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Case Report: Nephron-Sparing Surgery in a Patient with Bilateral Multifocal Wilms Tumor

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Abstract

We present a case of bilateral multifocal Wilms tumor in a non-syndromic 12 month old male. Our management approach included twelve weeks of preoperative chemotherapy for maximal tumor shrinkage and, despite the central location of the tumors, successful staged bilateral nephron-sparing surgery. We advocate for a broader application of nephron-sparing surgery in Wilms tumor cases with the goal of preserving renal function without compromising oncologic outcomes.

Introduction

Although great strides in protocol-based Wilms tumor (WT) treatment have been made in the last few decades, bilateral WT still represents a management dilemma. Current Childrens Oncology Group (COG) protocol recommends neoadjuvant chemotherapy (NAC) with assessment of tumor response at 6 weeks and potentially 6 additional weeks to maximize tumor shrinkage with the goal of performing nephron-sparing surgery (NSS). Beyond those recommendations there is no consensus on the management of bilateral WT, such as whether to stage the attempts at NSS (1) Recently, the results of COG trial AREN 0534 in the bilateral WT population showed excellent survival which, coupled with the risk for development of metachronous tumors, provides a strong rationale for NSS and preservation of renal function. (2)

Case Report

A 12 month old otherwise healthy male with bilateral palpable renal masses presented to our clinic for a second opinion. He had no clinical evidence of a predisposing syndrome. CT scan demonstrated large bilateral multifocal renal tumors without renal vein involvement with a presumptive diagnosis of non-metastatic WT. We recommended he undergo NAC and staged bilateral NSS with MRI review of tumor response at 6 and 12 weeks of therapy. An attempt at surgical resection was then deemed feasible after 12 weeks of Regimen DD-4A, which includes vincristine, doxorubicin, dactinomycin. [Figure 1]

One week following his last chemotherapy dose, he underwent right open NSS for two tumors in close proximity to the hilum. His preoperative ANC was 800. A right ureteral stent was placed cystoscopically prior to a transverse right upper abdominal incision for tumor resection. Intraoperative ultrasound confirmed tumor locations and complete excision. The renal hilum was clamped after IV furosemide and mannitol, as well as renal cooling with ice slush. The parenchyma was closed with hemostatic pledgets and hilar lymph node dissection (LND) was performed. With a starting hemoglobin of 9.6 g/dL, estimated blood loss was 600cc and he received a blood transfusion. Of note, at the end of the case, the laboratory revised his ANC from 800 to 80, citing a lab error. GCSF was started immediately after surgery, resulting in normalization of his ANC two days later and antibiotics were stopped. He experienced transient hypertension (HTN) but was discharged with no new medications on day 5. Pathology confirmed WT, favorable histology and negative margins for both tumors with negative lymph nodes. The medial tumor contained 5% viable

elements with blastemal predominance (intermediate risk) and the lateral tumor 40% viable, blastemal predominant (high risk) with focal involvement of the hilar fat.

An MRI 6 weeks following his first surgery showed no new or residual right renal lesions and the two endophytic masses of the left kidney were unchanged. The right ureteral stent was removed and an open left partial nephrectomy with stent placement and hilar LND was performed. Both tumors were very adherent and abutted the renal vein and collecting system, however they were able to be removed while preserving a robust amount of renal parenchyma [Figure 2]. Post-operatively the patient exhibited severe HTN requiring a triple intravenous drug regimen. Serum creatinine remained at his baseline 0.3 mg/dL and Doppler ultrasound revealed good renal perfusion bilaterally. He was discharged one week later on two oral anti-hypertensive medications. Follow-up MRI at three months revealed healing parenchyma and no new lesions [Figure 3]. Renal volume measurement by ultrasound is 46.1 mL (right) and 98.4 mL (left), creatinine 0.24 mg/dL, and he remains on low dose amlodipine for mild HTN. For outpatient adjuvant chemotherapy, he was switched to the more intensive Regimen M (vincristine, dactinomycin, doxorubicin, cyclophosphamide, etoposide) after the first partial nephrectomy due to the blastemal predominant histology. Comprehensive SNP array analysis on his tumors was performed showing cnLOH at 11p15 in tumor but not normal kidney; he did not have LOH at 1p and 16q.

