—Case Reports—

Hypertensive Cardiomyopathy with Congestive Heart Failure in an Infant with Unilateral Wilms Tumor: A Case Report

Jun Kuwabara[1,†], Satoshi Akita[1], Mitsunori Sato[1,†], Katsuya Watanabe[1], Takayasu Kawamoto[1], Kazufumi Tanigawa[1], Sayuri Matsui[1], Yusuke Matsuno[2], Yousuke Abe[2], Satoshi Kikuchi[1], Motohira Yoshida[1], Shigehiro Koga[1], Kei Ishimaru[1], Hiroyuki Egi[1] and Yuji Watanabe[1]

[1]Department of Gastrointestinal Surgery and Surgical Oncology, Ehime University Graduate School of Medicine, Ehime, Japan
[2]Department of Surgery, Saijo Central Hospital, Ehime, Japan

Wilms tumor (WT) is the most common malignant kidney tumor in children. High blood pressure is seen in up to 55% of children with WT. However, hypertensive cardiomyopathy with congestive heart failure due to WT is remarkably rare, with only several cases reported worldwide. In this report, a pediatric case of WT with hypertension causing hypertensive cardiomyopathy and congestive heart failure is presented. An 8-month-old male child with abdominal distension was seen by his primary physician. He was referred to our hospital for further examination and treatment. Abdominal contrast-enhanced computed tomography demonstrated a weakly enhancing, large abdominal mass, which was larger than 12 cm. Two-dimensional transthoracic echocardiography showed a diffuse hypokinetic left ventricle. The patient was diagnosed with cardiomyopathy caused by hypertension. Open surgical resection of the mass was successfully performed. His postoperative course was uncomplicated, and the patient was successfully discharged. The plasma renin activity was maintained at a high level even after left nephrectomy, suggesting that the right kidney was likely the source of renin secretion. Mechanical compression of the right renal blood vessels by a greatly enlarged left kidney can cause right renal ischemia, which activates renin excretion. Nephrectomy can be an effective treatment for a WT patient with hypertension causing hypertensive cardiomyopathy, and then cardiac function will be improved within several weeks. We recommend routine echocardiography surveillance in patients with WT. This report can help pediatric surgeons become more familiar with cardiomyopathy caused by WT.
(J Nippon Med Sch 2021; 88: 551–555)

Key words: Wilms tumor, hypertensive cardiomyopathy, hypertension, renin

Introduction

Wilms tumor (WT), also called nephroblastoma, is the most common malignant kidney tumor in children and is typically found between 3 and 5 years[1]. WT accounts for nearly 6% of all childhood tumors and more than 95% of all pediatric tumors of the kidney[2]. There is no significant sex predilection. Although most cases of WT are sporadic, about 1.5% of cases have a positive family history[3]. Most tumors are solitary and well circumscribed[4], and they typically present as an asymptomatic abdominal mass discovered by parents. Macroscopic hematuria occurs in approximately 25% of cases. Abdominal pain is reported in 30% of the patients, and high blood pressure (BP) is seen in up to 55% of children with WT[5,6]. However, hypertensive cardiomyopathy with subsequent congestive heart failure due to WT is remarkably rare, with only several cases reported worldwide (**Table 1**)[7–12]. In this report, a pediatric case of WT with hypertension causing hypertensive cardiomyopathy and congestive heart failure is presented.

Case Report

An 8-month-old male child with abdominal distension was brought to his primary physician. A large elastic left abdominal wall mass was felt on physical examination. He was referred to our hospital for further examination and treatment. At the time of admission, his vital signs were as follows: heart rate 136 beats/min, respiratory rate 30 breaths/min, BP 156/90 mmHg, and arterial oxygen saturation (SpO_2) 98%, and the patient presented

[†]These authors contributed equally to this work.
Correspondence to Mitsunori Sato, Department of Gastrointestinal Surgery and Surgical Oncology, Ehime University Graduate School of Medicine, Shitsukawa, Toon, Ehime 790–0295, Japan
E-mail: mit-sato@m.ehime-u.ac.jp
https://doi.org/10.1272/jnms.JNMS.2021_88-513
Journal Website (https://www.nms.ac.jp/sh/jnms/)

