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Function-guided renal parenchyma preservation in a giant bilateral Wilms tumor following SIOP-2016–based multistage chemotherapy and staged surgery: a case-based review

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Abstract *Synchronous bilateral Wilms tumor (BWT) demands oncologic control while protecting lifelong kidney function. In mesenchymal-predominant tumors, radiologic shrinkage after neoadjuvant therapy may be minimal and can mislead size-based surgical sequencing. In BWT with discordant radiologic response, split renal function can decisively guide sequencing and expand nephron preservation.*

Keywords: bilateral Wilms tumor; nephron-sparing surgery; renal scintigraphy; kidney preservation; SIOP

1. Introduction

Wilms tumor is the most common malignant renal neoplasm in children and accounts for approximately 6% of pediatric cancers. [1] Bilateral Wilms tumor occurs in ~5–8% of cases but presents disproportionately greater clinical challenges due to the competing demands of oncologic control and long-term renal functional preservation. [2,3] Massive bilateral tumors amplify these challenges, as radiologic size regression after neoadjuvant chemotherapy may be limited and can be

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discordant with treatment effect; response patterns may reflect histologic subtype rather than treatment failure. [4,5]

The UMBRELLA SIOP–RTSG 2016 framework supports preoperative chemotherapy for stage V disease followed by individualized surgical planning, with nephron-sparing surgery (NSS) pursued whenever feasible to reduce late chronic kidney disease risk and future kidney replacement therapy burden. [2,6] However, when radiologic response is poor despite favorable post-therapy histology, particularly in the presence of marked inter-renal functional asymmetry, practical guidance on how to prioritize tumor size versus functional status for surgical sequencing remains variable in real-world settings. [5]

We present an infant with a giant bilateral Wilms tumor in whom conventional size-based surgical logic would have mandated initial resection of the larger left-sided mass. Instead, functional scintigraphy redirected the strategy toward preservation of the solitary functioning kidney, enabling successful NSS despite massive tumor burden and collecting system involvement.

2. Case Report

A 16-month-old boy, weighing 8.5 kg and measuring 75 cm in height, presented to our clinic with a 1-month history of progressive abdominal distension, general fatigue, and pallor of the skin and mucous membranes. Physical examination revealed pronounced abdominal distension and a large palpable abdominal mass.

Initial laboratory evaluation showed abnormalities consistent with tumor burden and renal stress. Values above the institutional reference ranges were documented for red blood cell distribution width (RDW; reference range: 12.9–15.6%), monocyte percentage (MONO%; reference range: 4.4–13.4%), basophil percentage (BASO%; reference range: 0–0.6%), serum creatinine (reference range: 27–62 µmol/L), blood urea nitrogen (BUN; reference range: 2.5–8.3 mmol/L), and lactate dehydrogenase (LDH; reference range: 50–295 U/L). Exact numerical baseline values for all requested laboratory parameters, including hemoglobin and total white blood cell count, could not be reliably retrieved from the archived record and therefore were not reported quantitatively.

Ultrasonography, computed tomography, and magnetic resonance imaging demonstrated synchronous bilateral renal tumors. The right kidney contained an approximately 86.5 × 86 mm heterogeneous hypervascular mass that completely involved the renal pelvis and caused grade 2 hydronephrosis. The left kidney was located in its normal anatomical position and contained an approximately 125.5 × 116.2 mm heterogeneous hypervascular mass with calcifications, extending from the mid-third of the kidney toward the renal pelvis. There was no evidence of renal vein or inferior vena cava tumor thrombus, and chest and abdominal CT showed no signs of distant

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metastasis. Clinical findings suggestive of Wilms tumor–associated syndromes, including Beckwith–Wiedemann, Perlman, Denys–Drash, WAGR, and Frasier syndromes, were not identified.