Discussion

Over the last several decades, overall survival for WT has improved dramatically to over 90% due to coordinated efforts led by the COG and National Wilms Tumor Study Group (NWTSG). (1) Radical nephrectomy (RN) remains the standard of care for unilateral, unifocal WT in children without a predisposing condition, while NSS has typically been reserved for cases where renal function preservation is a priority, as in cases of solitary kidney, bilateral disease, and patients with predisposition syndromes and higher risk to develop metachronous tumors. However a multi-institutional retrospective review of unilateral WT highlighted the implications of RN vs. NSS at two year follow-up, with a the median increase in eGFR was 28.6 mL/min/1.73m² in 15 patients who had undergone NSS vs. median loss of 19 mL/min/1.73m² in the RN group.(3)

Preoperative chemotherapy typically reduces the WT burden by at least 50-60% and facilitates NSS.(4) Despite this, most institutional series of bilateral WT demonstrate small numbers of patients who actually received bilateral NSS, usually undergoing RN on one side with NSS reserved for the less involved side. (5) (6) However, one single institution cohort of 42 patients with bilateral WT all underwent bilateral NSS, emphasizing the realistic applicability of this approach. (5) Furthermore, most recently the COG trial AREN0534 demonstrated excellent survival with NSS in bilateral WT. (2)

The optimal surgical strategy and timing to synchronous bilateral disease is debated and is individualized based on the number and location of tumors as

well as response to NAC. The risks of potential contralateral tumor growth during recovery and the need for an additional surgery with the staged approach used in this case must be weighed against the risks of simultaneous surgery, namely prolonged exposure to anesthesia, increased blood loss, and the risk for transient renal failure due to bilateral kidney manipulation.

Tumor location plays a critical role in determining the surgical approach and intra-operative techniques. In the authors' opinion, while hand compression of the kidney may be used for smaller peripheral lesions, the location of these tumors necessitated hilar clamping. Although a recent clinical trial in adults is suggestive that mannitol during vessel clamping may not be protective of renal function, studies in young children are not yet available.(7)

Finally, there is no standardized measure to grade tumor complexity in children with WT. Cost et al applied the adult RENAL Nephrometry score retrospectively to preoperative imaging of 65 patients, however RN was performed in nearly all of the "highly complex" tumors (48 of 51), limiting its usefulness in correlating score to surgical outcome. (8) Ferrer et al found less than 8% of even very low-risk WT patients' preoperative imaging would be deemed appropriate for NSS, based on criteria that includes absence of tumor involvement and/or direct contact with the renal hilar vessels. (9) Importantly, if our patient had had a solitary tumor, his tumor location and proximity to the hilum would have made him "high-complexity" by Nephrometry score, and excluded him as a candidate for NSS in the Ferrer study.

Conclusion

Our patient had bilateral multifocal WT disease, making bilateral NSS the optimal approach. Although if solitary his tumors would not have been considered for NSS by current COG protocols, through tumor volume reduction with chemotherapy and despite close proximity to the hilum, successful resection with negative margins was achieved. In the future a clinical trial to study the NSS approach in children with unilateral disease should be considered.

