CASE REPORT

Renal Cell Carcinoma in Children and Young Adults

Hsin-Lin Tsai[1,3], Tai-Wai Chin[1,3]*, Jei-Wen Chang[2,3], Chin-Su Liu[1,3], Chou-Fu Wei[1,3]

[1]*Division of Pediatric Surgery, Department of Surgery, Taipei Veterans General Hospital,* [2]*Department of Pediatrics, Tao Yuan Veterans Hospital, and* [3]*Institute of Clinical Medicine, National Yang-Ming University School of Medicine, Taipei, Taiwan, R.O.C.*

Renal cell carcinoma (RCC) is a relatively uncommon tumor in childhood. Its biologic behavior and prognostic factors have rarely been documented. We report treatment and survival of 4 children (aged 8, 9, 11, and 14 years) who had RCC, along with a review of the literature to analyze the frequency of major symptoms, clinical stage, and prognostic factors based on 130 published cases of RCC in individuals younger than 20 years of age. Two of our cases had renal tumors detected by ultrasound screening, and all 4 cases were followed for a considerable length of time and were alive and free of disease after treatment. An analysis of these 130 published cases of pediatric RCC showed tumor staging and cell type to be the factors that affected patient survival. Tumors composed of granular cells or mixed cells, or at advanced stages, had a poor prognosis. Age, sex, tumor size, symptom duration, and cellular pattern were not related to patient prognosis. Children older than 10 years of age, who have an abdominal mass, flank pain, and/or hematuria should alert clinicians to consider the possibility of RCC. The importance of early diagnosis of renal tumors, using ultrasound as a tool of screening, is emphasized, since surgical treatment leads to a favorable prognosis only in the early stage of RCC. [*J Chin Med Assoc* 2006;69(5):240–244]

Key Words: abdominal ultrasound, nephrectomy, renal cell carcinoma

Introduction

Renal cell carcinoma (RCC) usually occurs in the age range of 50 to 70 years. It is extremely rare in children, similar to Wilms' tumor. The incidence of RCC tumor in childhood is estimated to be from 1.8% to 6.3% of all malignant renal tumors.[1] In Riches' study, less than 0.5% of RCC patients were younger than 20 years of age. However, an increasing number of reports during recent decades suggests that the incidence may not be as rare in children as previously thought. Surgery is the mainstay of treatment and results in cure when the tumor is localized and completely resected. The biologic behavior and the prognostic factors of RCC in young patients are still poorly understood. So far, no treatment protocols have been defined for children with RCC. In an effort to gain a clearer perspective of childhood RCC, we analyzed the presentation, diagnosis, and therapeutic results of 4 patients who were younger than 20 years of age at our hospital since 1980. In addition, 130 cases from the English literature are reviewed to identify prognostic factors for RCC in young patients.

Case Reports

Case 1

A 9-year-old boy had an abdominal mass noticed by his parents several days before admission to the hospital. Upon admission, ultrasound study showed a huge echo-complex lesion with hypervascularity at the lower pole of the right kidney. An abdominal computed tomography (CT) scan also disclosed a right renal mass with a distorted collecting system. The boy subsequently received a right radical nephrectomy. The tumor was 8 cm in diameter, the renal capsule was intact, and there was no tumor thrombus in the renal

*Correspondence to: Dr. Tai-Wai Chin, Division of Pediatric Surgery, Department of Surgery, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, R.O.C.
E-mail: twchin@vghtpe.gov.tw • Received: April 1, 2005 • Accepted: December 29, 2005

vein or inferior vena cava. Histopathology revealed RCC with granular cytoplasm and pleomorphic nuclei. Hilar lymph nodes were negative, indicating he was a stage I RCC requiring no further therapy. He was followed for the next 9 years. Eight years after his nephrectomy, he presented with severe headache after a minor trauma. A brain CT scan showed hydrocephalus and a suspected tectum tumor. He recovered rapidly after a ventriculoperitoneal shunt. Since then, there has been no evidence of RCC recurrence or metastasis.