Table 1 Clinical characteristics in patients with Wilms tumor and heart failure

Author & Year	Age	Sex	Primary tumor location	Maximum tumor diameter (cm)	Clinical symptoms	Hyperreninemia	LVEF (%)	LVFS (%)
Stine et al.[7], 1986	9 months	M	Bilateral kidneys	11 (right kidney) 13 (left kidney)	HT, abdominal distension	Yes	NA	NA
Pujol et al.[8], 1992	2 months	M	Left kidney	NA	HT	Yes	NA	NA
Agarwala et al.[9], 1997	2 years	F	Right kidney	15	HT, DCM, pulmonary edema	Yes	NA	NA
Sakaguchi et al.[10], 2009	2 years	F	Left kidney	12	HT, pleural effusion	Yes	<30	NA
Sethasathien et al.[11], 2019	3 years	M	Left kidney	9.7	HT, DCM	Yes	29	NA
Chung et al.[12], 2020	11 months	M	Left kidney	8.1	HT, DCM, pulmonary edema	NA	29.4	NA
Present case	8 months	M	Left kidney	15	HT, abdominal distension	Yes	33.7	15.6

LVEF: Left ventricular ejection fraction, LVFS: Left ventricular fractional shortening, HT: Hypertension, DCM: Dilated cardiomyopathy, NA: not available

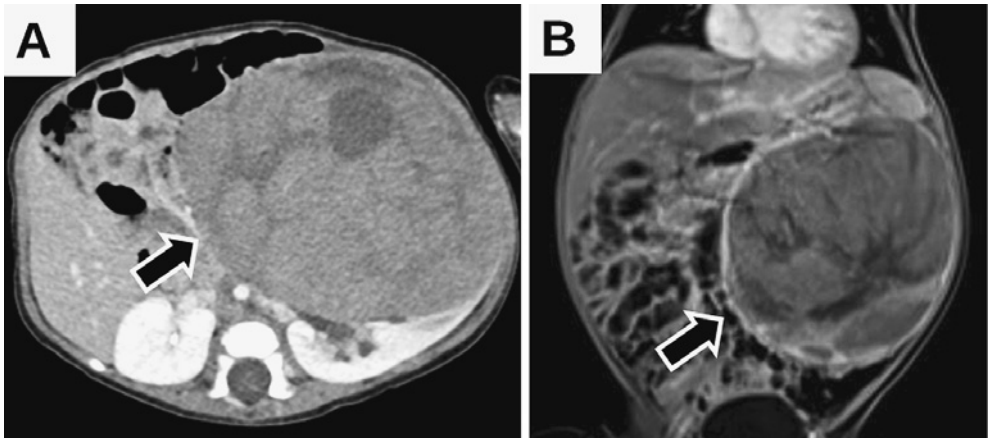

Fig. 1 Abdominal contrast-enhanced computed tomography and magnetic resonance imaging findings
Abdominal contrast-enhanced computed tomography shows a large, weakly enhancing, abdominal mass (arrow), larger than 12 cm (A). Abdominal magnetic resonance imaging shows a mixed solid and fluid-filled tumor (arrow) (B).

dyspnea. On cardiovascular examination, the first and second heart sounds were normal, with regular rhythm and no murmurs. Abdominal contrast-enhanced computed tomography showed a weakly enhancing, large abdominal mass, larger than 12 cm, and no evidence of metastatic lesions (**Fig. 1A**). Abdominal magnetic resonance imaging showed a mixed solid and fluid-filled tumor (**Fig. 1B**). The blood chemistry results showed elevated levels of lactate dehydrogenase (2,964 IU/L, normal: 202-437 IU/L), brain natriuretic peptide (104.2 pg/mL, normal: < 18.4 pg/mL), cortisol (97.6 μg/dL, normal: 4.3-22.4 μg/dL), aldosterone (44.1 ng/dL, normal: 3.6-22.4 ng/dL), and plasma renin activity (43.6 ng/mL/h, normal: 0.2-2.3 ng/mL/h). Electrocardiography showed left ventricular hypertrophy (LVH). The sum of the S wave in V1 (2.5 mV) and the R wave in V5 (2.9 mV) exceeded 3.5 mV (5.4 mV). Two-dimensional transthoracic echocardiography showed a diffuse hypokinetic left ventricle with an ejection fraction (EF) of 33.7% and fractional shortening of 15.6% (**Fig. 2**). The chest X-ray showed cardiomegaly with a cardiothoracic ratio of 55% (**Fig. 3**). The patient was diagnosed with cardiomyopathy caused by hypertension and was treated with furosemide, dobutamine, milrinone, and enalapril for treatment of the LV

