Renal cell carcinoma in children

Prognostic factors

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ABSTRACT

Objective: To determine the outcome in childhood renal cell carcinoma and the role of surgical and radiation treatment.

Methods: The records of 21 children with renal cell carcinoma were reviewed, 15 patients treated in the University of Toronto centers from 1959 through to 1997 and 6 patients treated in King Faisal Specialist Hospital, Riyadh, Kingdom of Saudi Arabia from 1975 through to 1998. The age was 3-17 (median 13) years. Systematic metastases were present at diagnosis in 5 patients. Regional nodal spread was present in 9 patients and 7 patients had localized disease alone. In the 16 M0 patients, the surgical treatment was radical nephrectomy (14 patients) partial nephrectomy (one patient) and wedge resection (one patient). Postoperative radiation treatment was utilized in 8 (50%) of these patients.

Results: The 5 year survival rate for all patients was 52%, and for M0 patients was 70%. No patient with systematic metastases at diagnosis survived beyond 26 months. Four of 7 node negative patients and 8 of 9 node positive patients remained in first complete remission, with the duration of follow up 1-30 (Median 5) years. Seven of 8 M0 patients who did not receive adjuvant radiation therapy continued in first remission (3N0, 2NI, 2N2), compared with 5 of 8 patients who received postoperativeradiation treatment (1 N0, 2 NI, 2 N2).

Conclusion: The prognosis of localized renal cell carcinoma in childhood may be better than in the adult. Gross complete resection is required for long term survival. Elective postoperativeradiation treatment is not indicated.

Saudi Med J 2004; Vol. 25 (11): 1583-1586

Renal cell carcinoma (RCC) is rare in children. It accounts for less than 0.1% of all malignant tumors and only 2-6% of all renal tumors in childhood.[1,2] Gross total tumor resection is a requirement for cure. The standard procedure is radical nephrectomy.[1,3] The value of postoperativeradiation therapy is uncertain.[1,4,5] Adjuvant chemotherapy is not given, due to lack of efficacy of the available agents.[3,5] The prognosis is less favorable than that of Wilm's tumor.[6] We reviewed our combined experience to further explore the natural history and the surgical and radiation treatment of renal cell carcinoma in children.

Methods. From 1959 through to 1997 15 young patients with RCC were referred to the Pediatric

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Received 17th May 2004. Accepted for publication in final form 10th July 2004.

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Table 1 - A summary of the clinical data for 21 patients.

Patient #	Age (years)	Size (cm)	TNM	Stage	Surgery	Radiation	Surv (mths)
1	5	X	TXN0M0	X	RN+L	W(25)L(10)	360 a+w*
2	11	X	TXN2M0	X	RN+L	L(40)	288 a+w
3	14	9	T2N2M0	4	RN+L	None	96 a+w
4	9	6.5	T1N1M0	3	RN	L(40)	216 a+w
5	6	2	T1N1M0	3	RN	L(45)	48 a+w
6	13	5	T1N2M0	4	RN	W(28)L(18)	48 dd**
7	14	9	T4N0M0	4	RN&L	None	96 dd
8	9	4	T4N0M0	4	RN+L	W(25)L(15)	48 dd
9	7	9	T2N2M0	4	RN+L	L(46)	84 a+w
10	13	5	T4N0M0	4	RN	L(41)	4 dd
11	10	5	T1N0M0	1	PN	None	26 a+w
12	3	2	T1N0M0	1	WR	None	54 a+w
13	3	9	T2N2M0	4	RN	None	58 a+w
14	13	4.5	T1N1M0	3	RN	None	18 a+w
15	14	10	T2N0M0	2	RN	None	48 a+w
16	8	10	T2N0M0	3	RN	None	42 a+w
17	9	X	TXNXM1	4	B	W(25)	26 dd
18	12	13.5	TXN2M1	4	B+RN	None	3 dd
19	16	15	TXN2M1	4	B	None	6 dd
20	17	X	TXNXM1	4	B	None	6 dd
21	15	X	TXNXM1	4	B	None	6 dd

RN - radical nephrectomy, PN - partial nephrectomy, B - biopsy, L - lymph node dissection
WR - wedge resection, W- whole abdomen, T- tumor bed and para aortic, a+w* - alive and well
dd** - dead, TNM - tumor node metastases, X - data not available