Case 2

An 11-year-old boy had an asymptomatic right renal tumor found during ultrasound screening. Abdominal CT scan revealed tumor thrombi in the right renal vein and the vena cava located above it, extending about 4 cm, with nearly complete obstruction of the inferior vena cava. Radical nephrectomy was performed. The tumor diameter was 9 cm, the renal capsule was intact, and a tumor thrombus was removed from the right renal vein and inferior vena cava. Typical RCC with anaplastic clear cells and granular cells in a tubular pattern could be seen in histopathologic sections. After surgery, he received irradiation (1,800 CGy in 10 fractions) and chemotherapy (adriamycin, oncovin, and actinomycin for 18 months). The patient recovered well and was free of tumor 11 years after surgery.

Case 3

A 14-year-old girl had a left renal tumor found during ultrasound screening. Radical nephrectomy was performed after a series of examinations, including CT scan and isotope tumor scanning. The tumor was 3.5 cm in diameter. Histopathology showed RCC with clear cells in a papillary pattern. The renal capsule was invaded, but the ureter and renal vessels were spared. A short course of chemotherapy (6 doses of actinomycin and oncovin) and radiotherapy (2,400 CGy in 12 fractions) were given postoperatively. She was tumor free 36 months after the surgery.

Case 4

An 8-year-old boy had intermittent gross hematuria for 4 months. A series of studies, including intravenous urography, renal sonography, and CT scan, demonstrated a right renal tumor. A tumor 3.5 cm in diameter was found in the upper pole of the right kidney during radical nephrectomy. Histopathologic studies showed RCC with clear cells in a sheet or papillary pattern. Hilar lymph node metastasis was found. Actinomycin D and oncovin were administered for 2 courses. The boy recovered well and was disease free during the follow-up period of 18 months.

Discussion

RCC occurs infrequently in children. In 411 cases of RCC recorded in our hospital since 1980, only 4 (0.98%) patients were younger than 20 years. It is generally hard to differentiate RCC from Wilms' tumor by preoperative evaluation, except that the rate of dystrophic calcification is higher in childhood RCC.[2] None of our patients were found to have tumor calcification in a preoperative image. While the peak patient age at presentation of Wilms' tumor is 3 years, in most series and in our study, the mean age of the presentation of RCC is approximately 8–9 years. Most research to date has been case reports. A few large series have been reported, such as by Dehner et al[3] and Lack et al.[4] Statistical analysis is not available for these reports.

From combined analysis of previously published reports, we have been able to perform statistical analyses on 130 RCC patients who were under 20 years of age.[3–15] The mean age of the patients was 9.1 years (n = 133, the number of patients with available information), ranging from 0.3 to 19 years. The peak incidence occurred between 7 and 11 years of age. The male to female ratio was 1:1.3 (n = 82). Right to left kidney involvement was 1:0.97 (n = 77). The tumors grew evenly from lower, middle, and upper portions of the kidney (n = 32). The mean tumor size was 7.4 cm, ranging from 1 to 18 cm (n = 65).

Detailed descriptions of symptoms were available in 61 patients. The major symptoms were hematuria, abdominal mass, and pain (Table 1). The classic triad of hematuria, a palpable mass, and pain was seen in only 1.6% of the cases. Systemic symptoms frequently reported were: fever (11.5%); nausea and vomiting (13.1%); and lassitude (8.2%). Tumor rupture occurred in 11.5% of the patients. There was a history of abdominal trauma shortly before diagnosis in 3.3% of the patients. Patients with smaller tumors (diameter ≤ 7 cm) usually presented with hematuria (75%), while

Table 1. Frequencies of major symptoms in cases of childhood renal cell carcinoma

Major symptoms	Percentage
Hematuria only	26.2
Mass only	14.8
Pain only	11.5
Hematuria + mass	6.6
Mass + pain	13.1
Hematuria + pain	16.4
Hematuria + mass + pain	1.6
No symptoms	6.6

those with larger tumors (diameter > 7 cm) tended to present with an abdominal mass (66.7%). All patients with the chief complaint of an abdominal mass had a tumor diameter larger than 6 cm. The mean duration of symptoms was 96 days, and ranged from 1 day to 2 years. Symptom duration was not related to the stage of the disease or the size of the tumors; however, the duration was usually short if there was tumor rupture. Paraneoplastic phenomena in adults are common but are infrequently documented in children.

