Published in final edited form as:

J Pediatr Surg. 2011 May ; 46(5): 983–988. doi:10.1016/j.jpedsurg.2011.01.025.

Laparoscopic nephron-sparing resection of synchronous Wilms tumors in a case of hyperplasticperilobarnephroblastomatosis

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Abstract

Diffuse hyperplasticperilobarnephroblastomatosis (DHPLN) is a rare precursor lesion of Wilms tumor (WT). Because of the increased risk to develop WT in either kidney, current management algorithms of DHPLN meritnephron-sparing strategies, beginning with chemotherapy and close radiographic monitoring into late childhood. After resolution of DHPLN, subsequent detection of a renal nodule mandates resection to exclude WT. Here, we report the case of a 4 year-old girl who developed two synchronous nodules in the right kidney more than two years after completion of therapy for DHPLN. Because of the early detection and peripheral location of these two nodules, laparoscopic nephron-sparing resection of each was performed using ultrasonic dissection. Both nodules were determined on pathology to be favorable histology WT with negative surgical margins. The child was placed onvincristine and actinomycin-D therapy for 18 weeks.

Keywords

Wilms tumor; nephroblastomatosis; laparoscopy; nephron-sparing surgery

Diffuse hyperplasticperilobarnephroblastomatosis (DHPLN) is a rare precursor lesion of Wilms tumor (WT)and may be considered an intermediate, pre-neoplastic stage in the sequence of Wilms tumorigenesis(1–5).Because the vast majority of DHPLN cases occur with bilateral renal involvement, current treatment algorithms emphasize nephron-sparing strategies(4).At time of diagnosis, DHPLN patients are recommended to receive 18 weeks of vincristine and actinomycin-D and may continue on extended therapy until all lesions resolve(5,6). Refractory, recurrent or new expanding nodules prompt tissue diagnosis with nephron-sparing resection to exclude WT initiation. Notably, in the seminal report outlining the natural history of DHPLN and the risk to develop WT, 24 of 52 (46.2%) patients who

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were followed for a minimum of five years developed WT, and 11 of these children developed two or more WT(4). Because of this risk to develop multiple WT in either kidney, conservative surgical strategies need to be followed to minimize late renal insufficiency, dialysis dependence, and need for renal transplantation(7).

Nephron-sparing strategies have been described for children presenting with bilateral WT(7–9). However, no description of a laparoscopic nephron-sparing resection of WT is currently available in the literature to serve as a technical guide to this advanced minimally invasive approach. A few case reports do describe laparoscopic radical nephrectomy for children having unilateral WT, yet these patients all received preoperative induction therapy and were not candidates for nephron-sparing strategies(10–12). One case report of a laparoscopic nephron-sparing resection of a metanephric adenoma in a 2 year-old child is available for review, but the authors do not describe in detail the technical considerations of the procedure(13). Much has been written on laparoscopic partial nephrectomy for various adult cancers and benign pathologies, and because of the challenging nature of this approach, some authors even advocate robotic assistance (14). Regarding the specific challenges of laparoscopic nephron-sparing resection for WT, care must be taken not to violate the tumor capsule, resulting in tumor spill, which upstages the patient. Further, an adequate and interpretable surgical margin needs to be included with the specimen, but not so extensive as to reduce functional nephronic units or to unnecessarily violate the renal calyces or renal pelvis. Finally, consideration must be given to meticulous hemostasis during parenchymal division and to the potential need for renal hilar vascular control, which poses the risk of protracted warm ischemia time and impairment of renal function.

Here, we report the case of a 4 year-old girl who has been followed since 10 months of age for DHPLN and who developed two nodules in her right kidney 24 months after completion of chemotherapy and resolution of the DHPLN. This case highlights the risk of children harboring DHPLN to develop WT, and potentially multiple WT, and illustrates a novel, minimally invasive approach to the nephron-sparing resection of WT arising in a predisposing condition.

