□ Case Report □

Wilms' tumor with polydipsia, polyuria, hyponatremic hypertension and congestive heart failure : a case report

**Chul Hee Woo, M.D., Ji Min Jang, M.D., Chan Wook Woo, M.D.
Ki Hyung Lee, M.D. and Kwang Chul Lee, M.D.**

Department of Pediatrics, College of Medicine, Korea University, Seoul, Korea

A 3-year-old girl presented with polydipsia, polyuria, hyponatremia, hypertension and congestive heart failure. Her polyuria was unresponsive to water restriction and vasopressin challenge tests, and her blood pressure was not effectively controlled by antihypertensive drugs. Radiologic examinations revealed a Wilms' tumor in the right kidney. Her plasma renin activity and aldosterone concentration were greatly increased. After surgical removal of the tumor, the congestive heart failure disappeared. Congestive heart failure due to Wilms' tumor is very rare and we report here on such a case, with a brief review of the literature. **(Korean J Pediatr 2006;49:99-102)**

Key Words : Wilms' tumor, Hypertension, Congestive heart failure, Hyperreninemia

Introduction

Wilms' tumor is one of the most common abdominal tumors of childhood with a peak incidence between 1 and 5 years age. Since the original study by Bradley and Pincoffs in 1983[1], it is well known that this renal tumor in children can be associated with hypertension. The incidence of hypertension has been reported over than 25%, but malignant hypertension with congestive heart failure is the rare manifestation[2-4]. For the case we are reporting on, the heart failure was secondary to the severe hypertension with extreme hyperreninemia, and it was difficult to control prior to surgical extirpation of the tumor. Such heart failure has been reported secondary to severe hypertension from extreme case of hyperreninemia and it is difficult to control prior to surgical extirpation of the tumor. Because understanding the congestive heart failure that occurs with Wilms' tumor is important to allow safe and appropriate management, we report here on our experience. To the best of our knowledge, this is the first report about a Korean child presenting with congestive heart failure due to Wilms' tumor.

접수 : 2005년 8월 12일, 승인 : 2005년 10월 4일
책임저자 : 이광철, 고려대학교 의과대학 소아과교실
Correspondence : Kwang Chul Lee, M.D.
Tel : 02)920-5090 Fax : 02)922-7476
E-mail : yh951637@chol.com

Case Report

Three months prior to her hospital admission, a 3-year-girl presented weight loss, anorexia, polydipsia and polyuria. Because of the generalized edema and respiratory difficulties, she was admitted to the Korea University Anam Hospital. She had been tested with water deprivation and vasopressin challenge before visiting our hospital and these tests were normal. The pulse rate was 150 per minute, the respiratory rate 35 per minute, the temperature 38 degrees ℃ and the blood pressure 90/50 mmHg. The physical examination showed a chronically ill, apparently dehydrated, malnourished girl. Her body weight was 9.8 kg and her height was 98 cm (below the 3r percentile for weight and in the 75-90 percentile for height). A small and hard mass was palpated at the right lower abdomen. Laboratory data showed a hemoglobin concentration of 10.7 g/dL and a white blood cell count of 11,400/mm^3 with a normal differential count. The serum sodium value was 119 mEq/L, potassium 3.2 mEq/L, chloride 83 mEq/L, bicarbonate 27.3 mEq/L, total bilirubin 0.9 mg/dL, AST/ALT 81/85 IU/L, protein/albumin 5.6/3.7 g/dL, glucose 142 mg/dL and a serum osmorality of 290 mOsm/L. The average urine output was 2,430 mL/day with a urinary sodium concentration of

