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Management of bilateral Wilms' tumour: A case report

Irfan Wahyudi^a, Johannes Aritonang^{a,*}, Agus Rizal A.H. Hamid^a, Gerhard R. Situmorang^a, HENDY Mirza^b, Fina Widia^a, Arry Rodjani^a^a Department of Urology, Cipto Mangunkusumo National General Hospital, Faculty of Medicine Universitas Indonesia, Indonesia^b Urology Division, Department of Surgery, Persahabatan Hospital, Jakarta, Indonesia

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ABSTRACT

INTRODUCTION: Wilms' tumour remains the most common renal tumour in children (6% of all pediatric malignancies) and present as one of the most challenging tasks for paediatric urologists as its management requires an advanced procedure. The ultimate goal in these cases is to preserve as much renal parenchyma as possible whilst still achieving complete tumour resection.

PRESENTATION OF CASE: Here we present a six year follow up report of a bilateral Wilms' tumour case in a 19-months old boy. This patient underwent neoadjuvant chemotherapy regimen, followed by right partial nephrectomy and left radical nephrectomy. Adjuvant radiotherapy was performed following the surgery. Follow-up imaging 5 months afterward revealed a firmly heterogeneous cystic lesion consist of fat and calcification at the upper pole of the right kidney, none of which created any problem for the patient. MRI was later performed on the 19th month after the surgery, showing marked decrease in the size of the cyst.

DISCUSSION: According to SIOP and NWTSG classification, the patient presented as stage V of the disease. The patient was on neoadjuvant chemotherapy (Regimen I) as recommended by NWTSG. This strategy was shown to be effective, as the tumour on the left kidney was reduced to less than 70% of the initial size. A routine follow-up using chest x-ray, abdominal ultrasonography (USG), and contrast studies such as MRI and MSCT scan, was performed in our reports.

CONCLUSION: From our experience, the combination of neo-adjuvant chemotherapy, renal salvage surgery and adjuvant radiotherapy is a feasible, safe and effective option for bilateral Wilms' tumour cases.

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1. Introduction

Wilms' tumour is the most common renal tumour in children. Globally, it accounts 6% of all pediatric malignancies, with 5–7% of Wilms' tumour manifested as bilateral case [1]. The male to female ratio is 0.60–1.00 in bilateral cases and the age at diagnosis is averagely 31 months in bilateral Wilms tumour [2,3]. Children with bilateral Wilms' tumour present one of the most challenging tasks for paediatric urologists. The ultimate goal of surgical intervention in bilateral Wilms' tumour is to achieve complete tumour resection whilst preserving as much normal renal parenchyma as possible [4]. The latest literature has limited records of bilateral Wilms' tumor approach. Therefore, this study tries to report our center approach to this issue.

2. Presentation of case

A 19-month-old boy was presented to our outpatient clinic with a palpable mass on his left abdomen since the age of 6 months. Patient and the mother did not have any history of drug consumption and no family history of same disease. Ultrasound-guided fine needle aspiration biopsy (FNAB) revealed typical features of unfavourable Wilms' tumour with an atypical undifferentiated malignant tumour appearance with findings of a discrete irregular shaped cells with hyperchromatic polymorphic nucleus, and necrotic tissues. A multi-slice computed tomography (MSCT) scan of the abdomen showed a 9 × 8.5 cm hypodense mass with necrotic area on the left kidney and a 3.5 × 3 cm mass on the right kidney, which appeared to be solitary and isolated to the superior pole. Contrast enhancement was clearly evident in both masses.

Patient was diagnosed with bilateral Wilms' tumour. He underwent 24 weeks of chemotherapy containing Doxorubicin, Vincristine, Cyclophosphamide and Etoposide. Following completion of chemotherapy, an abdominal MSCT scan with contrast was performed. A marked reduction of tumour size was observed on left

* Corresponding author at: Jl. Pangeran Diponegoro No.71, Kec. Senen, Central Jakarta, DKI Jakarta, 10430, Indonesia.

E-mail address: johannesaritonangmd@gmail.com (J. Aritonang).

