Management of Bilateral Wilms' Tumor: Our Experience

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Abstract Management of bilateral Wilms' tumor is particularly challenging, considering the chances of recurrence and long-term renal function for affected patients. Aggressive surgical resection to prevent recurrence must be balanced with the desire to preserve renal function. We evaluated our experience in the management of bilateral Wilms' tumor stressing the challenges encountered in decision making and the role of nephron sparing surgery. We had four children presenting with bilateral Wilms' tumor. All of them were appropriately staged and given standard chemotherapy as per NWTS-5 guidelines. Tumors were considered to have a 'good' response to chemotherapy if sufficient tumor shrinkage was observed so that renal hilum was seen free of tumor and vice versa. Nephron-sparing surgery was considered in all and was performed when feasible, followed by completion adjuvant chemotherapy. All patients were followed up with serial ultrasound scans (3–6 monthly) and CECT abdomen (yearly once). Blood urea and serum creatinine, hypertension, and proteinuria were assessed during follow-up visits. All four children received neo-adjuvant chemotherapy as per NWTS-5 guidelines. The first child had poor response to chemotherapy and was considered for left radical and right partial nephrectomy. However, patient attenders refused any surgical intervention and the child was taken home. The second child had a 'good' response

on left side and was planned for left partial and right radical nephroureterectomy based on pre-operative imaging analysis. However, intra-operatively, bilateral partial nephrectomy with good margins was feasible. The third child though, showed 'poor' response to pre-op chemotherapy and warranted bilateral nephroureterectomy, right partial and left radical nephroureterectomy was feasible. However, in the fourth child, we were not able to perform nephron sparing surgery and left nephroureterectomy with right tumor biopsy was done. Following this, child was started on 2nd-line chemotherapy, now awaiting right partial nephrectomy. The second child is on follow up for 1.5 years, doing well. However, the third child expired 1.5 years following surgery due to recurrence (lung metastasis). Management of bilateral Wilm's tumor is challenging and nephron-sparing surgery should be considered in all patients having bilateral Wilm's tumor with favorable histology, even if pre-operative imaging studies suggest that the lesions are unresectable.

Keywords Bilateral Wilm's tumor · Nephron sparing surgery

Introduction

Synchronous bilateral nephroblastoma occurs in about 5 % of children with Wilm's tumor, with metachronous lesions developing in 1 % [1, 2]. Treatment of such patients is a challenging problem, where one has to balance between cure following radical nephrectomy and preservation of renal function. Recent reports from NWTS indicate that the incidence of renal failure in patients with bilateral Wilms' tumor without associated anomalies is 11.5 at 20 years [3], the most common cause being the need for bilateral nephrectomy for persistent or recurrent tumor in the remaining kidney after initial

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nephrectomy [4]. A lot of literature regarding the role of nephron-sparing surgery in the management of BWT is available, but none from India so far [1–5]. We would like to share our small experience in the management of these children.

Materials and Methods

Four children who had presented with bilateral Wilms' tumor between Jan. 2013 and Jan. 2015 to our institute were reviewed. Medical records, operative reports and pathology findings were re-examined. Patient's age at diagnosis, associated congenital syndromes or anomalies, hypertension at diagnosis and initial renal function (Blood urea and serum creatinine) were documented. All children were appropriately staged and given standard chemotherapy as per NWTs 5 guidelines. Tumors were considered to have 'good' response to chemotherapy if sufficient tumor shrinkage was observed so that renal hilum was seen free of tumor and vice versa. Nephron-sparing surgery was considered in all and was performed when feasible, followed by completion chemotherapy. All patients were followed up with serial ultrasound scans (3–6 monthly) and CECT abdomen (yearly once). Blood urea and serum creatinine, hypertension, and proteinuria were assessed during follow-up visits. All cases of BWT were attempted partial nephrectomies rather than enucleation when possible, with inclusion of a rim of grossly uninvolved renal parenchyma along with the resected tumor.

