Short Communication

Prognostic Factors of Wilms' Tumor Complicated with Nephroblastomatosis

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Introduction

Nephrogenic rests (NRs) are abnormally persistent clusters of embryonal cells, representing microscopic dysplasias of the developing kidney. NRs are found in approximately 1% of infant kidneys at autopsy. Nephroblastomatosis signifies the presence of multiple or diffuse NRs. Both NRs and nephroblastomatosis were known as precursor lesions of Wilms' tumor.[1] Nephroblastomatosis can be classified into four categories: Perilobar (PLNR only); intralobar (ILNR only); combined (PLNR and ILNR); and universal. The diagnosis and treatment of Wilms' tumor have been improved constantly and achieved common sense. However, little information is available regarding Wilms' tumor associated with nephroblastomatosis for lower prevalence. This study aimed to investigate the prognostic factors of Wilms' tumor associated with nephroblastomatosis.

Methods

Study approval was obtained from the Institutional Review Board and Ethics Committee of Capital Medical University, and the informed consents were obtained from all patients' parents or guardians. We retrospectively reviewed the records of 30 consecutive patients who were diagnosed as Wilms' tumor associated with nephroblastomatosis and received treatment in Beijing Children's Hospital from March 2008 to April 2013.

The gender, age, initial symptoms, bilateral lesions, multicentric lesions, the number of lesions, and grading were recorded and analyzed. All children received surgical treatment, including transperitoneal radical nephrectomy or nephron-sparing surgery (NSS), depending on the location of the tumor. Preoperative chemotherapy or radiotherapy was performed according to standard SIOP protocols. All tumors were identified and categorized into blastemal, epithelial, stromal, mixed type, and anaplasia by pathologist after excision, according to National Wilms' Tumor Study (NWTS). Nephroblastomatosis was classified into ILNR, PLNR, combined and universal, also by pathologists. Follow-up consisted of the prognosis, such as recurrence, metastasis or death, for >12 months postoperatively.

Data were analyzed using Logistic regression with SPSS software (version 18.0; SPSS Inc., Chicago, IL, USA). Gender, age, initial symptoms, bilateral lesions, multicentric lesions, the number of lesions, pathological type, grading, preoperative chemotherapy, surgical approach, and radiotherapy were regarded as independent variables; prognosis, such as recurrence, metastasis and death, were regarded as dependent variables. Univariate analysis was taken first to select potential factors, and then these factors were analyzed by multivariate logistic regression. $P < 0.05$ was considered significant.

Results

A series of 30 patients were studied [Table 1]. The patients aged from 4 months to 11 years and 4 months (average 3.45 ± 2.75 years). Sixteen children presented with an asymptomatic abdominal mass, 9 with abdominal pain, 7 with

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hematuresis, 2 with frequent urination, 1 with hypertension, 2 patients had abdominal pain associated with hematuresis, 1 child had abdominal mass associated with abdominal pain, 1 had abdominal mass complicated with hematuresis, and 1 had hypertension associated with frequent urination. Twelve patients had bilateral lesions. Multicentric lesions [Figure 1] were found in 11 patients; the maximum number of lesions was 12. Regarding the pattern of Wilms' tumor, 6 children were diagnosed to be suffering tumor with predominantly epithelial differentiation, 8 were diagnosed to be blastemal-predominant Wilms tumor, 6 were stromal-predominant, 9 were mixed type, and only 1 was identified to be anaplastic-type. In viewing of the location of NRs, 16 cases of ILNR were observed, 9 of PLNR were observed, and 5 were found to be both ILNR and PLNR. Wilms' tumor was generally classified into five stages using Roman numerals I through V according to NWTS. Five patients were found in Stage I, 4 were in Stage II, 6 were in Stage III, 3 were in Stage IV, and 12 in Stage V. Twenty children had received nephrectomy; 10 cases had undergone- NSS. Thirteen patients had received preoperative chemotherapy; all children underwent chemotherapy after surgery. Four patients were treated by radiotherapy.

Two children relapsed; 6 tumors had metastasized to different locations, including pulmonary (4), lymph node (1), and small bowel (1). Two patients died from this disease in the follow-up period. One child relapsed and died; 1 relapsed and metastasized to pulmonary.

When the prognosis was taken as the dependent variable, the results filtered out by univariate analysis showed that bilateral lesions ($P = 0.053$), multicentric lesions ($P = 0.002$), the number of lesions ($P = 0.011$) were the potential factors [Table 2]. Although P value of the bilateral lesions was close to 0.05, which means close to the significance borderline, the bilateral lesions were considered as a factor. Logistic regression indicated that multicentric lesions ($P = 0.030$) were correlated with the prognosis [Table 3].

Table 1: Clinical characteristic distribution of the patients with Wilms' tumor complicated with nephroblastomatosis

Variables	Favorable prognosis	Unfavorable prognosis
Gender, *n*		
Male	12	3
Female	10	5
Mean age, years	3.06 ± 2.44	4.76 ± 3.29
Bilateral lesions, *n*	6	6
Multicentric lesions, *n*	5	7
Pathological type of Wilms' tumor, *n*		
Epithelial	4	2
Blastemal	7	1
Stromal	3	3
Mixed	7	2
Anaplastic	1	0
Categories of nephroblastomatosis, *n*		
ILNR	12	5
PLNR	4	5
ILNR + PLNR	4	1
Grading, *n*		
Stage I	5	0
Stage II	3	1
Stage III	6	1
Stage IV	2	1
Stage V	6	6
Surgical methods, *n*		
Radical nephrectomy	17	3
Nephron sparing surgery	5	5
Preoperative chemotherapy, *n*	6	5
Radiotherapy, *n*	2	2

ILNR: Intralobar; PLNR: Perilobar.