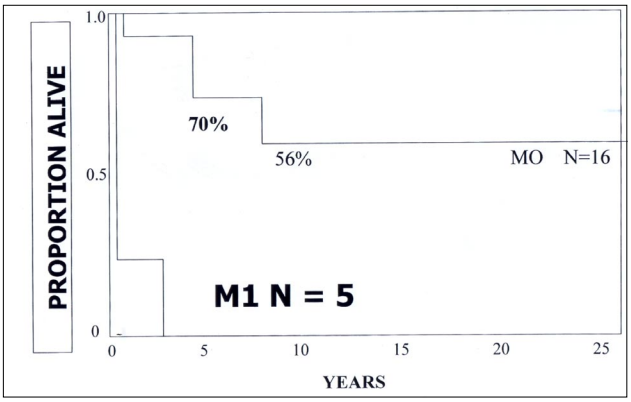

Figure 1 - Overall survival for patients with (M1) and without (M0) distant metastases.

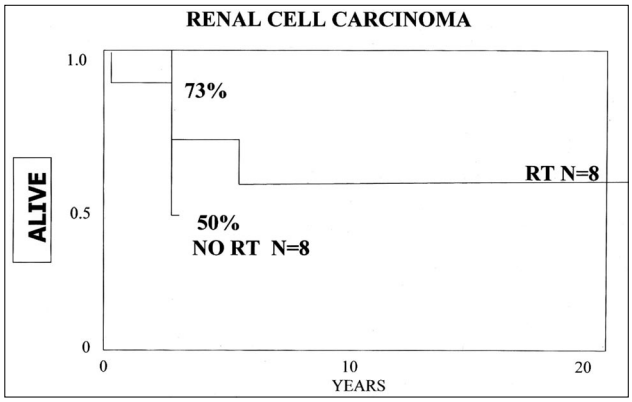

Figure 2 - Survival for 16 M0 patients with regional lymph node involvement.

Departments of the University of Toronto and were treated once or more at The Hospital for Sick Children, Princess Margaret Hospital or Toronto-Sunnybrook Regional Cancer Center, Toronto, Canada. Six additional patients were treated at King Faisal Specialist Hospital, Riyadh, Kingdom of Saudi Arabia, from 1975 through to 1998. The hospital charts were retrospectively reviewed. Postoperative radiation treatment was given to 8 patients. The indications for adjuvant radiation included gross nodal residual disease, histologically positive lymph nodes without gross residual, unknown nodal status and node negative patients. This nearly 40-year study covered many different practices. Adjuvant radiation treatment was not used after 1994. The radiation volumes were: tumor bed and regional para-aortic nodes with a margin (5 patients) and whole abdomen followed by a tumor bed and para-aortic node boost (3 patients). The doses varied, but most of the patients received 40-45 Gy to the tumor bed. No patient received adjuvant systemic treatment. The clinical data are summarized in **Table 1**. The end-points used were death and relapse. All deaths were due to disease. No patient with systemic metastases, progressive disease or relapse survived. At the time of this review all surviving patients were in first complete remission. Survival rates were used for

comparison of sub-groups. Survival and relapse free survival were computed according to the methods of Kaplan-Meyer and were compared using the Log Rank Test.