38 mEq/L, a urinary potassium of 25 mEq/L, a urinary chloride of 35 mEq/L and a urinary osmorality of 212 mOsm/L. The electrocardiogram (ECG) showed sinus tachycardia with severe left ventricular hypertrophy. Inverted T waves and ST changes were noted at V_4-V_6. Two-dimensional and Doppler echocardiography demonstrated left ventricular enlargement, a decrease of the fractional shortening to 15% (normal >25%) and moderate to severe mitral, aortic and pulmonary valve regurgitation. Radiographs of the chest, abdomen and skull were unremarkable. Abdominal ultrasonography demonstrated a mass in the kidney of about 5 cm diameter, and mild hydronephrosis was noted (Fig. 1). Computer tomography and a bone scan revealed no evidence of metastasis. A hormonal study was performed and the plasma renin in the peripheral blood was 142 ng/mL/hr (normal <16.6 ng/mL/hr), the angiotensin I was 27,000 pg/mL (normal <500 pg/mL), the angiotensin II was 998 pg/mL (normal 9 to 47 pg/mL), the aldosterone was 756.4 pg/mL (normal 10 to 160 pg/mL). The urinary homovanilic acid (HVA) was measured at 0.09 ng/mL/day (normal <22 ng/mL/day) and the urinary epinephrine was 1.1 μg/day (normal 4-29 μg/day).

The patient was treated with digoxin, furosemide, fluid restriction and electrolyte replacement. Her blood pressure fluctuated from 170/120 to 100/50 and it was not effectively controlled with calcium channel blockers and angiotension converting enzyme inhibitors. On the 9th hospital day, nephrectomy was done and a well encapsulated tumor (5×4×5 cm) was removed (Fig. 2). Histologically, it had the characteristics of a favorable Wilms' tumor with a combination of epithelial, blastemal and stromal tubular formation and immature glomeruli (Fig. 3). Shortly after surgery, her craving for water decreased; her urine output was markedly reduced and the blood pressure was significantly improved. On the fourth postoperative day, the serum renin concentration was decreased to 0.2 ng/mL/hr and the se-

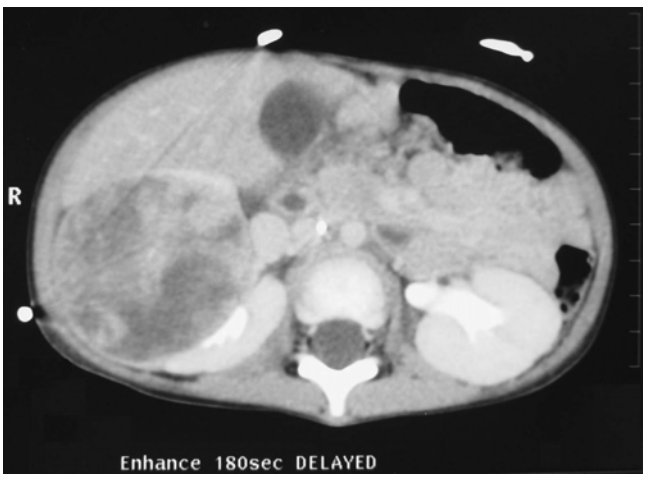

Fig. 1. Abdominal CT shows a large heterogenous low density mass leision, about 5cm in diameter in right kidney.

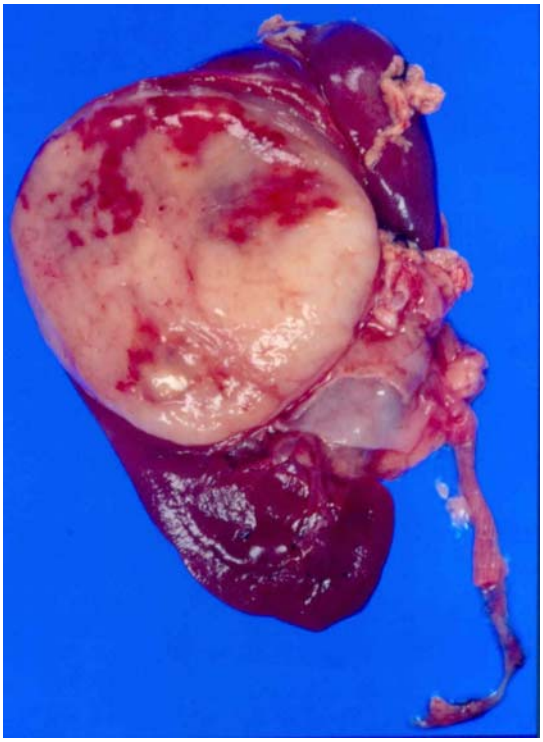

Fig. 2. Gross picture of the resected specimen. There is no specific renovascular obstruction and pelvic involvement of tumor.