Neoadjuvant polychemotherapy was initiated according to SIOP-based recommendations. The initial regimen included vincristine 0.4 mg during weeks 1, 2, 3, 4, and 5, and dactinomycin 270 mcg during weeks 1, 3, and 5. Follow-up ultrasonography during and at the end of chemotherapy showed no meaningful reduction in tumor size. Therefore, an additional week of chemotherapy was administered in week 6, consisting of vincristine 0.4 mg and doxorubicin 15 mg.

Renal radionuclide scintigraphy demonstrated marked functional asymmetry. Perfusion of the left kidney was simultaneous with the abdominal aorta and within normal limits; the kidney was enlarged but located in its typical anatomical position. The renogram curve of the left kidney showed a partially obstructive pattern. In contrast, right renal perfusion was severely reduced, no active uptake was detected in the projection of the right kidney, and the renogram curve showed an afunctional pattern. Split renal function was calculated as 1% for the right kidney and 99% for the left kidney. Based on these findings, the surgical strategy was planned according to renal function rather than tumor size.

A staged, function-guided surgical strategy was adopted. The first stage consisted of right nephrectomy through a transverse incision to obtain definitive histology, determine the pathomorphological regression grade and histological subtype, and reduce total tumor burden with minimal functional sacrifice. The second stage was planned as nephron-sparing surgery of the functionally dominant left kidney after continuation of chemotherapy. The patient was closely monitored, and preliminary discussions were held with the kidney transplantation team in case postoperative renal failure developed.

The scheduled surgery was temporarily postponed because of varicella-zoster virus infection. Under the supervision of an infectious disease specialist, intravenous acyclovir was administered at a dose of 10 mg/kg every 8 hours for 7 days. After clinical recovery and confirmation by polymerase chain reaction testing, a short observation period was maintained during the subsequent asthenic phase. The patient was then re-evaluated by ultrasonography, and a short CE regimen was administered, consisting of carboplatin 50 mg and etoposide 40 mg.

Four weeks after the last chemotherapy cycle, first-stage right nephrectomy was performed. Histopathological and immunohistochemical examinations confirmed biphasic nephroblastoma/Wilms tumor composed of approximately 70% mesenchymal and 30% epithelial components. Tumor regression was graded as pathomorphosis grade III. Surgical margin status, lymph node assessment, and quantitative residual viable tumor percentage were not documented in the available archived pathology report. Based on

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postoperative risk assessment, radiotherapy was not administered. After a 1-month rehabilitation period, follow-up CT demonstrated persistent tumor burden in the left kidney, measuring approximately 133.6 × 104.7 mm. According to the UMBRELLA SIOP–RTSG 2016–aligned approach, chemotherapy was continued with vincristine 0.4 mg during weeks 1 to 11, dactinomycin 270 mcg during weeks 2, 5, 8, and 11, and doxorubicin 15 mg during weeks 6 and 10. CT performed at the end of this chemotherapy course showed no meaningful change in tumor size, with the residual left-sided tumor measuring approximately 133 × 103.8 mm.

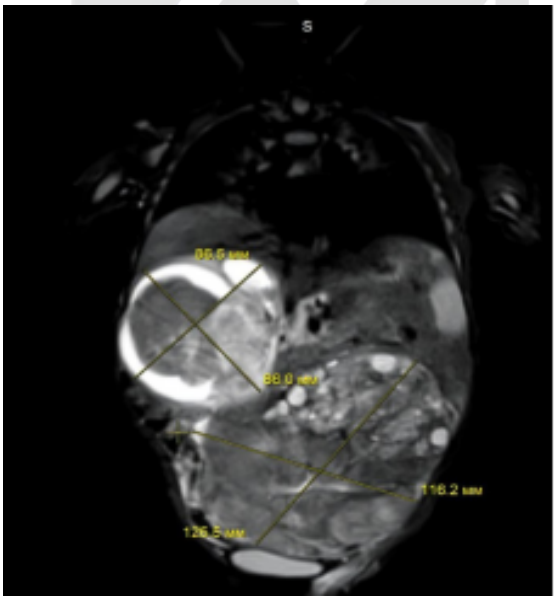

Figure 1A: Pretreatment MRI demonstrating massive synchronous bilateral renal tumors with marked abdominal distension.