Clear cells were the most common histologic type, accounting for 72% (n = 84) of the cell types reported. Granular cell and mixed cell were less frequently encountered, and accounted for 11.1% (n = 13) and 17.1% (n = 20), respectively. The rates of metastasis were 20.4%, 62.5%, and 38.5% for clear cell, granular cell, and mixed cell tumors, respectively. The granular cell RCC had a significantly higher incidence of metastasis when compared with other cell types ($p < 0.05$, Chi-square test). No correlation was found between cell type, age, sex, or tumor size and symptom duration.

The histologic patterns commonly described were papillary, trabecular, and tubular type. The incidence was 57.3% (n = 43) for papillary, 12% for trabecular (n = 9), and 30.7% for tubular (n = 23). No correlation was found between the histologic patterns and the other factors.

The patients were staged according to the pathologic system of Robson et al.[16,17] Information for tumor staging was available in 68 cases (Table 2). Tumor staging was not related to age, sex, symptom duration, cell types, or histologic patterns. The overall 1-year, 2-year, and 5-year survival rates were 78.9%, 68.4%, and 62.4%, respectively.

Several factors were reported to have prognostic value. Symptom duration, cell type, pseudocapsule formation, and vascular invasion were survival-related in Dehner et al's series.[3] In Castellanos et al's report,[5] tumor staging was the only prognostic factor. Summary of previous studies about variables affecting the 5-year survival of RCC in children and young adults is shown in Table 3.[3–15] Five-year survival was estimated using the Kaplan-Meier method, with differences between groups being analyzed by the 2-tailed log-rank test. In the previous study, cell type and tumor staging were the 2 most significant factors affecting patient survival. Patients with clear cell RCC had higher survival rates and lower metastatic rates than those with mixed or granular cell RCC. Similar observations were reported by Dehner et al.[3] Disease staging is the most important factor. The 5-year survival rate of stage I patients was 96%, in contrast to 9% for stage IV patients.[18] Rupture of tumors was not a sign of poor prognosis.[11,15] All 6 patients who had tumor rupture survived without tumor recurrence or metastasis in the follow-up period (from 15 months to 10 years). Patients with tumor rupture had a rather favorable prognosis, probably resulting from an earlier diagnosis of the disease.

Information about treatment was available in 51 patients. Among stage I patients, 9 patients received nephrectomy only, and 12 received nephrectomy plus adjuvant radiotherapy and chemotherapy. There was no difference in survival between these 2 groups. Most of the stage II and III patients received irradiation and/or chemotherapy in addition to surgery. Therefore, the effect of adjuvant therapy in these patients could not be analyzed in this retrospective study. Immunotherapy has shown promise in treating selected adults with advanced stage RCC. However, its effect has only been reported in a few children. Radical nephrectomy with lymphadenectomy provides a satisfactory outcome in stage I patients.

As with other malignancies, early diagnosis is the key to successful treatment. Abdominal ultrasound screening is a useful tool in detecting early renal tumors and other urinary tract abnormalities. The

Table 2. Clinical staging according to Robson's Staging System

		No. patients
Stage I	Tumor limited to the kidney	31
Stage II	Tumor invading perinephric fat but still contained within Gerota's fascia	8
Stage III		19
	A. Tumor invading the renal vein or inferior vena cava	8
	B. Regional lymph node metastasis	11
	C. Combination of IIIA and IIIB	0
Stage IV		10
	A. Spread to contiguous organs except ipsilateral adrenal	
	B. Distant metastasis	

Table 3. Summary of previous studies of the 5-year survival rates in children

Factors	Five-year survival, %	No. patients	*p*
1. Age			0.130
Age < 9 years	70.4	61	
Age ≥ 9 years	52.5	49	
2. Sex			0.279
Male	50.6	29	
Female	75.5	43	
3. Tumor size			0.223
Tumor ≤ 7cm	75.1	37	
Tumor > 7cm	70.0	28	
4. Symptom duration			0.243
Symptoms < 1 month	77.0	19	
Symptoms ≥ 1 month	58.6	16	
5. Cell type			0.048*
Clear cell	69.9	71	
Granular cell	22.8	10	
Mixed cell	65.2	15	
6. Pattern of growth			0.177
Papillary pattern	59.8	33	
Tubular pattern	62.6	21	
Trabecular pattern	100	8	
7. Tumor staging			0.000*
Stage I	91.3	28	
Stage II	60.0	8	
Stage IIIA	12.5	8	
Stage IIIB	71.6	11	
Stage IIIC		0	
Stage IV	0	8	
8. Treatment for Stage I			
Nephrectomy only	100	9	
Nephrectomy + adjuvant	91.7	12	