Case 1

A 1.4-year-old male child presented with bilateral Wilms' tumor (left > right) without any syndromic features. Poor response was noted to chemotherapy. Child was planned for left radical and right partial nephrectomy. However, they were explained that bilateral nephrectomies may be needed and child might require dialysis till future transplant. But, patient attenders refused any surgical intervention in spite of explaining to them that all charges related to surgery, hospital stay, and future dialysis would be waived off. Child was taken against medical advice.

Case 2

A 1.5-year-old boy presented with bilateral Wilms' tumor, without any syndromic features. Good response was noted to pre-op chemotherapy on left side, while poor response was noted on right side; hence was planned for left partial and right radical nephroureterectomy. However, on table,

we were able to perform bilateral partial nephrectomies. Post-operatively, child had an uneventful recovery except for transient urinary leak and hypertension along with raised blood urea and serum creatinine, which gradually settled. Histo-pathological evaluation revealed bilateral classic Wilms' tumor with favorable histology with negative margins. Following this, child completed chemotherapy and is on follow-up since 1.5 years, doing well.

Case 3

The 3rd child was 2.5-year-old and presented with bilateral Wilms' tumor (left > right), without any syndromic features (Figs. 1 and 2).

The child did not show any response to chemotherapy. The child was planned for left radical and right partial nephroureterectomy. Option of bench surgery with auto-transplant were also considered for the right side if required (Figs. 3 and 4).

Initially, the right kidney was approached. Intra-operatively, a good margin was achieved and partial nephrectomy was possibly sparing the upper pole. Left nephroureterectomy was done (Figs. 5 and 6).

Child completed adjuvant chemotherapy and was on follow up. Unfortunately, he presented with massive pulmonary metastasis and finally expired 1.5 years following surgery. However, child did not have any recurrence at the operated site and his blood urea and serum creatinine levels were within normal limits. Perhaps, this could be due to flaring up of some micro metastasis in the lungs, not responding to chemotherapy.

Fig. 1 Clinical presentation

Fig. 2 CT scan findings after chemotherapy

Case 4

Our 4th child was a two-year-old female who received pre-op chemotherapy with poor response. Intra-operatively, nephron-sparing surgery was not amenable due to massive tumor. Hence, left nephroureterectomy with right renal biopsy was done with a hope that the right-sided tumor may become amenable for partial nephrectomy following second-line chemotherapy. HPE was consistent with bilateral classic Wilms's tumor with favorable histology. The child was started on

Fig. 3 Intra-op finding (right side)

Fig. 4 Vessels being isolated

second-line chemotherapy, presently awaiting right partial nephrectomy.

Discussion

Although synchronous BWT accounts for only 5 to 7 % of all Wilms tumors, they represent a particular challenge to practitioners involved in treating these patients. Treatment of such

Fig. 5 Tumor tissue resected

Fig. 6 Excised specimen

patients should balance the desire of positive oncological outcomes achieved through aggressive surgical resection and adjunctive therapies with maintenance of long-term renal function of potential cancer survivors. Because studies have demonstrated that patients with bilateral Wilm's tumor are at higher risk for renal failure [3], the management of BWT has successfully evolved from primary renal extirpation to renal preserving surgical approaches augmented by pre-operative chemotherapy.

Bishop and Hope first recommended a conservative surgical approach with initial biopsy and chemotherapy before surgical resection [5]. In 1979, NWTs-3 formally recommended initial biopsy and chemotherapy before surgical resection of bilateral tumors [6]. Since that time, multiple studies have confirmed the beneficial effects of neo-adjuvant chemotherapy followed by conservative surgical resection in amenable, favorable histology BWT cases [7, 8]. This demonstrates that pre-operative chemotherapy allows tumor shrinkage, leading to easier resection with preservation of unaffected parenchyma as well as decreased tumor spillage. This approach has resulted in an overall decrease in the incidence of renal failure in BWT, as evidenced by the fact that the renal failure rate in NWTs-1 and NWTs-2 was 16.4 % compared with 3.8 % in NWTs-4 [4].

