Extrarenal Wilms tumor with hypertension and dilated cardiomyopathy in an infant: A case report and review of the literature

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Title page

Extrarenal Wilms tumor with hypertension and dilated cardiomyopathy in an infant: A case report and review of the literature

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Abbreviations table

Abbreviation	Full term
ERWT	Extrarenal Wilms tumors
CHF	Congestive heart failure
ICU	Intensive care unit
BP	Blood pressure
MRI	Magnetic resonance imaging
CT	Computed tomography

Abstract

While Wilms tumors are the most frequently detected renal cancer type in children, extrarenal Wilms tumors (ERWTs) remain rare. This report is the first to describe hypertension and dilated cardiomyopathy in a patient with an ERWT. A six-month-old male infant presented with an abdominal mass and paroxysmal hypertension, echocardiography revealed dilated cardiomyopathy with an ejection fraction of 34%, as well as substantially increased plasma renin activity. Pathology yielded a definitive diagnosis of ERWT. Cardiac function and blood pressure gradually returned to normal after tumorectomy. The early diagnosis of such a tumor together with efficient oncologic treatment are vital to optimal patient outcomes.

1 | INTRODUCTION

Wilms tumor, also referred to as nephroblastoma, accounts for ˜90% of all pediatric renal malignancies[1]. However, extrarenal Wilms tumor (ERWT) manifestation remains rare, occurring in approximately 3% of all Wilms tumor cases[2]. Such extrarenal tumors typically present in the form of an asymptomatic mass within the abdomen, although they can be accompanied by abdominal pain, hematuria, and/or hypertension, with each occurring in roughly a quarter of such cases[3]. Dilated cardiomyopathy and congestive heart failure (CHF) are rare presentations for such tumors, with only a few previously reported cases exhibiting these symptoms. There have not been any published reports to date of a case of ERWT presenting with hypertension, dilated cardiomyopathy, and CHF. Here we present the first case of ERWT with these rare symptoms and review the relevant literature.

2 | CASE DESCRIPTION

Our patient is a six-month-old male infant. He was found to exhibit right cryptorchidism after birth, and one month ago his parents took him to see a doctor because of this cryptorchidism. During the doctor's examination, a mass was discovered in the lower abdomen, and the patient was therefore admitted to the Department of Thoracic and oncological surgery of our hospital for further examination and treatment. However, just after hospitalization, the patient exhibited progressive hepatomegaly, dyspnea, paroxysmal tachycardia, and paroxysmal hypertension, that had not been previously detected. Chest radiography revealed cardiomegaly, and echocardiography revealed cardiomyopathy with an ejection fraction of 34%. The patient was diagnosed with acute heart failure and treated using digoxin, milrinone, furosemide, and spironolactone, which failed to resolve these symptoms. He was therefore transferred to the intensive care unit (ICU) due to acute heart failure, hypertension, and poor left ventricular contractility.

After transferring to the ICU, The patient exhibited a heart rate of 160 beats per minute, a respiratory rate of 55 breaths per minute, 100% blood oxygen saturation, and the blood pressure (BP) was 134/102 mmHg. Cardiac examinations revealed grade II systolic murmur, low heart sound, and a regular rhythm. A hard 5 cm x 5 cm x 4 cm mass was detected within the lower right abdomen upon palpation. The liver was palpated 3 cm below the right costal margin. We performed a series of laboratory tests, and blood chemistry analyses revealed elevated levels of liver enzymes (aspartate aminotransferase 417.2 U/L, normal: 0-40 U/L; alanine aminotransferase 351.5 U/L, normal: 0-40 U/L), elevated troponin T (348.8 ng/L, normal:[?] 14 ng/L), and markedly elevated pro-B-type natriuretic peptide (>35000 pg/mL, normal: < 646 pg/mL). Substantial increases were also detected in plasma renin activity (684.7 μIU/mL, normal: 3.11-41.2 μIU/mL), angiotensin I (18.74 ng/mL/hr, normal 0.15-2.33 ng/mL/hr), angiotensin II (76.78 ng/mL/hr, normal 25-60 ng/mL/hr