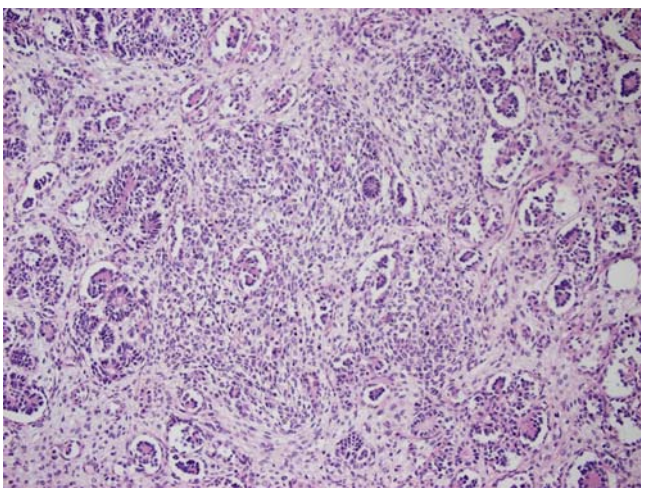

Fig. 3. Pathologic finding shows a combination of epithelia, blstema and stromal tubular formation and immature glomeruli (H&E ×200).

rum aldosterone was reduced to 203.5 pg/mL. The cardiac function improved both clinically and on the echocardiography. An echocardiographic examination showed that the left ventricular function was improved with a fractional shortening of 22% and only mild mitral regurgitation was detected. After surgery, chemotherapy was started with actinomycin D and vincristine. Five months after surgery, the patient has remained normotensive and she is off all vasoactive or cardiotropic drugs. The congestive heart failure has disappeared, and the echocardiogram has returned to normal.

Discussion

Congestive heart failure as a presenting sign of Wilms' tumor is very rare. Since Stine et al.[3] described a 9-month-old infant with bilateral Wilms tumor, it has been suggested that the congestive heart failure seen with Wilms' tumor was apparently produced by the hyperreninemia. This proposal was substantiated by the improvement of the congestive heart failure with specific renin blocking drugs or because of the effectiveness of nephrectomy for eliminating the cardiac dysfunction with the coincident return of the renin levels to normal. In our case the congestive heart failure was refractory to vasodilators and angiotension coverting enzyme inhibitor, but after nephrectomy, the patient's sign and symptoms were alleviated and the serum renin level returned to normal.

For this patient with congestive heart failure, the renin-angiotensin-aldosterone system has an important roles in the hyperreninemia. First, angiotensin II and aldosterone constrict the peripheral vascular muscle and decrease the renal excretion of sodium and water[5]. Especially. Renin-angiotensin II can increase the pulmonary artery pressure by direct vasoconstriction[6] and it may also increase the capillary permeability[7]. Angiotensin II is also a dipsogenic hormone and it can stimulate drinking by the activation of the receptors in the subfornical organ of the brain[8-10]. Many studies have shown that the angiotensin-sensitive neurons are distributed throughout the subfornical organ and these can influence autonomic function and water intake. Thus, it is probable that the elevated renin production caused the marked hypertension and so it led to the congestive heart failure.

Second, another important hormone may be atrial natriuretic factor (ANF). Silberman et al.[11] reported ANF is elevated in the Wilms' tumor patients with malignant hypertenion. Atrial distention and acute salt loading lead to significant increases in ANF. In the case of hyperreninemia, the initial hypervolemia that is induced by the highly elevated angiotensin level and then the subsequent chronic atrial distension that is secondary to the left ventricular dysfunction may be the stimulus for the initial secretion and then the chronic secretion of ANF. ANF abolishes the vasoconstrictor effect of angiotensin II and it decreases the release of the hormone and antagonizes the effect of the renin/angiotensin system; it also promotes natriuresis and decreases the cardiac output and plasma volume. Hypersecretion of ANF may explain the hypovolemia and sodium diuresis.