Six weeks after the last chemotherapy cycle, planned second-stage nephron-sparing surgery of the left kidney was performed. Through a transverse abdominal incision, the left renal tumor was exposed, mobilized, and excised with preservation of viable renal parenchyma. Because of renal pelvis involvement, the tumor-invaded portion of the renal pelvis was also resected. Pelvic reconstruction was performed using 6-0 polydioxanone sutures, and the renal parenchyma was closed with 3-0 Vicryl sutures.

Histopathological evaluation of the resected left-sided specimen showed a biphasic Wilms tumor composed of approximately 90% mesenchymal and 10% epithelial components, with pathomorphosis grade III. Surgical margin status, lymph node status, and a quantitative estimate of residual viable tumor were not documented in the available archived pathology report.

Postoperative CT was performed to assess the surgical site and preserved renal parenchyma. During the postoperative period, laboratory and instrumental assessments did not reveal surgical or renal complications. Renal function remained clinically stable, and no signs of renal failure were observed; therefore, kidney replacement therapy and the previously discussed transplantation pathway were not required.

Postoperative chemotherapy was resumed according to the SIOP-based protocol, with vincristine 0.4 mg administered during weeks

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1 to 4 and dactinomycin 270 mcg administered during weeks 2 and 4. Treatment was concluded after completion of this chemotherapy regimen.

In brief, the treatment sequence was as follows: initial diagnosis, SIOP-based neoadjuvant chemotherapy with vincristine and dactinomycin, addition of doxorubicin after limited radiologic regression, differential renal scintigraphy demonstrating 1% right and 99% left renal function, first-stage right nephrectomy, second-stage left nephron-sparing surgery with pelvic reconstruction, completion of postoperative chemotherapy, and 6-month surveillance imaging.

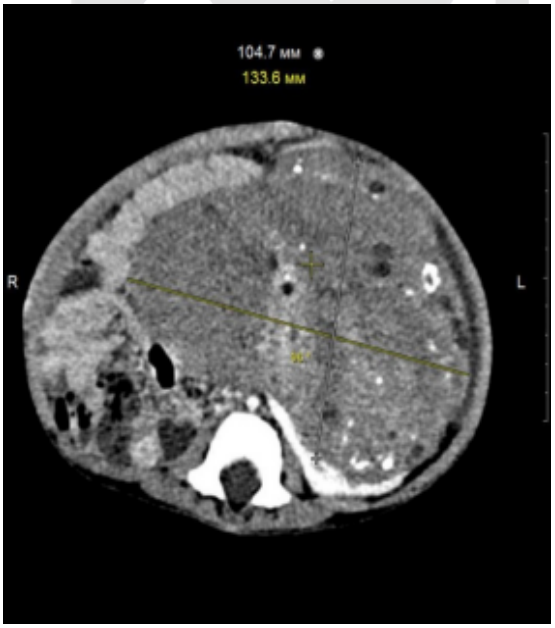

Figure 1B: Differential renal scintigraphy demonstrating extreme split renal function (right kidney 1%, left kidney 99%), which shifted the surgical priority from tumor size to preservation of the only functioning kidney.

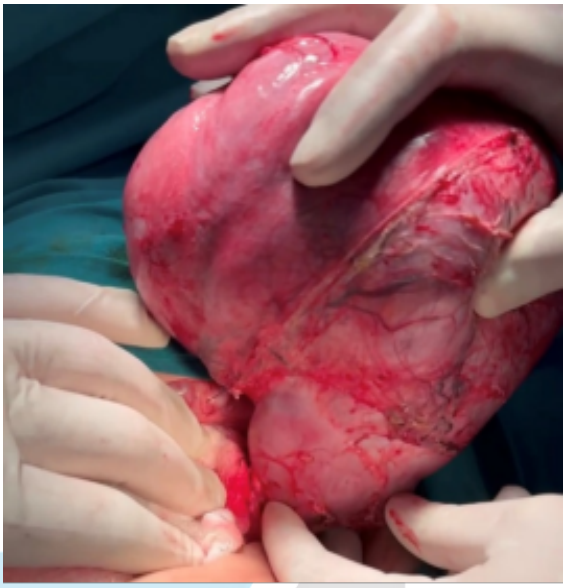

Figure 1C: Intraoperative nephron-sparing surgery (NSS) on the left kidney showing tumor exposure and collecting system reconstruction (pelvic closure followed by layered parenchymal repair).