Results. There were 13 girls and 8 boys. The median age was 13.5-years (range 3-17-years). The clinical presentations included: hematuria (10 patients), abdominal pain (10 patients), palpable abdominal mass (8 patients, 3 asymptomatic), and fever (4 patients). Three patients presented with severe abdominal pain as a result of abdominal traumatism and subsequently developed hypovolemic shock due to hemorrhage. One patient who presented with a poor appetite and failure to thrive demonstrated polycythemia. Tissue diagnosis was obtained in all patients. The histology findings were typical of the clear cell type in 17 patients and of the papillary variant in 4 patients. The maximum linear tumor size was available for 14 M0 patients. The range was 2-10 (Median 5.5) cm. Fourteen of 16 non-metastatic patients underwent radical nephrectomy, one a partial nephrectomy, and one a wedge resection (the patient with polycythemia and a 2cm tumor). The 1997 TNM staging system was employed.[7] For seven patients with localized (N0M0) disease the T distribution was: 2 T1, 1 T2, 3 T4 and one TX. All 3 patients with T4 disease had presented with gross pre-operative tumor rapture. Nine patients demonstrated spread to the regional lymph nodes. (4 N1, 5 N2). The stage grouping for 14 evaluable M0 patients was: stage 1 (T1, N0), 2 patients, stage 2 (T2,N0) one patient, stage 3 (T1,2,N1 and T3,N0,1) 4 patients and stage 4, (T4 or any T,N2) 7 patients. For all 21 patients the 5 and 10-year survival rates were 52% and 40%, and for 16 M0 patients were 70% and 56%, No patients with systemic metastases at diagnosis survived to 5-years (maximum survival 26-months) **(Figure 1)**. Four out of seven node negative patients and 8 out of 9 node positive patients were alive in first complete remission, 1-30 (Median 5) years from diagnosis. The 5-year survival rates for these subsets were 57% and 80% **(Figure 2)**. Eight of 16 M0 patients were treated with radical nephrectomy without node dissection. Six of these patients were alive. Six patients underwent nephrectomy and lymph node dissection. Four were alive at last follow up. The two patients who underwent local resections for small tumors were alive. Eight patients were given postoperativeradiation treatment. Five were alive in first remission (1 N0, 2 N1, 2N2) and 3 died (2 N0, 1 N2). The N2 patient failed locally and distally. One N0 patient failed locally and one distally. Eight M0 patients were not irradiated. Seven were alive (3 N0, 2 N1, 2 N2) and one (N0) relapsed (local and distal relapsed) and died. All 3 patients (patients no.7, 8, and 10) with gross pre-operative tumor rupture died. They all had both local and distant relapse. These patients, who otherwise had localized disease, were allocated as T4, stage IV by virtue of gross tumor rupture. All underwent radical nephrectomy and 2 received postoperativeradiation treatment. When these patients were excluded from the irradiated group, of the remaining 6 patients 5 are long-term survivors with duration of follow up 18-96 (median 48) months. Overall, for 14 M0 evaluable patients the survival results by stage grouping, were: Stage I, 2 patients, both alive, Stage II, 1 patient alive, Stage III, 4 patients. All alive and Stage IV, 7 patients, 3 alive 4 dead.

Discussion. Renal cell carcinoma is a rare disease in the young and the experience with management is limited. As in this report, it is seen mainly in older children. The overall 5-year survival of 70% reported for M0 patients is consistent with other pediatric reports, 56-64%[1,8,9] and superior to the results of some of the reported adult series 17-53%.[9,10,11] All long term survivors underwent total resection of the primary tumor and had no gross, or confirmed microscopic, residual disease post-operatively. A finding that emphasized the importance of achieving total resection of all gross disease as reported in other series.[5,11] In a literature review of 84 children with RCC, there was no survival rate difference between patients treated with resection alone and those treated with resection and postoperativeradiation, with a 10-year overall survival rate of 50%. For 39 patients with stage I disease treated by nephrectomy alone, the 10-year survival rate was 80%.[1] The small number of patients in this report does not allow useful analysis of the benefit of lymph node dissection as opposed to biopsy of suspicious nodes. It is appropriate to apply the larger adult experience to the young, but for both lymph node dissection and radiation treatment controversy remains.[1,3-5,12,13] Pediatric RCC with isolated regional node metastasis have significantly better survival than adults.[1,2] In the current series 8 of 9 node positive patients were alive with no evidence of disease at a median follow up 48-months. In this series as in many other series, there was no obvious benefit for postoperativeradiation treatment. The large volume high dose radiation treatment required in RCC should not be used in children in the absence of unequivocal evidence of a survival benefit. Therefore, elective postoperative radiation treatment should not be given in the young. This has been our practice since 1994. In the unusual event of gross residual unresectable disease, radiation treatment may be given, but must be assumed to be palliative. Curative treatment of RCC with radiation has not been described. The clinical stage has been shown

to be an important prognostic factor.[1,14] In this study, only one of 13 patients with M0 disease and without gross tumor rupture died, regardless of the stage grouping. Four of 7 patients with stage IV M0 disease died from their disease as did all 5 M1 Stage IV patients. The overall prognosis of young patients with M0 disease appears to be superior to the adult experience.[10,11,15] However, in 2473 adults with RCC the overall 5-year survival rate was 53%, not different from the results reported in children. The survival rates were 75% for stage I, 63% for stage II, 38% for stage III, and 10% for stage IV.[8]

In conclusion, the available literature and this review suggest that children with N1, N2 M0 RCC have a relatively favorable outcome compared with adults. The addition of adjuvant radiotherapy to the tumor bed did not improve local control or survival. In the absence of clear evidence that radiation treatment improves survival, this modality should not be used electively in these young patients.

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