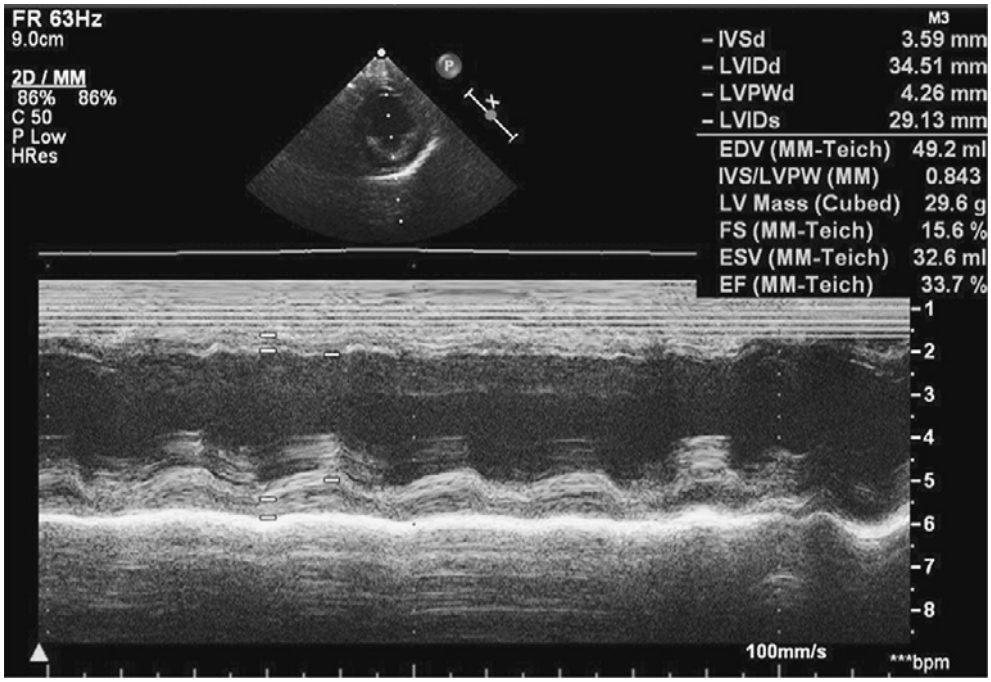

Fig. 2 Echocardiography findings
Two-dimensional transthoracic echocardiography shows a diffuse hypokinetic left ventricle with an ejection fraction of 33.7% and fractional shortening of 15.6%.

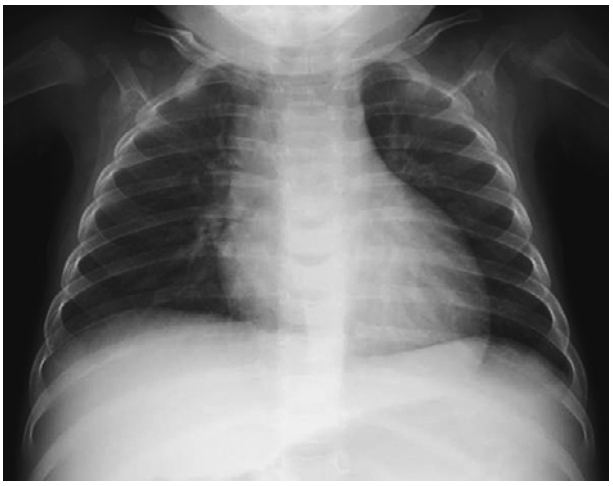

Fig. 3 Chest X-ray findings
The chest X-ray shows cardiomegaly with a cardiothoracic ratio of 55%.

systolic dysfunction in hypertension. After the completion of treatment, the patient showed clinical improvement in LVEF (from 33.7% to 40.5%) and BP (from 156/90 mmHg to 116/58 mmHg).