), and plasma aldosterone (2000 pg/mL, normal: 30-160 pg/mL). Plasma metanephrine levels were within the normal range (1615.9 pmol/L, normal: 413.9-4434.2 pmol/L), and low urinary metanephrine levels were detected (3 nmol/d, normal: 68.9-378 μg/d). Cardiomegaly and diffuse pulmonary infiltration were detected through chest radiographic imaging (Fig. 1A), with echocardiography revealing dilated cardiomyopathy with an ejection fraction of 38.4%, a shortening fraction of 18.1%, grade 2 mitral regurgitation, and no evidence of intracardiac thrombus or heart defects (Fig. 1C). Abdominal magnetic resonance imaging (MRI) revealed an inhomogeneous quasi-circular soft tissue mass (48.7 mm × 49.5 mm × 52.8 mm) (Figs. 1E and 1F), ascites, and bilateral pleural effusion.

The patient underwent emergency ICU treatment for CHF, hypertension, and left ventricular dysfunction with oral digoxin, spironolactone and intravenous milrinone and furosemide. However, owing to elevated renin-angiotensin-aldosterone levels, BP control was difficult. When the patient was treated with low-dose captopril (0.3 mg/kg), he developed severe hypotension, with BP dropping from 134/75mmHg to 69/32mmHg within 30 minutes and the drug was immediately discontinued. Antihypertensive drugs were then exchanged for urapidil and then sodium nitroprusside, with BP gradually returning to the normal range. However, there was still an occasional paroxysmal increase in BP. Owing to dyspnea, non-invasive ventilation was required to provide breathing assistance. After all of these treatments, the patient exhibited improved left ventricular ejection fraction (LVEF; from 34% to 58%) and BP (from 158/110mmHg to 117/68mmHg). After hemodynamic stabilization had largely been achieved, the mass was resected through an open surgical procedure on day 22 of hospitalization.

Pathologic examination revealed a well-circumscribed 6.0 cm x 5.0 cm x 5.0 cm mass consistent with ERWT without anaplasia (Fig. 2A). Microscopic analyses revealed triphasic histological findings characteristics of a Wilms tumor, including stromal, epithelial, and renal blastema elements. Testicular tissue was observed covering the tumor surface intraoperatively, but there was no evidence of tumor invasion of the surrounding tissues, including epididymal or testicular tissue. Embryonic renal tissue remnants were observed around the tumor. The tumor exhibited positive immunohistochemical staining for WT-1 (Fig. 2B), EGFR, CK19, AE1/AE3, and CAM5.2.

Postoperatively, the patient's BP returned to the normal range and antihypertensive drugs were discontinued immediately following surgery, whereupon BP remained stable. Plasma renin activity returned to the normal range within one day postoperatively, and cardiac size and function returned to normal within 24 days after surgery (Fig. 1B and 1D). He is currently undergoing adjuvant chemotherapy treatment (vincristine, doxorubicin, and actinomycin D) as per the recommendations of the International Society of Pediatric Oncology (SIOP)[4] at a local hospital.

A follow-up was conducted in our hospital two months after surgery. Cardiotonic drug use was gradually tapered until being fully discontinued, and the patient's heart rate, BP, and cardiac function have since remained stable. To date, it has been 4 months since the operation, and a recent telephone follow-up indicated that he has undergone four courses of chemotherapy and remains in stable condition. Additionally, his chest and abdominal computed tomography (CT) scans performed at a local hospital have shown no evidence of recurrence four months after treatment.

3 | DISCUSSION

Given their rarity, accurately diagnosing ERWTs prior to surgical resection remains challenging. The primary diagnosis in the present case was pheochromocytoma owing to the observed paroxysmal tachycardia and hypertension, but the normal urinary and plasma catecholamine levels did not support this diagnosis. We also considered neuroblastoma, as about 10% of neuroblastoma cases present with high BP[5], and there have also been case reports of neuroblastoma with hypertension and dilated cardiomyopathy, suggesting that this tumor type can cause the activation of the reninangiotensin aldosterone system[6]. However, about 90% of cases exhibited elevated urinary catecholamine metabolites[7], which was not evident in the present case. In addition to the above differential diagnosis, as some of these tumors arise within the pelvis, they may be incorrectly diagnosed as ovarian cysts or pelvic teratomas[8], but these rarely cause high blood