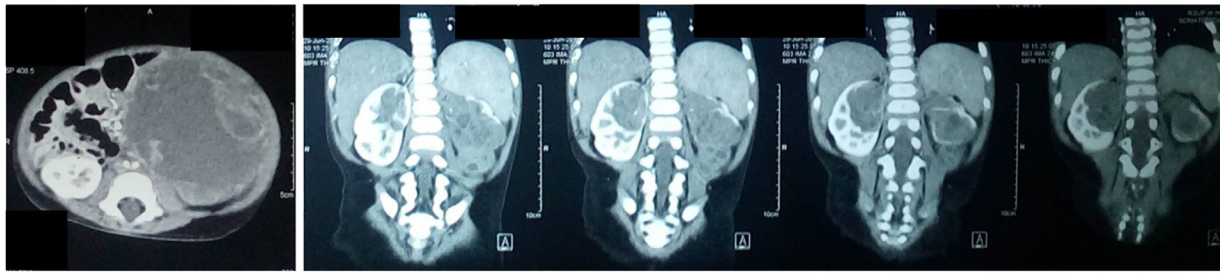


Fig. 1. Pre-operative abdominal MSCT scan with intravenous contrast agent, showing a large hypodense lesion in the left kidney on transverse section (A). Coronal sections of the abdominal CT-scan showing lesions with similar density in both kidneys. Notice that the lesion in the right kidney was relatively confined to the upper and medial part, leaving a proportion of normal kidney parenchyma (B).

and right kidneys (9×8.5 cm to 6×5.2 cm and 3.5×3 cm to 3×2.1 cm respectively) (see Fig. 1). The patient was also diagnosed with right palpable undescended testis. Blood analysis showed elevated liver enzymes (AST of 163 u/L, and ALT of 140 u/L). Other laboratory findings were within normal.

Patient underwent left radical nephrectomy and zero ischemic partial-nephrectomy of the right kidney at the age of 20-months by pediatric urologist. The limitation of partial nephrectomy is the probability of incision border is not tumor-free tissues. After that, inguinal exploration and right orchidopexy were performed. All procedures were performed in one-stage. The operation lasted for 4 h, with no intra-operative complication reported. Pathology report revealed a typical presentation of unfavourable Wilms' tumour with the presence of blastemal, stromal and epithelial components accompanied by hyperchromatic tumour cells. The patient was discharged after ten days of hospitalization until stable vital and general signs were achieved. Subsequently, the patient received 7 cycles of adjuvant radiotherapy (10.5 Gy). In this study, follow-up abdominal MSCT scan performed at 25-months detected a firm cystic lesion at the upper-posterior pole of the right kidney sized $22 \times 18 \times 15$ mm (see Fig. 2). The renal function laboratory result also showed good function of the kidney without any symptoms. Therefore, we decided to conduct further imaging examination to re-evaluate the patient in the next 12 months.

An abdominal-pelvic magnetic resonance imaging (MRI) with 2.4 ml intravenous of gadoteric acid contrast was performed at the age of 39 months to screen for recurrence and further evaluate the progression of the cyst (see Fig. 3). There were no findings of residual or progressive mass or abdominal lymphadenopathy. However, the cystic lesion remained visible on the upper pole of the right kidney, which size decreased to $1.2 \times 1.2 \times 1.2$ cm. Focal caliectasis at the superior pole was also detected.

The most recent follow-up (70-months) showed normal renal function (ureum 23.8 mg/dL; creatinine 0.50 mg/dL), electrolyte level, and urinalysis. Liver enzymes results which was increased before the surgery was also found to be within the normal reference range (AST 29 U/L; ALT 15 U/L). Patient parents informed their child condition is improving significantly after the intervention.

3. Discussion

According to SIOP and NWTSG classification, the patient presented as stage V of the disease [4]. This was evident as the disease involved both kidneys as well as from the histopathological features found from fine-needle aspiration biopsy. We decided to put the patient on neoadjuvant chemotherapy (Regimen I) as recommended by NWTSG in an attempt to reduce the tumour size and to salvage as much renal parenchyma as possible (see Table 1). This

strategy was shown to be effective, as the tumour on the left kidney was reduced to less than 70% of the initial size.

After completion of chemotherapy, the patient underwent partial nephrectomy of the right kidney, radical nephrectomy of the left kidney, and right orchidopexy procedures at the age of 20-months old (see Fig. 4). During the nephron-sparing surgery, a modified Chevron was performed to expose the right kidney. This method is generally performed in nephron sparing surgery for bilateral Wilms' tumour [5]. Non-clamping or zero ischemia partial nephrectomy was performed on the right kidney. Vessel loop was applied only if required for bleeding control, which was not performed in this case. The 25 kHz Cavitron Ultrasonic Surgical Aspirator / CUSA (SONOCA 300®) was utilized to decrease the effect of reperfusion injury [6]. Both of the tumours were removed by slicing the renal surface and separating the tumour from the healthy renal parenchyma. An approximate two-third of one kidney must be intact post-operatively for the renal-sparing surgery to be effective without the needs for renal transplant [4].