At the 6-month postoperative follow-up, CT showed no radiologic evidence of residual or recurrent disease. The patient remained clinically stable under pediatric and oncological surveillance.

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Targeted literature synthesis

To contextualize our function-based sequence strategy within existing practice examples and evidence topics, we present a targeted, text-based evidence map instead of a direct comparison table. Reports and series of bilateral Wilms tumors are inherently heterogeneous in terms of tumor burden, histology, response to treatment, surgical techniques, and follow-up duration; therefore, the evidence map format better allows for transparent interpretation of the results without over-generalizing them. In this synthesis, each body of evidence is tied to a practical decision point related to our assessment of the response to the condition, functional asymmetry, surgical sequence, reconstructive feasibility, and long-term renal risk. When an element was not reported consistently across sources, it was explicitly marked as NR (not reported) to avoid drawing conclusions beyond the available data. Representative reports informing staged nephron-sparing strategies and renal outcomes in bilateral Wilms tumor are summarized in Table1.

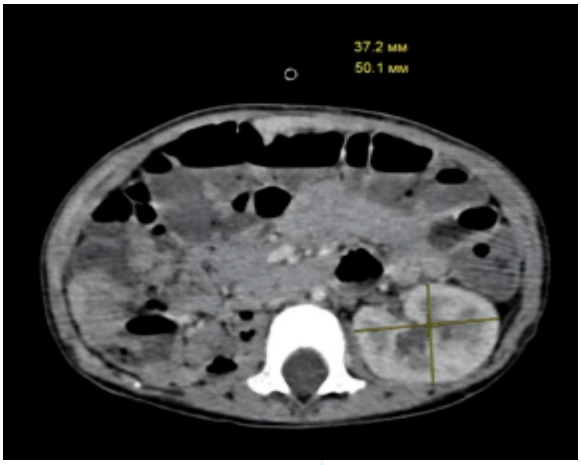

Figure 1D: Six-month postoperative CT demonstrating preserved renal parenchyma with compensatory hypertrophy and no radiologic evidence of residual or recurrent disease.

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Table 1. Evidence snapshot: bilateral Wilms tumor, staged surgery, nephron-sparing surgery, and complications (representative reports)

Study (year)	Design/cohort	Key sequencing concept	NSS / reconstruction notes	Complications / renal outcomes	Why it matters for our case
Hamilton et al. (2011)	NWTS-4 analysis; 188 patients with synchronous BWT	Highlights long-term renal risk in BWT	Emphasizes nephron preservation strategies	ESRD risk persists in BWT cohorts	Supports renal preservation as a central goal in BWT.
Sudour-Bonnange et al. (2024)	SIOP-2001; 174 synchronous BWT	Standardized SIOP strategy; response-guided surgery	High rate of nephron-sparing approach reported	Demonstrates feasibility of NSS in a modern cooperative setting	Supports SIOP-based staged decision-making.
Davidoff et al. (2008)	Single-center St Jude series; 12 synchronous BWT patients, 1999–2006	Aggressive bilateral NSS when feasible	Collecting system entry/repair is part of real-world NSS	Urine leak in 3 patients, UPJ obstruction in 1, renal failure in 1	Shows real-world feasibility of complex bilateral NSS.
Spiegl et al. (2020)	Retrospective study; 55 NSS patients	NSS increases surgical complexity compared with radical nephrectomy	NSS linked with higher estimated blood loss and margin positivity	NSS complications 36.4%; urine leak 9; positive margins 36.4%	Frames NSS complexity and complication risk.
Kieran et al. (2013)	Retrospective study; 21 BWT patients after NSS	Margin status is not the sole driver of recurrence	Some patients received flank radiotherapy	Recurrence 33%; renal failure in 1 high-risk patient	Reinforces careful surveillance after NSS.
de Souza et al. (2023)	Single-center study; 33 BWT patients; median follow-up 83 months	Surgery within a multidisciplinary protocol	70.4% underwent bilateral NSS; reconstruction occasionally needed	No urinary fistulas or early surgical complications; 5-year survival 76%	Shows complication-free NSS is achievable.
Meier et al. (2023)	Large SIOP/GPOH analysis, 1989–2022	Avoid overly prolonged pretreatment in non-metastatic BWT	Indirectly supports timely conversion to surgery	In non-metastatic BWT, relapse risk increased after >120 days	Supports avoiding excessive chemotherapy delay.
Murphy and Davidoff (2023)	Focused review	Summarizes NSS indications and technical principles	Emphasizes reconstruction and collecting system management	Highlights balance between oncologic safety and renal preservation	Provides practical NSS principles.