pressure and heart failure. In general, only postoperative pathological analyses ultimately lead to definitive ERWT diagnoses. Per Beckwith and Palmer[9], ERWTs are diagnosed based upon the following criteria: a primary extrarenal tumor exhibiting a primitive blastematous spindle or round cell component, with an abortive, embryonal tubular, or glomeruloid structure and no evidence of teratoma or renal carcinoma. WT1 is the most sensitive immunohistochemical marker for Wilms tumor diagnosis, being detectable in $> 90\%$ of cases[10]. Ultimately, in this medical record, pathological results were instead consistent with an ERWT, with WT1 positivity being observed upon immunohistochemical staining, diagnosis is definitive. Another rare aspect of this case is that the tumor arose next to the undescended testis. There have only been a few prior reports of paratesticular ERWTs to date[11].

To date, there have only been six published cases of Wilms tumor patients suffering from hypertensive cardiomyopathy and subsequent CHF[12-17], with all of these cases being tied to primary intrarenal tumors. This report is the first to describe hypertension and CHF in a patient with an ERWT. The two mechanisms that are generally believed to contribute to hyperreninemia are Wilms tumor-mediated renin production and the tumor-mediated compression of the renal artery. Immunohistochemical staining of the tumor tissues from five Wilms tumor patients revealed detectable renin expression in the blastemal portion of the tumor tissue, supporting a model wherein the production of renin by these tumors is the primary driver of hypertension[18]. In the present case, preoperative renin levels were significantly elevated but rapidly returned to normal ranges within the days following surgery. Moreover, the tumor was located within the pelvis, thus precluding the potential for renal artery compression. We thus speculate that this tumor was capable of directly secreting renin, contributing to secondary complications including dilated cardiomyopathy, hypertension, and CHF. Tumor resection alleviated the observed deterioration in cardiac function, with gradual postoperative improvements in LV contractility, performance, and function. It is thus evident that tumor-induced hyperreninemia led to increased angiotensin II and aldosterone, resulting in hypertension and hypertensive cardiomyopathy. However, Perry *et al* [19] reported cases of Wilms tumors with dilated cardiomyopathy without hyperreninemia. They note that in addition to renin, there may be other vasoactive mediators that can contribute to dilated cardiomyopathy and CHF, but further research will be required to confirm this possibility.

When assessing patients presenting with pelvic tumors complicated by heart failure and hypertension, ERWTs must be considered in the differential diagnosis. Hypertension can frequently lead to the potential for misdiagnosis in these cases, underscoring the need to raise awareness of this rare complication of such extrarenal tumors. Preoperatively controlling BP is critical in the treatment of ERWTs patients, and the use of angiotensin-converting enzyme inhibitors may represent the most effective means of treating renin-mediated hypertension in these patients prior to surgical intervention[20]. In the present case, the patient exhibited pronounced hypotension following the administration of low-dose captopril (0.3 mg/kg), suggesting that even lower doses should be used in the future in an effort to prevent this complication. The overall prognosis of ERWT patients is similar to that of intrarenal Wilms tumor patients, with surgical resection of the tumor representing the most effective means of controlling tumor growth and associated complications. Following tumorectomy, the prognosis of affected patients is generally good. However, in patients presenting with unexplained pelvic or abdominal tumors, early diagnosis and prompt surgical intervention are recommended to prevent or mitigate hypertension, dilated cardiomyopathy, and heart failure, thus contributing to a better patient prognosis.

4 | CONCLUSION

ERWTs should be considered in the differential diagnosis of children exhibiting a pelvic mass and suffering from hypertension and dilated cardiomyopathy. The clinical symptoms observed in the present case were likely attributable to the secretion of renin by the Wilms tumor. Tumor resection represents a highly effective treatment for affected patients, but ERWTs presenting with CHF and dilated cardiomyopathy are nonetheless life-threatening, underscoring the need for early diagnosis and the timely provision of intensive care and oncological treatment in order to ensure the best possible clinical outcomes.

CONFLICTS OF INTEREST

The authors declare no conflict of interests for this manuscript.