1. Case Report

Oncologic care and imaging

At 10 months of age, another wise healthy female infant presented with a urinary tract infection, prompting renal ultrasound. Large bilateral renal masses were observed sonographically, and an MRI was obtained that showed features suggestive of bilateral DHPLN, typified by the reniform appearance of the right kidney mass (Figure 1A,B). These radiographic findings were not suggestive of WT, which classically appears as a solid mass protruding from the renal parenchyma with the uninvolved kidney variably investing the tumor in a claw-like manner. The infant was initiated on and completed per protocol 18 weeks of vincristine and actinomycin-D therapy. On follow up imaging 3 months off therapy, however, MRI showed significant interval enlargement of three masses within the right kidney, yet the imaging features were indeterminate for HPLNR or WT. Because of the extensive involvement of the right kidney with these new lesions, because of the risk over time to develop WT in either kidney, and because of the necessity to observe nephron-sparing treatment strategies, the child was initiated on vincristine, actinomycin-D and doxorubicin. However, the child was only able to tolerate two doses of the doxorubicin, which was terminated due to neutropenia, and so, she completed 24 weeks of the two-drug therapy. To monitor for development of new HPLNR or WT, MRI was performed every 3 months for the first year off therapy, then every 6 months for the second year.

Approximately 24 months after completing chemotherapy for DHPLN, which had resolved on imaging, the child was noted on surveillance MRI to develop enlargement of a nodule in the lower pole cortex of the right kidney, which had grown from 0.5 to 1.0 cm. This nodule had been previously dormant without change over the preceding 12 months. On this same imaging study, a 5 mm nodule persisted in the posterior aspect of the upper pole cortex but had regressed in size when compared with imaging 12 months earlier. Significant bilateral renal cortical scarring remained unchanged. Because of the concerning increase in size of the lower pole lesion, a repeat MRI was obtained two months later to determine any additional growth that would suggest potential WT development. On this subsequent MRI, the lower pole solid nodule now measured 1.6 cm in greatest dimension, and the upper pole nodule had increased in size to 1.0 cm, showing enhancement characteristics of a heterogeneous and cystic lesion (Figure 1C-F).

Operative procedure—Given the continued interval growth in the lower pole lesion of the right kidney, and new growth observed in the upper pole lesion, we determined that both nodules needed nephron-sparing resection to distinguish malignant transformation from benign hyperplastic change within a nephrogenic rest. Because on MRI the lesions were localized to the renal cortex and did not appear to encroach on the calyceal system or renal pelvis, we determined a laparoscopic approach would be feasible.

The child was placed in the left lateral decubitus position at 60° on a beanbag, as described for a laparoscopic left donor nephrectomy but in mirror image (15). The operating table was flexed between the iliac crest and lower costal margin, and a soft kidney bump was placed. After standard aseptic preparation of the operative field, a 10 mm port was placed in the infraumbilical location, and three 5 mm ports were placed respectively in the right lower quadrant 1 cm medial to the anterior iliac spine, in the midclavicular line of the right hypogastrium, and subcostal in the midclavicular line of the right upper quadrant. Pneumoperitoneum was maintained at 15 mmHg. The right colon was reflected medially providing exposure of the right kidney. The lower pole nodule was immediately apparent (Figure 2A). Grossly, this lesion was worrisome for WT because of superficial angiogenesis, which in contrast was not present on the background of cortical scar. The proper plane between the nodule and scar was determined by gentle compressing of the kidney. This nodule was resected using the Harmonic scalpel (Ethicon Endo-Surgery, Inc., Cincinnati, OH), and a minimum gross margin was maintained at 3 mm without tumor spill (Figure 2B). Excellent hemostasis was achieved with this device throughout the resection, which facilitated visualization of the tumor border. This specimen was placed in a bag and removed through the 10 mm port site.

We next approached the upper pole lesion with an identical technique (Figure 2C,D). This lesion was interesting because of its desmoplastic reaction to the retroperitoneal musculature, but nevertheless was able to be resected in a nephron-sparing manner without spill or violation of its capsule. In order to expose these two lesions in both poles of the kidney, it was necessary to dissect thoroughly the renal hilar vessels and the anteromedial border of the inferior vena cava for the entire length of the kidney. As predicted from the preoperative MRI, no visible lymph nodes were encountered along this extent of the dissection, and so none were included with the final specimens.

The two resection beds within the renal parenchyma were observed for urine leak, which was not identified. Fibrin sealant was applied to both beds for hemostasis and to minimize delayed urine leak. No drain was placed because of the cortical location of the two nodules and the depth of the resection margin did not penetrate the renal medulla. The child was discharged home on postoperative day two, and renal ultrasound on postoperative day four showed no perinephric fluid collection and no intraperitoneal free fluid. On

postoperative day seven, a subcutaneous reservoir was placed for the child to receive 18 weeks of vincristine and actinomycin-D.