For the treatment of Wilms' tumor, pre-operative blood pressure stabilization may be important to reduce the post-treatment morbidity. As the renin-mediated hypertension is produced by the angiotensin cascade, the most effective classes of drugs may be the angiotensin converting enzyme inhibitors and the competitive angiotensin II antagonists[12]. Peri-operative tumor handling may also cause severe hypertension and it should be treated with short-acting agents such as sodium nitroprusside. Nephrectomy may be the definitive treatment for this hypertension and then the cardiac function will be normalized within some months.

In summary, we report here on a case of Wilms' tumor presenting with polydipsia, polyuria, hyponatremic/hypertension and congestive heart failure. This case shows that congestive heart failure developed secondary to the severe hypertension and this was due to hyperreninemia. Physicians should be aware of this complication and recognize it for better treatment.

한 글 요 약

다음, 다뇨, 저나트륨성 고혈압, 심부전증을 보이는 윌름씨 종양 1례

고려대학교 의과대학 소아과교실

우철희 · 장지민 · 우찬욱 · 이기형 · 이광철

윌름씨 종양은 주로 1-5세에 복부에 생기는 종양으로 약 25% 이상에서 고혈압을 동반하지만 심각한 고혈압에 의하여 심부전을 보이는 경우는 매우 드물다. 저자들은 3세된 여자 아이가 윌름씨 종양으로 인한 고레닌 혈증으로 다음, 다뇨, 저나트륨성 고혈압과 심부전을 보였으나 수술적으로 종양을 제거한 후 증상

호전을 보였기에 문헌 고찰과 함께 보고하는 바이다.

References

1) Bradley JE, Pincoffs MC. The association of adenomyosarcoma of the kidney (Wilms' tumor) with arterial hypertension. Ann Intern Med 1938;11:1613-28
2) Agarwala B, Mehrotra N, Waldman JD. Congestive heart failure caused by Wilms' tumor. Pediatr Cardiol 1997;18:43-4.
3) Stine KC, Goertz KK, Poisner AM, Lowman JT. Congestive heart failure, hypertension and hyperreninemia in bilateral Wilms' tumor : successful medical management. Med Pediatr Oncol 1986;14:63-6
4) Trebo MM, Mann G, Dworzak M, Zoubek A, Gadner H. Wilms tumor and cardiomyopathy. Med Pediatr Oncol 2003;41:574.
5) Brewster UC, Perazella MA. The renin-angiotensin-aldosterone system and the kidngy : effects on kidney disease. Am J Med 2004;116:263-72.
6) Boe J, Simonesson B. Effects of angiotensin II and bradykinin on isolated human pulmonary arteries. Eur J Respir Dis 1981;62:95-101.
7) Grubb R, Raichle M. Intraventricular angiotensin II incresases brain vascular permeability. Brian Res 1981;210:426-30.
8) Simpson JB, Routenberg A. Subfornical organ : site of drinking elicitation by angiotension II. Science 1973;181:1172-5.
9) Saavedra JM, Ando H, Armando I, Baiardi G, Bregonzio C, Jezova M, et al. Brain angiotensin II, an important stress hormone: regulatory site and therapeutic opportunities. Ann N Y Acad Sci 2004;1018:76-84.
10) Mckinley MJ, Cairns MJ, Denton DA, Egan G, Mathai ML, Uschakov A, et al. Physiological and pathophysiological influences on thirst. Physiol Behav 2004;81:795-803.
11) Silberman TLP, Blau EB. Wilms' tumor, the hyponatremic/hypertension syndrome, and an elevated atrial natriuretic factor. Am J Pediatr Hematol Oncol 1992;14:273-5.
12) Wong W, Mauger D. Treatment of Wilms' tumor-related hypertension with losartan and captopril. Pediatr Nephrol 2004;19:805-7.