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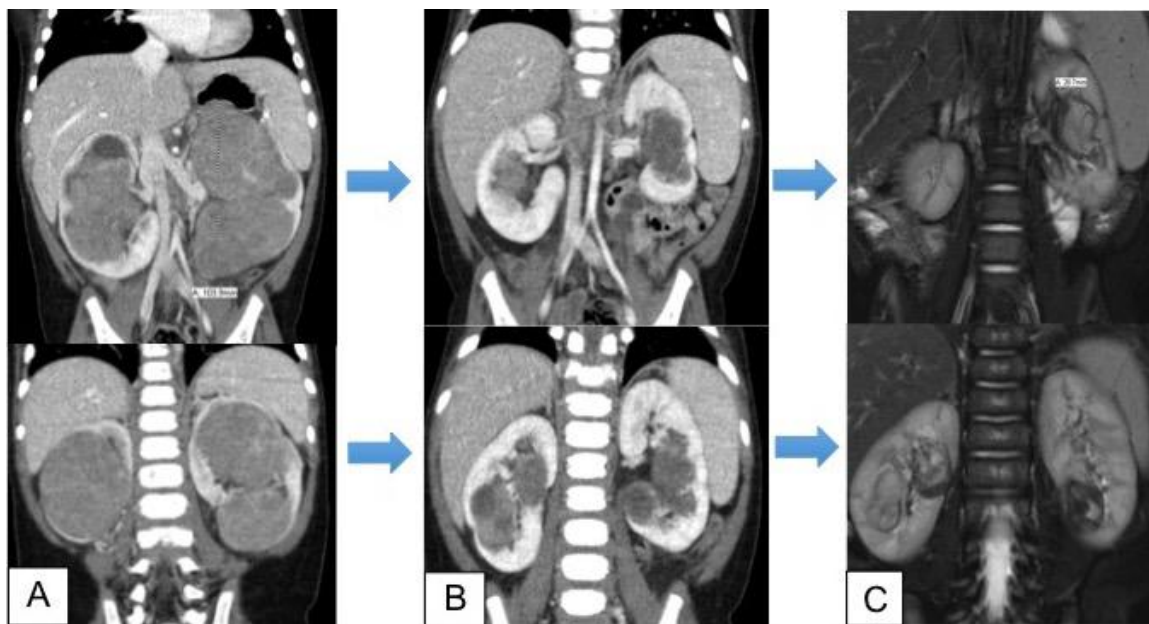
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Figure Legends:

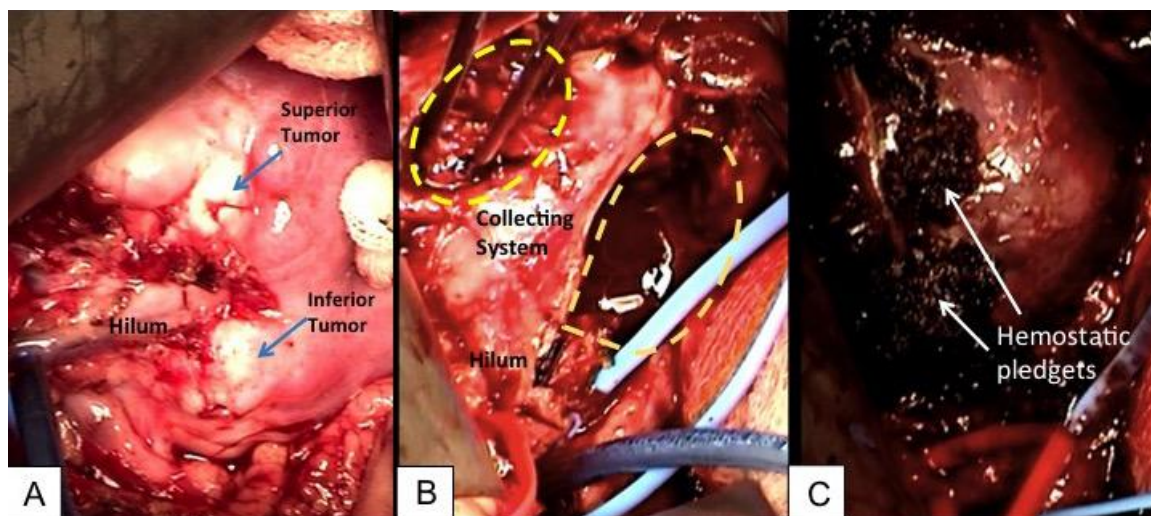
Figure 1. Comparison of initial imaging prior to treatment (A) and subsequently at the 6 week (B) and 12 week (C) interval marks. The greatest tumor size reduction in each kidney was 8.3cm to 2.2cm in the right, and 10.4cm to 2.9cm in the left kidney.