Pathology—Pathologic examination of the lower pole nodule showed a favorable histology, blastemal-predominant WT with a minimum surgical margin of 2mm (Figure 3A-D). Importantly, use of the ultrasonic dissector did not distort any aspect of the surgical margin. To establish the diagnosis of WT, in contradistinction to HPLNR, a pathologist must observe a capsule surrounding the lesion, which compresses the adjacent normal renal parenchyma, as shown (Figure 3A,B). HPLNR would not have this capsule and would simply appear immediately adjacent to and interfacing with the renal parenchyma without compression (Figure 3B). Another histologic feature distinguishing WT from HPLNR is evidence of tumor invasion into the adjacent normal renal parenchyma, as was present in the lower pole specimen (Figure 3A,C).

2. Discussion

This case illustrates a minimally invasive approach to the nephron-sparing resection of WT in a background of bilateral DHPLN. However, the wider applicability of definitive laparoscopic nephron-sparing resection of WT is extremely limited in North America, given the current recommendations of the Children's Oncology Group (COG) to perform primary resection and thorough surgical staging upfront, which determines the most appropriate adjuvant therapy regimen (5,6).

The current literature contains several reports of laparoscopic radical nephrectomy for WT after neoadjuvant therapy, as typically administered at international centers that follow recommendations of the International Society of Pediatric Oncology (SIOP)(10–12). Only one report of a laparoscopic nephron-sparing resection of a renal tumor (metanephric adenoma) in a two year-old child is found in the current literature, but the technical considerations are lacking(13). Several series describing laparoscopic partial nephrectomy for adult cancers are indeed reported(14,16); however, no description of a laparoscopic nephron-sparing resection of WT has been reported to guide the minimally invasive approach to similar cases as ours.

Conditions such as DHPLN, which predispose to the development of WT and which require frequent imaging surveillance, are ideally suited to definitive minimally invasive techniques because of the potential for early detection of relatively small size WT. Of further advantage in cases of DHPLN is the peripheral and cortical location of these perilobar lesions, which may be remote from the hilar vascular branches and from the major urinary collecting system of the kidney. Although laparoscopic partial nephrectomy potentially can be performed for deeper seated and intralobar WT, significant consideration must be given to vascular control, warm ischemia time, and repair of the major collecting system if violated. Our case of laparoscopic nephron-sparing resection of two WT using the ultrasonic dissector was facilitated by early detection and the perilobar nature of these lesions, which did not require hilar vascular control. More complex partial nephrectomy resections attempted with laparoscopy might be facilitated by use of a hand-assist device to achieve hilar control, to place antegrade a ureteral stent, and to position the kidney during collecting system repair.

To distinguish WT from a hyperplastic nephrogenic rest, the pathologic specimen must contain an adequate margin of normal renal parenchyma to identify the presence or absence of a tumor capsule, which typically pushes on and compresses the adjacent kidney (4,17). If this tumor capsule does not exist, and no other microscopic features of tumor invasion into parenchyma or vessels are present, then the lesion may be classified as a benign but hyperplastic perilobar nephrogenic rest (HPLNR). In our two specimens, importantly, the

ultrasonic dissector preserved the surgical margins and the peritumoral capsule, which permitted conclusive diagnosis of favorable histology WT.

