%.[18] In another study by User *et al.,* 20 children with BWT were followed up for a median duration of 5.8 years (range 6 months to 14 years).[11] Of those who survived, there were no recurrences while there were two recurrences among the seven patients who died from the disease. It was further suggested that with effective adjuvant radiation and chemotherapy, positive surgical margins might not actually lead to higher locoregional recurrence. Most of the studies on NSS have been single-center experiences of a small number of patients so drawing a definitive conclusion may not be possible.[11]

We have presented a small experience of two cases of BWT managed with chemotherapy and NSS. The number of cases is not sufficient to draw a conclusion or a recommendation which is the greatest limitation. Another limitation is the short follow-up period of up to 2 years which may not be sufficient as late recurrences are known.

To conclude, bilateral NSS is a viable, safe, and effective treatment in BWT. Radiological assessment of the feasibility of NSS has a high sensitivity, specificity, and accuracy; however, it can underestimate the amount of salvageable parenchyma. Contrast CT with CT angiogram prepares the road map for subsequent surgery. Intraoperative ultrasound can delineate the tumor in relation to hilar anatomy and demarcate surgical margin and thus help preserve maximum parenchyma with negative margins.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Sulkowski J, Kolon T, Mattei P. Nephron-sparing partial nephrectomy for bilateral Wilms' tumor. J Pediatr Surg 2012;47:1234-8.
2. Kieran K, Davidoff AM. Nephron-sparing surgery for bilateral Wilms tumor. Pediatr Surg Int 2015;31:229-36.
3. Giel DW, Williams MA, Jones DP, Davidoff AM, Dome JS. Renal function outcomes in patients treated with nephron sparing surgery for bilateral Wilms tumor. J Urol 2007;178(4 Pt 2):1786-9.
4. Wilde JC, Aronson DC, Sznajder B, Van Tinteren H, Powis M, Okoye B, *et al.* Nephron sparing surgery (NSS) for unilateral wilms tumor (UWT): The SIOP 2001 experience. Pediatr Blood Cancer 2014;61:2175-9.
5. Bhosale PR, Wei W, Ernst RD, Bathala TK, Reading RM, Wood CG, *et al.* Intraoperative sonography during open partial nephrectomy for renal cell cancer: Does it alter surgical management? AJR Am J Roentgenol 2014;203:822-7.
6. Uzzo RG, Novick AC. Nephron sparing surgery for renal tumors: Indications, techniques and outcomes. J Urol 2001;166:6-18.
7. Harel M, Makari JH, Ferrer FA Jr. Oncology: The role of partial nephrectomy in Wilms tumor. Curr Urol Rep 2013;14:350-8.
8. Davidoff AM, Giel DW, Jones DP, Jenkins JJ, Krasin MJ, Hoffer FA, *et al.* The feasibility and outcome of nephron-sparing surgery for children with bilateral Wilms tumor. The St Jude Children's Research Hospital experience: 1999-2006. Cancer 2008;112:2060-70.
9. Fuchs J, Szavay P, Seitz G, Handgretinger R, Schäfer JF, Warmann SW. Nephron sparing surgery for synchronous bilateral nephroblastoma involving the renal hilus. J Urol 2011;186:1430-6.
10. Ritchey ML, Shamberger RC. Nephron sparing surgery for Wilms' tumor. J Urol 2011;186:1179-80.
11. User IR, Ekinci S, Kale G, Akyüz C, Büyükpamukçu M, Karnak I, *et al.* Management of bilateral Wilms tumor over three decades: The perspective of a single center. J Pediatr Urol 2015;11:118.e1-6.
12. Polascik TJ, Meng MV, Epstein JI, Marshall FF. Intraoperative sonography for the evaluation and management of renal tumors: Experience with 100 patients. J Urol 1995;154:1676-80.
13. Agarwala S, Mittal D, Bhatnagar V, Srinivas M, Bakhshi S, Bajpai M, *et al.* Management and outcomes in massive bilateral Wilms' tumors. J Indian Assoc Pediatr Surg 2014;19:208-12.
14. Kieran K, Williams MA, McGregor LM, Dome JS, Krasin MJ, Davidoff AM. Repeat nephron-sparing surgery for children with bilateral Wilms tumor. J Pediatr Surg 2014;49:149-53.
15. Lange J, Peterson SM, Takashima JR, Grigoriev Y, Ritchey ML, Shamberger RC, *et al.* Risk factors for end stage renal disease in non-WT1-syndromic Wilms tumor. J Urol 2011;186:378-86.
16. Cost NG, Lubahn JD, Granberg CF, Sagalowsky AI, Wickiser JE, Gargollo PC, *et al.* Pathological review of Wilms tumor nephrectomy specimens and potential implications for nephron sparing surgery in Wilms tumor. J Urol 2012;188 4 Suppl: 1506-10.
17. Kopp RP, Dicks BM, Goldstein I, Mehrazin R, Silberstein JL, Colangelo CJ, *et al.* Does radical nephrectomy increase the risk of erectile dysfunction compared with partial nephrectomy? A cohort analysis. BJU Int 2013;111:E98-102.
18. Vanden Berg RN, Bierman EN, Noord MV, Rice HE, Routh JC. Nephron-sparing surgery for Wilms tumor: A systematic review. Urol Oncol 2016;34:24-32.