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3. Limitations

This is a single-case report, limiting generalizability and precluding comparative conclusions about sequencing strategies. Ultrasound images were not available for inclusion despite documented examinations, and follow-up remains limited, which is insufficient to fully assess long-term renal stability and late relapse risk. Molecular profiling was not performed, preventing correlation of mesenchymal predominance with specific genetic alterations such as WT1, CTNNB1, and TP53 that may refine future risk stratification and treatment planning. In addition, exact baseline laboratory values, objective serial postoperative creatinine/eGFR values, surgical margin status, lymph node assessment, and quantitative residual viable tumor percentage were not fully retrievable from the archived record. Larger multicenter case series with standardized reporting of split renal function, postoperative renal outcomes, surgical margins, lymph node status, and long-term relapse data are needed to validate function-guided sequencing strategies in bilateral Wilms tumor.

4. Discussion

In the present case, neoadjuvant chemotherapy (preoperative chemotherapy, PCT) delivered according to SIOP-based (UMBRELLA/SIOP-RTSG 2016–aligned) principles did not result in meaningful radiologic tumor shrinkage, despite a high grade of post-treatment pathomorphosis. This apparent discordance is clinically plausible in mesenchymal-rich (stromal-predominant) tumors, where volumetric regression may be limited even when histologic treatment effect is substantial. Duncan et al. reported that apparent radiologic response in bilateral Wilms tumor can vary by histologic subtype and that limited size reduction may occur despite favorable post-therapy pathology. [7] Our findings are consistent with this response–histology dissociation and support interpreting the benefit of PCT not solely through size metrics, but also through histologic effect and operative feasibility.

Although tumor shrinkage was limited, the achievement of a high pathomorphosis grade remains clinically relevant because post-treatment histology is incorporated into risk stratification and can influence subsequent local and systemic therapy decisions. In this context, the principal value of SIOP-based PCT may lie in improving tumor biology and surgical conditions supporting safer dissection and resectability rather than guaranteeing radiologic regression, particularly in mesenchymal-predominant bilateral disease. [7]

Nephron-sparing surgery (NSS) in very young children has increasing support in the literature, with reports describing kidney-preserving strategies and favorable early oncologic outcomes in carefully selected patients. [8] In our patient, NSS was performed on the functionally dominant kidney with preservation of clinically stable renal function. Figure 1 summarizes the clinical course and operative milestones, whereas the focused evidence map (Table 1,

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text-only) links published themes to the decision nodes that were most relevant to our management response assessment, functional asymmetry, sequencing, reconstructive feasibility, and long-term renal risk.