Open surgical resection of the mass (nephrectomy) was successfully performed (**Fig. 4**). Blood loss was 13 mL. The surgical time was 220 minutes. The resected specimen weighted 695 g and measured 13 × 11 × 10 cm^3 (**Fig. 5**).

Postoperative plasma renin activity was also examined (**Fig. 6**). Plasma renin activity reached a peak value of 138.8 ng/mL/h on day 15 after surgery and gradually fell to normal. Clinical genetic testing showed a mutation in the gene coding Wilms tumor suppressor gene 1 (WT 1). On histopathological examination, the left tumor was WT of the nephroblastic type, classified as stage I (National Wilms Tumor Study-5), focal nephroblastic subtype.

After surgery, adjuvant vincristine and actinomycin D (regimen EE4A) were given for 6 weeks to prevent recurrence. Normalization of BP and brain natriuretic peptide was achieved within 2 weeks after operation. One month after surgery, improvements of LVEF (63.0%) and LV fractional shortening (36.8%) were observed, and normalization of lactate dehydrogenase was achieved. The sum of the S wave in V1 and the R wave in V5 was not greater than 3.5 mV within 2 months after the operation.

The patient's postoperative course was uncomplicated, and the patient was successfully discharged on hospital day 180 in good clinical condition.

Written, informed consent was obtained from the parents of the patient for the publication of this case report and any accompanying images.

Discussion

It is well known that children with WT may have hypertension due to high plasma renin activity[13].

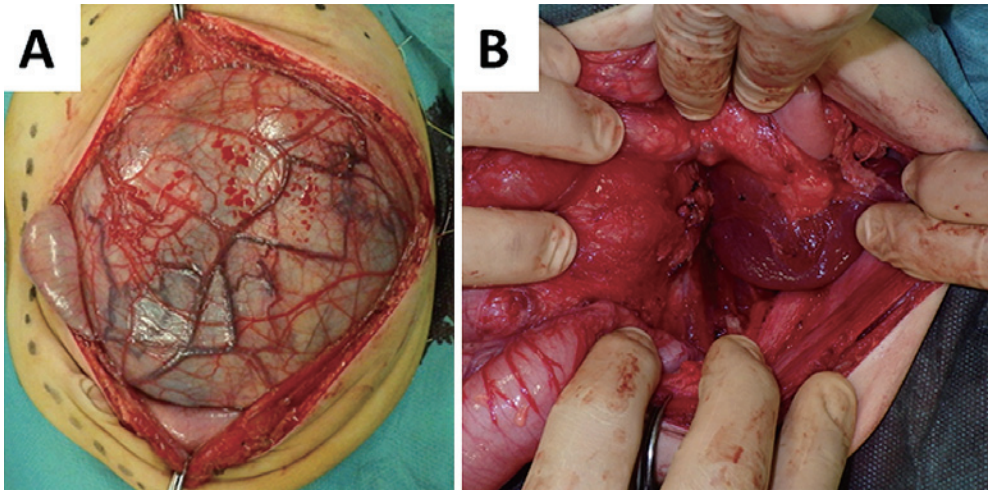

Fig. 4 Intraoperative findings
Intraoperative photographs (A) before and (B) after surgical resection of Wilms tumor.

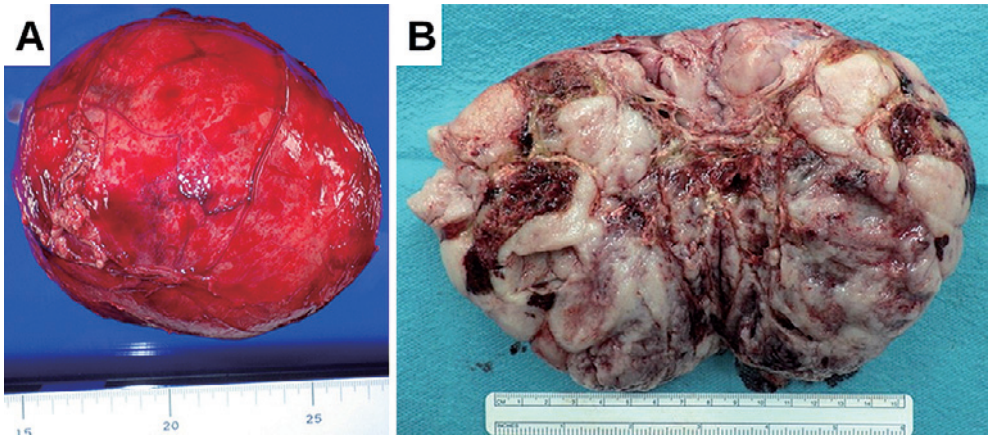

Fig. 5 Resected specimen
The surgical specimen shows a 12-cm-long abdominal mass (A). Gross appearance of the cut surface of the resected specimen (B).