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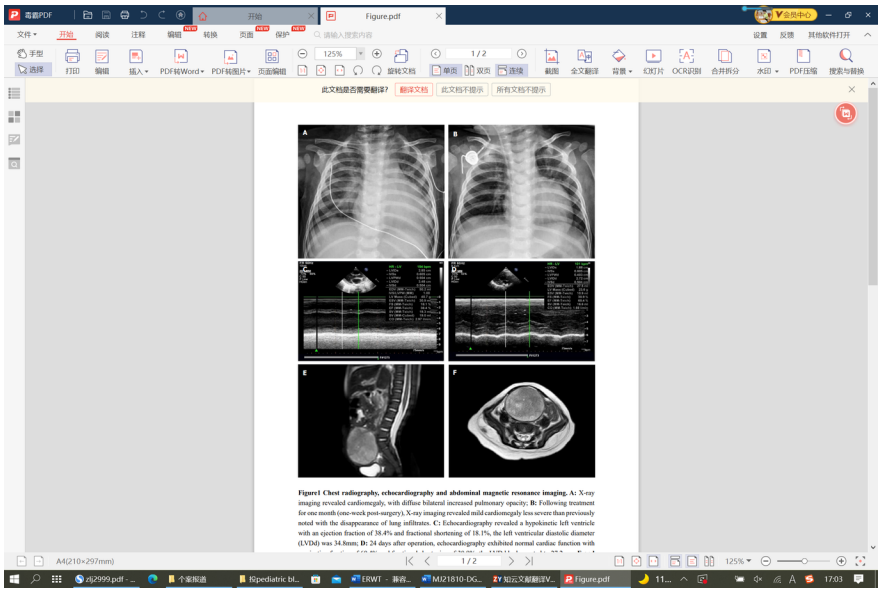

FIGURE 1 Imaging examination. (A) X-ray imaging revealed cardiomegaly, with diffuse bilateral increased pulmonary opacity; (B) Following treatment for one month (one-week post-surgery), X-ray imaging revealed mild cardiomegaly less severe than previously noted with the disappearance of lung infiltrates; (C) Echocardiography revealed a hypokinetic left ventricle with an ejection fraction of 38.4% and fractional shortening of 18.1%, the left ventricular diastolic diameter (LVDd) was 34.8mm; (D) 24 days after operation, echocardiography exhibited normal cardiac function with an ejection fraction of 60.4% and fractional shortening of 30.9%; the LVDd had reverted to 27.2mm; (E-F) MRI revealed an inhomogeneous quasi-circular 48.7 mm × 49.5 mm × 52.8 mm soft tissue mass.

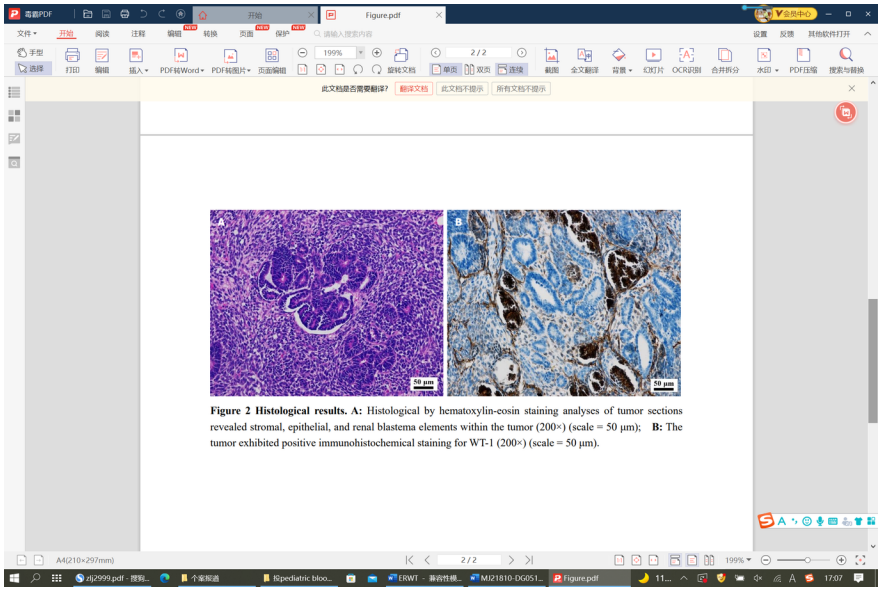

FIGURE 2 Histological results. (A) Histological by hematoxylin-eosin staining analyses of tumor sections revealed stromal, epithelial, and renal blastema elements within the tumor (200×) (scale = 50 μm); (B) The tumor exhibited positive immunohistochemical staining for WT-1 (200×) (scale = 50 μm).