Discussions

Wilms' tumor is the most common form of renal malignancy in childhood. The nephroblastomatosis was known as

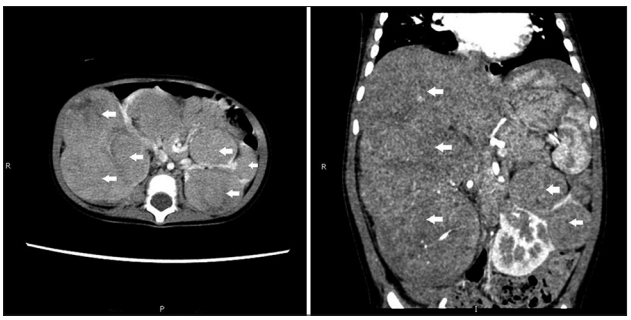

Figure 1: Case 13, female, contrast enhanced computed tomography shows multiple nodules (white arrows) of both kidneys.

Table 2: Results filtered out by univariate analysis when the prognosis was taken as the dependent variable

Lesions	Favorable prognosis	Unfavorable prognosis	χ^2	*P*
Bilateral lesions	5	7	3.758	0.053
Multicentric lesions	5	6	9.459	0.002
The number of lesions				
1	18	1	14.922	0.011
2	1	0		
3	2	2		
4	1	3		
5	0	1		
12	1	0		

Table 3: Final step of logistic regression when the prognosis was taken as the dependent variable

Lesions	*B*	SE	*P*	*OR*	*OR* 95% *CI*	
					Lower	Upper
Bilateral lesions	−0.055	1.407	0.969	0.947	0.060	14.906
Multicentric lesions	−3.547	1.635	0.030	0.029	0.001	0.709
The number of lesions	−0.158	0.268	0.557	0.854	0.505	1.445
Constant	4.305	2.546	0.091	74.077		

SE: Standard error; *CI*: Confidence interval; *OR*: Odds ratio.

precursor lesions of Wilms' tumor. The natural history of nephroblastomatosis seems to present significant variation as some lesions may regress spontaneously, while others may grow and expand or relapse and develop into Wilms' tumor later in childhood.[2] The risk of developing one or more Wilms' tumors during the natural history of the disease is increased, especially in cases with diffuse hyperplastic PLNR.[1] The cases of Wilms tumor associated with nephroblastomatosis are rare. Wilms' tumor usually occurs in the first 2–5 years of life. Bilateral Wilms' tumors account for about 6–7% of all Wilms' tumor. Our study showed the bilateral lesions were account for 40% of Wilms' tumor associated with nephroblastomatosis. Long-term survival of Wilms' tumor approaches 90%. Recurrence rates are low. Up to 10% of patients have metastatic disease at presentation, the most common sites being the lungs (80%), regional lymph nodes, liver, and bone. However, the Wilms' tumor associated with nephroblastomatosis in this study was of higher recurrence and metastatic rates.

Our study indicates that patients with multicentric lesions were correlated with adverse prognosis of Wilms' tumor complicated with nephroblastomatosis. Moreover, we found most patients with multicentric lesions (9/11) received NSS. It may be that residual tumor cells or NRs, after tumor resection, might develop into another neoplasm. Similar results had been reported in a previous study, which investigated that the event-free survival of Wilms' tumor with nephroblastomatosis was significantly lower than that of Wilms' tumor only. The authors believe that the discovery of nephroblastomatosis in the nontumoral part of the kidney with Wilms' tumor can be an adverse factor, and in particular, favors the subsequent development of a new Wilms' tumor.[3] It is recommended that removing the tumor by ultrasonic dissection and a minimum gross margin was maintained at 3 mm without tumor spill. Ultrasonic dissector can be the best choice to retain peritumoral capsule and removal margins.[4] The pediatric urological surgeon is facing the dilemma that NSS could be maximized to preserve renal function, but faced the risk of recurrence.

In the current series of patients, we found that bilateral lesions made the Wilms' tumor associated with nephroblastomatosis trend to unfavorable prognosis. We speculated that the bilateral lesions may usually be unfavorable histology; this kind of tumor cells may be more easily metastasized, which could contribute to the poor outcome. The earlier studies assessed 81 cases with Wilms' tumor and nephroblastomatosis, demonstrated that Wilms' tumor complicated with nephroblastomatosis would present more clinical symptoms and bilateral lesions.[3] A significantly higher incidence of metachronous bilateral Wilms' tumor was found in girls and infants.[5] Compared with unilateral lesions, the incidence age of this patients was younger, the opportunity of completed with other congenital malformations may be higher.

We recorded only 30 patients who were diagnosed as Wilms' tumor associated with nephroblastomatosis for the lower incidence. Our results may be partly influenced by the small sample size. The conclusion still needs to be supported by enlarged sample size and prolong the follow-up period in the further study.

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Conflicts of interest

There are no conflicts of interest.

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