In our centre, 10.5 Gy irradiation was performed, which was divided into seven fractions for the whole abdomen. Recall that the recommended dose for pediatric patients underwent radiation after surgery is 10–12 Gy [7]. The dose was limited primarily due to the potential diffuse spillage and nephrotoxicity. In addition, it is important to note that the damaging risks of radiotherapy are not only for the renal function, but also the growth and development of kidney normal tissue as well as fertility [8].

Following these procedures, some clinically important consequences may occur late. One of the most commonly reported is cardiotoxicity, followed by reproductive problems, renal dysfunction, and the development of benign and malignant second tumours [1]. During post-operative follow-up (26 months-old), the levels of blood urea nitrogen and creatinine clearance rate (CCR) in our patient was 31 mg/dl and 123.8 mL/min/1.73 m² [calculated with Schwartz equation; body weight and length at measurement: 10.5 kg and 90 cm; normal range of CCR: 85–150 mL/min/1.73 m² [9–11]. In addition, laboratory examination at the age of 70 months, including renal function, electrolyte and liver enzymes, were found to be normal.

A routine follow-up using chest x-ray, abdominal ultrasonography (USG), and contrast studies such as MRI and MSCT scan, was performed to further evaluate the presence of metastases, occurrence of contralateral tumour, or relapse [12]. Tongaonkar et al. mentioned that both USG and MSCT scan are imaging modalities for Wilms's tumour [13]. The alternative modality that can be used is MRI. The cost-effectiveness of MRI is yet to be confirmed. Nevertheless, a previous study by Rohrschneider et al. suggested that both contrast-enhanced CT and T1-weighted MRI had similar potential and both modalities were superior to ultrasound in diagnosing nephroblastomatosis [14].

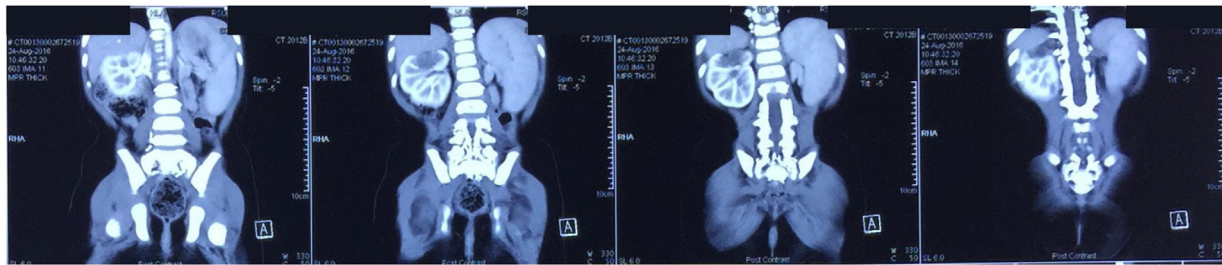


Fig. 2. MSCT scan examination after undergoing 24-weeks of neoadjuvant chemotherapy, right partial nephrectomy, left radical nephrectomy, and 7 fractions of 10.6 Gy radiotherapy.

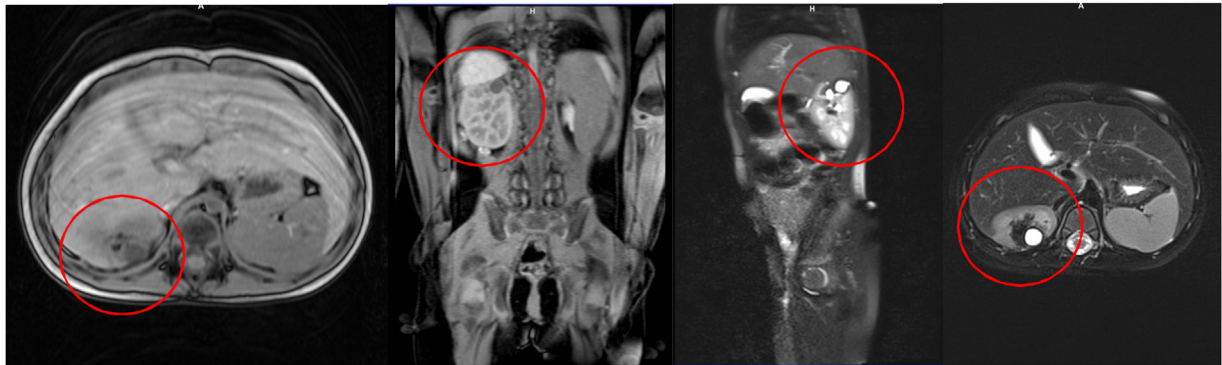


Fig. 3. A 1.2 cm cystic lesion (red circle) remained at the superior pole of right kidney. (A: T1-weighted axial slice; B: T1-weighted coronal slice; C: T2-weighted sagittal slice; D: T2-weighted axial slice).