Figure 2. Intra-operative images of the left kidney. A) Superior and inferior tumors of the left kidney prior to resection. B) After resection, both tumor bed defects surrounding the collecting system. C) Reconstructed left kidney with closure of the capsule by hemostatic pledgets.

Figure 3. Post-operative MRI at 3 months from last surgery.

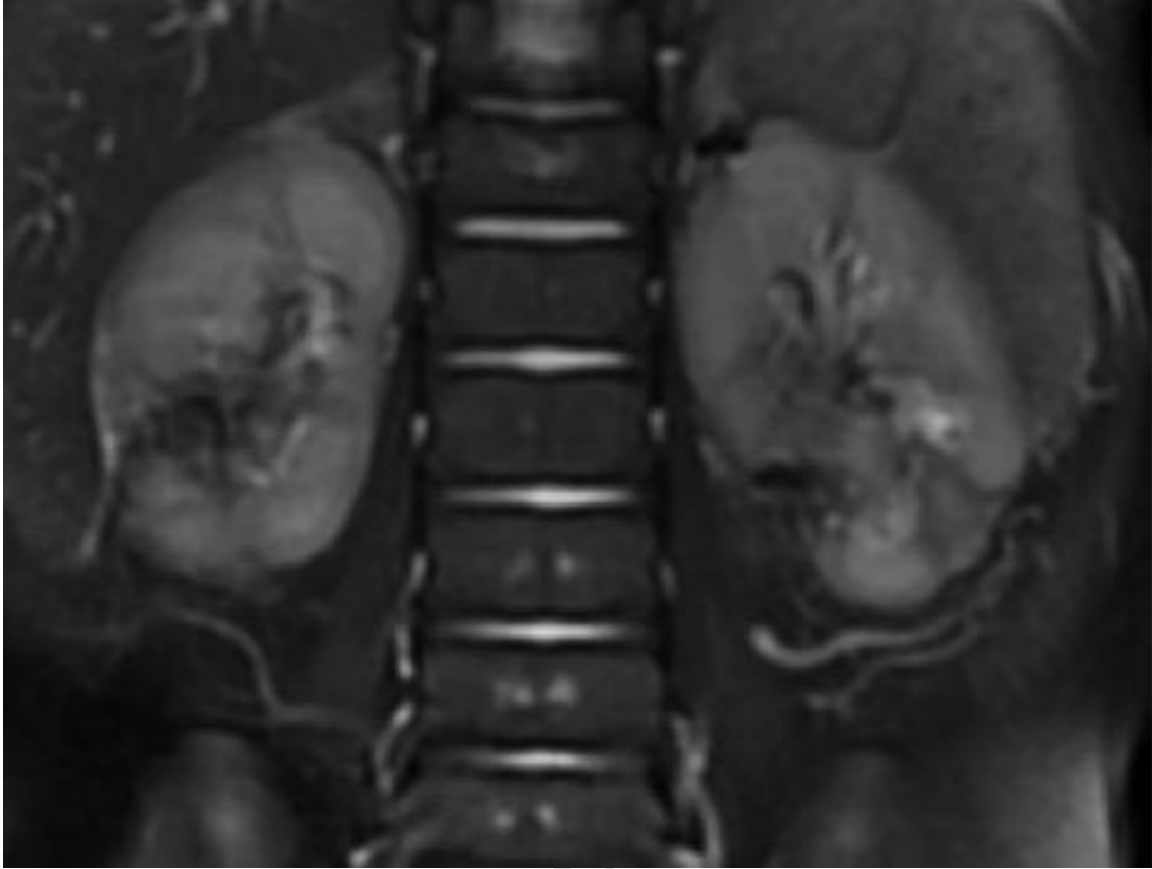


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