** $p < 0.05$.*

frequency of renal abnormalities was 0.5% in a mass screening project using ultrasound.[19] Two of our patients were able to achieve an early diagnosis through ultrasound screening. In summary, although Wilms' tumor is the most common pediatric renal tumor, children older than 10 years who have an abdominal mass, flank pain, and/or hematuria should alert clinicians to consider the possibility of RCC. The importance of early diagnosis of renal tumors, using ultrasound as a tool of screening, is emphasized since surgical treatment leads to a favorable prognosis only in the early stage of RCC. For an advanced stage tumor, immunotherapy, alone or combined with chemotherapy, is warranted. Tumor staging and cell type are the important factors for patient survival. Because of the very low incidence of RCC in children, a multicenter study may be necessary to develop an optimal therapeutic strategy.

References

1. Riches EW, Griffiths IH, Thackray AC. New growths of the kidney and ureter. *Br J Urol* 1951;23:297–356.
2. Strouse PJ. Pediatric renal neoplasms. *Radiol Clin North Am* 1996;34:1091–100.
3. Dehner LP, Leestma JE, Price EB. Renal cell carcinoma in children: a clinicopathologic study of 15 cases and review of the literature. *J Pediatr* 1970;76:358–68.
4. Lack EE, Cassady JR, Sallan SE. Renal cell carcinoma in childhood and adolescence: a clinical and pathological study of 17 cases. *J Urol* 1985;133:822–7.
5. Castellanos RD, Aron BS, Evans A. Renal adenocarcinoma in children: incidence, therapy and prognosis. *J Urol* 1974;111:534–7.
6. Pochedly C, Suwansirikul S, Penzer P, Meadow E, Island L. Renal-cell carcinoma with extrarenal manifestations in a 10-month-old child. *Am J Dis Child* 1971;121:528–30.
7. Lynne CM, Machiz S. Renal cell carcinoma in children: a report of four cases and a review of the literature. *J Pediatr Surg* 1973;8:925–9.
8. Goto S, Ikeda K, Nakagawara A, Daimara Y, Tsuneyoshi M, Enjoji M. Renal cell carcinoma in Japanese children. *J Urol*

1986;136:1261–3.
9. Strimer RM, Richardson JR. Adenocarcinoma of kidney in a child. *Urology* 1975;5:649–51.
10. Hicks CC, O'Brien DP, Majmudar B, Parrott TS. Hypernephroma in children. *Urology* 1975;6:598–602.
11. Futrell JW, Filston HC, Reid JD. Rupture of a renal cell carcinoma in a child. *Cancer* 1978;41:1565–70.
12. Fisher RG, Granmayeh M, Wallace S, Johnson DE. Renal adenocarcinoma in adolescence and childhood: emphasis on angiographic findings. *J Urol* 1976;118:83–6.
13. Palma LD, Kenny GM, Murphy GP. Childhood renal carcinoma. *Cancer* 1970;26:1321–4.
14. Laurenti C, Racheli T, Dal Forno S. Long survival after renal carcinoma in a female child. *Br J Urol* 1980;52:64.
15. Booth CM. Renal parenchymal carcinoma in children. *Br J Surg* 1986;73:313–7.
16. Robson CJ, Churchill BM, Anderson W. The results of radical nephrectomy for renal cell carcinoma. *J Urol* 1969;101: 297–301.
17. Robson CJ. Radical nephrecomy for renal cell carcinoma. *J Urol* 1963;89:37–42.
18. Uchiyama M, Iwafuchi M, Yagi M, Iinuma Y, Masahiro O, Tomita Y, Hirota M, et al. Treatment of childhood renal carcinoma with lymph node metastasis: two cases and a review of literature. *J Surg Oncol* 2000;75:266–9.
19. Sheih CP, Liu MB, Hung CS, Yang KH, Chen WY, Lin CY. Renal abnormalities in schoolchildren. *Pediatrics* 1989;84: 1086–90.