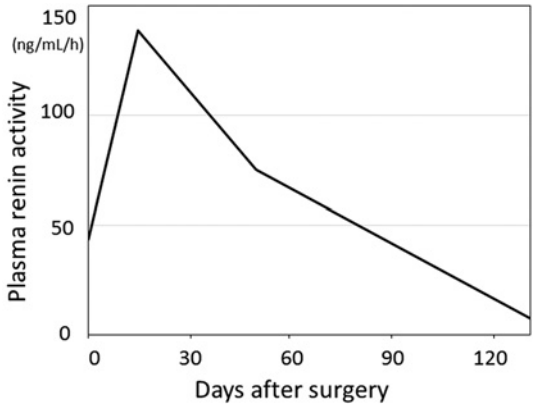

Fig. 6 Course of plasma renin activity
The postoperative plasma renin activity is maintained at a high level over 4 months after surgery, and then it gradually decreases.

However, hypertensive cardiomyopathy and subsequent congestive heart failure due to WT are remarkably rare, with only several cases reported worldwide (**Table 1**)[7–12]. In this report, a case of an unusual presentation of hypertensive cardiomyopathy caused by hypertension associated with WT was described.

Although hypertensive cardiomyopathy is uncommon in patients with WT, hypertension with elevated renin activity is common. Two mechanisms have been put forward for the etiology of hyperreninemia: (1) renal artery stenosis-related renal ischemia; and (2) WT secreting renin[14,15]. As shown in **Figure 6**, the postoperative plasma renin activity was maintained at a high level over 4 months after surgery, and it then gradually decreased. The plasma renin activity was maintained at a high level even after left nephrectomy, suggesting that the right kidney was the likely source of renin secretion. Mechanical

compression of right renal blood vessels by a greatly enlarged left kidney can cause right renal ischemia, which activates renin excretion. Therefore, renin would be secreted from the juxtaglomerular kidney cells.

Reinhold et al.[16] reported that, in the 2-kidney-1-clip Goldblatt rat model of renovascular hypertension, renal renin gene expression was higher at all time points in the clipped kidney than in the unclipped kidney. They also demonstrated that plasma renin activity was significantly higher in the 2-kidney-1-clip Goldblatt rat model than in the control group, and it then decreased to 2-fold of the control group on day 70 after surgery[16]. In the present case, renin was secreted from the ischemic right kidney, correlated with the right kidney deterioration. Recovery from right renal ischemia would require several months. Consequently, elevation of renin secretion was observed for over 4 months after surgery.

Hyperreninemia led to increased angiotensin II and aldosterone, resulting in hypertension and hypertensive cardiomyopathy. WT resection alleviated the deteriorating cardiac function in the present case. After the left WT resection, LV contractility, function, and performance gradually improved.

Preoperative BP control is important to reduce postoperative complications after WT treatment. Angiotensin-converting enzyme inhibitors may be the most effective group of drugs in WT patients with renin-mediated hypertension before surgery[15]. The present patient was treated with enalapril, and his BP improved from 156/90 mmHg to 116/58 mmHg.

Nephrectomy can be an effective treatment for WT patients with hypertension causing hypertensive cardiomyopathy, and then cardiac function will improve within several weeks. We recommend routine echocardiography surveillance in patients with WT. In a patient with hypertensive cardiomyopathy due to hypertension, abdominal imaging should probably be performed. Pediatric surgeons should keep in mind the need to identify cardiomyopathy when assessing WT patients with hypertension. In inferior vena cava, tumor thrombus is observed in 4-10% of patients, with 1-3% of right atrium involvement[17]. Therefore, preoperative cardiac examinations should be performed to prevent cardiovascular complication. This report can help pediatric surgeons become more familiar with cardiomyopathy caused by WT.