Table 1
Management of Wilms tumour according to NWTS/COG.

Stadium	Histology	NWTS/COG Management (post-operative)
I	FH	18 weeks of
	UH	DAM/VCR
II	FH	18 weeks of DAM/VCR
	UH	24 weeks of DAM/VCR/DOX/CPM/Etoposide, RT of tumour bed + any regions involved
III	FH	24 weeks of DAM/VCR/DOX, RT of tumour bed + any regions involved
	UH	24 weeks of DAM/VCR/DOX/CPM/Etoposide, RT of tumour bed + any regions involved
IV	FH	24 weeks of DAM/VCR/DOX, RT of tumour bed + any regions involved
	UH	24 weeks of DAM/VCR/DOX/CPM/Etoposide, RT of tumour bed + any regions involved

UH: Unfavorable Histology; FH: Favorable Histology; DAM: Dactinomycin; VCR: Vincristine; DOX; Doxorubicin; CPM; Cyclophosphamide; RT: Radiotherapy. Adapted from: Hamid ARAH, Umbas R, Oka AAG, Mochtar CA, Djatisoesanto W, et al. Guidelines of renal cancer. IAUI; 2019.

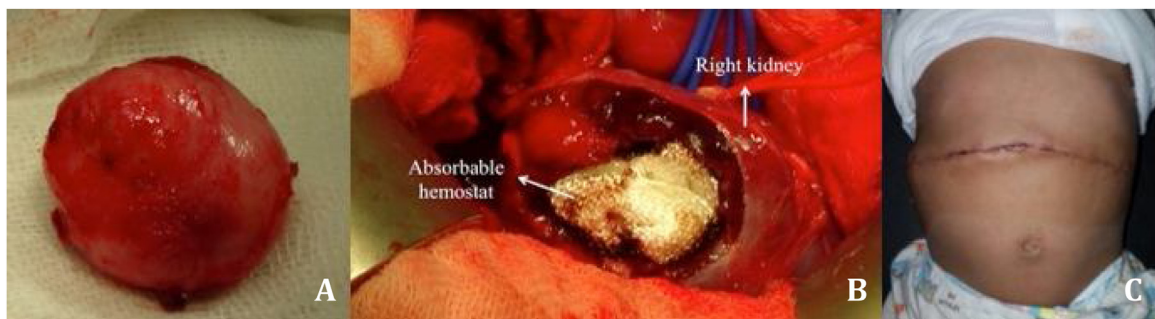


Fig. 4. Tumour of the right kidney (A); absorbable haemostat was applied during the procedure of partial right nephrectomy (B); post-surgical scar day-6.

In our patient, the MSCT scan revealed a cystic mass at the right upper-posterior pole of the right kidney after finalising radiotherapy. We suspected that this mass was a residual of blood clot or hematoma. Despite this assumption, we recommended the patient to undergo an MRI examination. Blute et al. stated that only 38% of stage V children from NWTS-3 study had all tumours eliminated

after one or more surgeries [15]. Thus, we felt that close monitoring through periodic follow-up sessions and imaging are key to achieving therapeutic success in this cohort of patients. To date, there are no clear recommendation on the timing of follow-up and imaging. However, in this patient, we plan to do routine follow-up every 12 months and periodic imaging using MRI.

4. Conclusion

From our experience, the combination of pre-chemotherapy biopsy followed by neo-adjuvant chemotherapy, renal salvage surgery and adjuvant radiotherapy resulted in a good clinical outcome for our patient. We propose that follow-up examinations to be performed every three months during the first year. This timeline can be adjusted during later follow-up years. Consensus should be developed internationally on the best practices in the diagnosis and management of this rare but challenging clinical condition.

5. Scare criteria

We confirmed that our work has been reported in line with the SCARE 2018 criteria [16].

Declaration of Competing Interest

The authors declare no conflict of interest.

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Ethical approval

The authors declare that we obtained permission from ethics committee in our institution. The Reference number for our ethical committee is 20-08-0966.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

- Irfan Wahyudi; Study concept or design, data collection, data analysis or interpretation, writing the paper
- Johannes Aritonang; Study concept or design, data collection, data interpretation, writing the paper
- Agus Rizal A. Hamid; Study concept or design, data collection, data interpretation
- Gerhard R. Situmorang; Study concept or design, data collection, data interpretation
- Hendy Mirza; Data collection, data interpretation

- Fina Widia; Data collection, data interpretation
- Arry Rodjani; Data collection, data interpretation

Registration of research studies

Our study design is case report, therefore we did not submit our report into any registry.

Guarantor

Irfan Wahyudi, MD. PhD.
Johannes Aritonang MD. B.MedSc.

Provenance and peer review

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