Surgical sequencing in bilateral Wilms tumor remains debated, including whether the side with greater tumor burden should be prioritized. [9] Our case demonstrates that tumor size alone should not dictate sequencing when renal contribution is profoundly asymmetric. Despite a smaller right-sided lesion, scintigraphy demonstrated that the right kidney contributed only 1% of total function and was extensively involved with the collecting system; therefore, right nephrectomy served primarily to secure definitive histology and reduce global tumor burden at minimal functional cost. This staged approach enabled subsequent NSS on the left kidney, which accounted for 99% of the overall renal function. The decision to remove the right kidney first was based on functional rather than size-based prioritization. Although the left-sided tumor was larger, the left kidney represented nearly all measurable renal function, whereas the right kidney contributed only 1% and had collecting system involvement. Attempting initial complex surgery on the left side would have exposed the child's only functioning renal unit to a higher risk of ischemic injury, urinary leakage, incomplete resection, or loss of renal reserve. In contrast, right nephrectomy provided definitive histology and reduced total tumor burden with minimal additional functional sacrifice. Therefore, the function-guided sequence was considered safer than a purely size-based strategy.

This case also illustrates why radiological tumor size alone may be insufficient for surgical sequencing in bilateral Wilms tumor. Despite the larger left-sided mass, renal scintigraphy demonstrated that the left kidney was the functionally dominant, near-solitary renal unit. Thus, differential renal scintigraphy changed the surgical priority from resection of the larger tumor to preservation of the only functioning kidney. In selected bilateral Wilms tumor cases, differential renal scintigraphy may therefore prevent misleading surgical sequencing when tumor size and renal contribution are discordant. The rationale for weighting renal function at least as heavily as tumor size is synthesized in the evidence map and underscores the practical role of functional assessment in operative planning.

Preservation of native renal tissue is particularly important given the long-term burdens associated with chronic kidney disease and potential kidney replacement therapy, including the risks of chronic immunosuppression in transplant recipients. [10,11] In addition, specialist-center experience suggests that preoperative imaging alone may not fully capture intraoperative resectability and that final NSS feasibility is sometimes clarified at exploration. [12,13] These comparative themes, integrated into the evidence map, support an individualized approach in which anatomy, response context, and critically

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split renal function jointly shape the operative plan.

Guidance documents similarly support individualized decision-making for nephron preservation, recognizing that collecting system involvement is not necessarily an absolute contraindication when adequate viable parenchyma can be preserved, and reconstruction is feasible. [14] In our case, multidisciplinary integration of cross-sectional imaging, renal scintigraphy, and intraoperative assessment enabled successful NSS with collecting system reconstruction despite massive bilateral disease (Figure 1B–C).

In summary, this case highlights that (i) limited radiologic shrinkage after PCT may occur despite substantial histologic treatment effect in mesenchymal-rich tumors, [7] and (ii) sequencing in bilateral Wilms tumors should incorporate functional dominance rather than relying on tumor size alone. [9] The evidence themes summarized in the text-only map support the central principle demonstrated here: when renal contribution is markedly asymmetric, function-guided staging can expand the feasibility of nephron preservation even in anatomically complex disease while maintaining early oncologic control. At 6 months, imaging showed no radiologic evidence of recurrence, and longer surveillance is ongoing. [10–14]

5. Conclusion

This case illustrates that giant synchronous bilateral Wilms tumor with mesenchymal predominance can be managed with a staged, multimodal strategy in which functional preservation is explicitly prioritized over size-based surgical sequencing. Despite extensive tumor burden, limited radiologic regression after SIOP-based preoperative chemotherapy, and collecting system involvement requiring reconstruction, nephron-sparing surgery of the functionally dominant near-solitary kidney was feasible and resulted in preserved clinical renal function without the need for kidney replacement therapy during follow-up.

More broadly, this report supports a practical decision pathway for complex bilateral Wilms tumor when imaging response appears discordant: histological treatment effect and split renal function assessment by scintigraphy should be integrated alongside anatomic imaging to guide operative sequencing. Differential renal scintigraphy may be particularly useful when radiological response does not accurately reflect functional renal preservation, allowing surgical sequencing to be individualized according to renal contribution rather than tumor size alone. Nevertheless, longer oncological and functional follow-up is required before this strategy can be generalized beyond carefully selected cases.

Declaration of conflicting interests

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