Partial nephrectomy for renal lesions dates back as far as 1884, when Wells described a technique for removing perirenal fibrolipoma [9]. In 1887, Czerny was the first to perform partial nephrectomy as therapy for renal malignancy [10]. However, excessive postoperative morbidity limited its application until the 1950s, when Vermooten suggested that peripheral encapsulated renal neoplasms should be locally

excised, leaving a margin of normal parenchyma around the tumor [11].

Enthusiasm for nephron-sparing surgery has been stimulated by several trends, including advances in renal imaging, improved surgical techniques and methods to prevent ischemic renal injury, better postoperative management, such as renal replacement therapy, and long-term prospective cancer-free survival data. Extended experience has now established that nephron-sparing surgery may be performed safely with low morbidity, preservation of renal function, a low local recurrence rate, and high patient satisfaction [12].

Various techniques to carry out nephron-sparing surgery have been described including enucleation, enucleo-resection (enucleation of the tumor with a rim of healthy parenchyma), segmental or partial nephrectomy (superior or inferior), wedge resection of the tumor, transverse resection of the tumor (for centrally located tumors), and extra-corporeal bench surgery with auto transplantation [13].

Presently, nephron-saving surgery is indicated in all settings of localized malignancies that would render the patient otherwise anephric with a subsequent immediate need for renal replacement therapy. Apart from this, it is also indicated in tumors involving a solitary kidney, bilateral renal involvement, and contralateral renal impairment [3]. Nephron-sparing surgery should also be attempted in select patients with a solid renal mass in whom the contralateral kidney is threatened by local, systemic, or genetic conditions that may affect future function or the likelihood of subsequent contralateral tumors [14].

While nephron-saving surgery leads to the possibility of positive margins, which causes concern for potentially higher recurrence rates from an oncological standpoint, it was shown that positive surgical margins do not invariably lead to local recurrence [15], reflecting the chemosensitivity and radiosensitivity of Wilm's tumor. Rather, the ability to leave the patient with functioning renal parenchyma in those with favorable histology BWT has given physicians the opportunity to maintain cure rates without sacrificing overall renal function.

Nephron-sparing surgery has its share of complications including urinary leak (1.4–17.4 %), acute or delayed hemorrhage (1.3–7.9 %), acute renal failure (1.3–12.7 %), and chronic renal insufficiency [16]. However, these complications have declined in the last decade owing to better patient selection, operating techniques, perioperative care, and surgical experience. Renal failure is often multifactorial in its etiology, resulting from intra-operative ischemia, recurrent tumor requiring further resection, an inadequate amount of remaining renal parenchyma, and the potential for hyperfiltration injury, nephrotoxic effects of chemotherapy and radiation, and a congenital predisposition to renal function abnormalities [3].

Though nephron-sparing surgery is not possible in all cases, an attempt should be made to do so without compromising with the margins. A positive mindset is necessary on the part of the surgeon. Pre-operative imaging may not be completely reliable [17]. Even in our series of patients, we had the similar experience. In cases 2 and 3, even though pre-operative imaging suggested that partial nephrectomy may not be feasible, still intra-op, partial nephrectomy could be carried out with negative margins. Thus, intra-operative evaluation is necessary before labeling the tumor as unresectable.

In our first case, even after explaining that all charges related to hospital stay, surgery and post-op dialysis would be waived off, patient attenders refused any surgical intervention. Perhaps, this could be related to ignorance or local social taboos. Thus, improved patient education, improved social grants, and improving knowledge on the part of the surgeons regarding the feasibility of nephron-sparing surgery is required.

Conclusion

Management of bilateral Wilm's tumor is challenging and nephron-sparing surgery could be considered for all patients who have bilateral Wilm's tumor with favorable histology, even if pre-operative imaging studies suggest that the lesions are unresectable.

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