DHPLN is a rare condition in which nephronic progenitor cells escape pathways of terminal differentiation and senescence, and persist indefinitely into the postnatal period(1–4,17). Although most of these nephroblastic cells reside dormant in the renal cortex, some may undergo hyperplastic and eventually malignant transformation due to unclear mechanisms(18). In the most comprehensive series reported to date outlining the natural history of DHPLN, 24 of 52 children ultimately developed WT, and 11 of these 24 developed multiple WT, as evident in our case(4). In that series, over 94% of children having DHPLN presented with bilateral disease, and so all cases are considered at risk to develop WT in either kidney up to approximately 8 years of age. As a result, nephron-sparing strategies are mandated to minimize the risk to develop late renal insufficiency(7–9). To assist the sparing of as many nephrons as possible, the rationale to administer vincristine and actinomycin-D at initial diagnosis of DHPLN is to reduce the burden of pre-malignant hyperplastic nephrogenic rests and any malignant clones hidden within these often huge lesions(4). The subsequent development of WT does not necessarily represent a failure in efficacy of these two drugs but more likely a novel malignant transformation of persistent nephrogenic rest tissue(5), which explains the longitudinal risk of DHPLN patients to develop WT across childhood. Each subsequent WT should be treated according to stage, and in our child's case, she received an additional 18 weeks of vincristine and actinomycin-D to eliminate any missed micrometastases, given the nephron-sparing strategy. One additional pathology consideration in cases of WT arising from DHPLN must be given to the potential "selection" of anaplastic clones through the extensive administration of chemotherapeutics over time. In the Perlman series, anaplastic features were identified in 7 of 34 (20%) total WT specimens documented at pathology, which significantly exceeds the 5% incidence of anaplasia found in all WT cases. However, these authors rationalized that this high incidence of anaplasia is overestimated, given the likelihood that a multitude of patients having DHPLN also harbored clones of favorable histology WT that were successfully treated with chemotherapy alone and never required resection, whereas the rare anaplastic clones were more likely to resist vincristine and actinomycin-D therapy, to persist into a tumorigenic phase and to become enriched in this patient population(4).

Given the necessary frequency of radiographic monitoring for DHPLN, MRI is the ideal modality to surveil these patients long term, due to enhanced detection capabilities not available with ultrasound and to the lack of exposure to ionizing radiation, as with computed tomography. We believe that proper MRI surveillance of children with DHPLN will afford early detection of WT, should it arise, and that such lesions will be, by definition of the perilobar origin of the nephrogenic rests, in a cortical location away from the hilum and major collecting system. MRI in these cases provides an excellent roadmap to plan operative details, including evaluation for lymphadenopathy. Subsequent nodules arising in a background of DHPLN, after initial resolution of the nephroblastic rind surrounding the kidney, may be ideally suited for a minimally invasive approach to the nephron-sparing strategy. Importantly, ultrasonic dissection appears to preserve the histologic integrity of specimen margins. Our case illustrates one minimally invasive approach to the nephron-sparing resection of WT that warrants assessment of its wider applicability as additional experience is gained.

Acknowledgments

This report is dedicated to the women and men serving our country in the armed services whose children are battling cancer, as is this family. This work was supported in part by the National Cancer Institute grant, 4R00CA135695-02 (HNL).

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Figure 1.

(A,B) Magnetic resonance imaging (MRI) of bilateral and diffuse hyperplastic perilobar nephroblastomatosis (DHPLN) in a 10 month-old girl (T2-weighted SPIR sequence: Spectral Presaturation with Inversion Recovery). Note nephroblastic rind (A, arrow) surrounding right kidney and maintaining reniform appearance. The left kidney was predominantly involved in the lower pole (B, arrow). (C-F) MRI 28 months after completing DD-4A therapy for DHPLN. (C,D) T2-weighted pre-contrast MRI shows two heterogeneous peripheral nodules (arrow), which are hyper-intense relative to the surrounding renal cortex. (E,F) T1-weighted post-contrast MRI: (E) Lower pole WT (arrow) arising in right kidney measures 1.6 cm in greatest dimension and shows mild heterogeneous enhancement; (F) Upper pole WT (arrow) measures 1.0 cm in greatest dimension and shows peripheral rim-like enhancement consistent with cystic change.

Figure 2. Laparoscopic nephron-sparing resection of right kidney lower pole (A, B) and upper pole (C, D) WT. (A) Arrow denotes WT protruding from lower pole cortex. Note angiogenesis on surface of WT. (B) Initiating resection plane of lower pole WT with ultrasonic dissector. Arrowhead denotes whitish appearance of cortical scar without angiogenesis typical of WT. U denotes right ureter. (C) Asterisk depicts upper pole WT on posterior aspect of right kidney. (D) Resection plane and margin along upper pole WT (asterisk).

Figure 3.

Pathology of lower pole WT. (A) Favorable histology WT (WT) separated from normal renal parenchyma by tumor capsule (c). Note invasion of WT (asterisk) into adjacent and compressed normal kidney. Surgical margin is shown (sm, arrow). (B) Margin of WT with adjacent perilobar nephrogenic rests (PLNR, arrow). Note that the WT is surrounded by a capsule (c) but that the PLNR interfaces directly with the normal adjacent kidney. (C) Lower pole WT breaching its capsule (c) and invading normal kidney. (D) High power view of blastemal-predominant favorable histology WT.