Conflict of Interest: The authors declare no conflict of interests.

References

1. Bhatnagar S. Management of Wilms' tumor: NWTS vs SIOP. J Indian Assoc Pediatr Surg. 2009 Jan;14(1):6–14.
2. Davidoff A. Wilms tumor. Curr Opin Pediatr. 2009 June; 21(3):357–64.
3. Ganesh S, Vennila JJ, Scholz H. An overview and perspectives of Wilms' tumor. Int J Canc Res. 2011 Apr;7(1):1–7.
4. Chung E, Graeber A, Conran R. Renal tumors of childhood: radiologic-pathologic correlation. Part 1. The 1st Decade. Radiographics. 2006 Apr;36(2):499–522.
5. Denes FT, Duarte RJ, Cristofani LM, et al. Pediatric genitourinary oncology. Front Pediatr. 2013 Dec 16;1(48):1–10.
6. Jastaniah W, Elimam N, Alluhaibi R, et al. The prognostic significance of hypertension at diagnosis in children with Wilms tumor. Saudi Med J. 2017 Mar;38(3):262–7.
7. Stine KC, Goertz KK, Poisner AM, et al. Congestive heart failure, hypertension, and hyperreninemia in bilateral Wilms' tumor: successful medical management. Med Pediatr Oncol. 1986;14(1):63–6.
8. Pujol JF, Perel Y, Fayon M, et al. Cardiac failure by major arterial hypertension secondary to nephroblastoma. Pediatrie. 1992;47(6):441–4.
9. Agarwala B, Mehrotra N, Waldman JD. Congestive heart failure caused by Wilms' tumor. Pediatr Cardiol. 1997 Feb;18(1):43–4.
10. Sakaguchi D, Doizaki S, Watanabe S, et al. Sashitsu shinkin chimitsuka shogai niyoru shinfuzen wo gappeishita jingashu no 1 rei [Clinical outcomes in Wilms tumor patient with left ventricular noncompaction and heart failure]. Shonigan [Japanese Journal of Pediatric Oncology]. 2009;46(1):59–60. Japanese.
11. Sethasathien S, Choed-Amphai C, Saengsin K, et al. Wilms tumor with dilated cardiomyopathy: A case report. World J Clin Oncol. 2019 Aug 24;10(8):293–9.
12. Chung JM, Lee SD. Wilms Tumor with dilated hypertensive cardiomyopathy, acute myocarditis, pulmonary edema, and heart failure. Urol Case Rep. 2020 Aug 25;33: 101391.
13. Mitchell JD, Baxter TJ, Blair-West JR, et al. Renin levels in nephroblastoma (Wilms' Tumour) report of a renin secreting tumour. Arch Dis Child. 1970 Jun;45(241):376–84.
14. Spahr J, Demers L, Shochat S. Renin producing Wilms' tumor. J Pediatr Surg. 1981 Feb;16(1):32–4.
15. Maas M, Cransberg K, Grotel M, et al. Renin-induced hypertension in Wilms tumor patients. Pediatr Blood Cancer. 2007 May 16;48(5):500–3.
16. Reinhold S, Uihlein D, Böger C, et al. Renin, endothelial NO synthase and endothelin gene expression in the 2 kidney-1clip Goldblatt model of long-term renovascular hypertension. Eur J Med Res. 2009 Dec 14;14(12):520–5.
17. Ratajczyk K, Czekaj A, Rogala J, et al. Adult Wilms tumor with inferior vena cava thrombus and distal deep vein thrombosis - a case report and literature review. World J Surg Oncol [Internet]. 2018 Feb 23;16(1):38. Available from: https://doi.org/10.1186/s12957-018-1343-4

(Received, July 30, 2020)
(Accepted, October 28, 2020)
(J-STAGE Advance Publication, November 30, 2020)

Journal of Nippon Medical School has adopted the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License (https://creativecommons.org/licenses/by-nc-nd/4.0/) for this article. The Medical Association of Nippon Medical School remains the copyright holder of all articles. Anyone may download, reuse, copy, reprint, or distribute articles for non-profit purposes under this license, on condition that the authors of the articles are properly credited.