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Renal cell carcinoma in children and adolescence: Our experience

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ABSTRACT

Background: Literature on renal cell carcinoma (RCC) in children is lacking. Occasional case report has been mentioned. Aims and objective of our study are to evaluate the clinical presentation and outcome in children with RCC. **Patients and Methods:** Records of 11 children and adolescence, from January 2007 to June 2011, who were treated for RCC were retrospectively analysed. Age, clinical presentation, any paraneoplastic symptom or sign, haematological, bio-chemical investigations, radiological imaging's, operative details, pathological reports and treatment details were taken from hospital records and results were analysed. All patients were followed-up with complete haemogram, biochemical investigations, ultrasonography - whole abdomen and chest X-ray at 6 months interval and patients with stages 2 and 3 were also followed-up with contrast enhanced computed tomography - whole abdomen. They were followed-up for 2-5 years. **Results:** All had undergone open radical nephrectomy with eight hilar lymph node dissection and three formal lymphadenectomy. None had received adjuvant therapy. Four patients with stage 1 were well at 5, 4, 2.5 and 2 years. One patient with stage 1 was lost to follow-up. Three patients with stage 2 were well at 4, 3 and 2 years of follow-up while three with stage 3 were well at 5, 4 and 2 years of follow-up. **Conclusions:** Lymph node dissection not only improves the survival, but it guides one the exact pathological staging and one can adopt the more aggressive follow-up in advanced pathological staging and strict follow-up is mandatory.

Key words: Childhood, lymphadenectomy, radical nephrectomy, renal cell carcinoma

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INTRODUCTION

Although renal cell carcinoma (RCC) is the most common primary renal malignant neoplasm in adults, accounting for 2-3% of all the adult malignancy, it occurs rarely in children. Incidence of this tumour in childhood is estimated to be 0.1-0.3% of all the neoplasm and 1.8-6.3% of all the malignant renal tumours.[1-3] No adequate therapy has been defined for children with RCC. Surgery remains the main stay of treatment and results in cure when tumour is localised and completely resectable. Therapeutic value of complete retroperitoneal lymph node dissection is still controversial. Role of adjuvant therapy including radiotherapy, chemotherapy and immunotherapy is not clear. Different chemotherapy regimens showed only minimal activity when tested in clinical trials. Patients with tumour localised in the kidney have a good prognosis compared with patients with regional lymph node involvement or distant metastasis. Rarity of this disease entity in children and routine lymphadenectomy at our centre prompted us to carry out a study to evaluate the clinical presentation and outcome in children with RCC. We report our experience of 11 children with RCC.

PATIENTS AND METHODS

All children less than 18 years from January 2007 to June 2011, who were found to have RCC were retrospectively analysed. Age, clinical presentation in the form of a palpable mass, haematuria, flank pain or classical triad, any paraneoplastic symptom or sign, site of metastatic disease, duration of presentation, abdominal ultrasonography, contrast enhanced computed tomography (CECT) - whole abdomen scan reports, haematological, bio-chemical investigations, operative details, pathological reports and treatment details were taken from hospital records and results analysed. All patients underwent open radical nephrectomy with hilar lymph node dissection. In addition, patients who presented with node positive disease on CT-scan (no. 3, 6

and 8 in series) underwent formal lymphadenectomy. All patients were followed-up with ultrasonography — whole abdomen, complete haemogram, serum creatinine, liver function test and chest X-ray at 6 months interval. Patients with stages 2 and 3 were also followed-up with CECT-whole abdomen at 1 year interval for 2 years and then at 2-year interval. Spectrum of presentation and follow-up is shown in Table 1.

RESULTS

Mean age at presentation was 10.9 years ranging from 4 to 18 years. Boys:girls ratio was 1.2:1. Clinical symptoms were haematuria, abdominal lump and flank pain. Only one patient presented with classical triad. Nine patients had solitary tumour while two patients had two tumours, one at each pole. None had a family history of RCC. No patient presented with paraneoplastic syndrome. No boy presented with varicocele. None of the 11 patients underwent pre-nephrectomy biopsy. Stage wise distribution was T1N0M0 in 5, T2N0M0 in 3 and T2N1M0 in 3. Histopathology was clear cell type in 45%, papillary type in 45% and unclassified in 9% [Table 2]. Median duration of follow-up was 40.2 months (range: 24-60 months). All patients were disease free with the mentioned duration of follow-up.

DISCUSSION

Literature revealed that RCC corresponds to 1.4% of renal tumours in patients under 4 years old, 15.2% between 5 and 9 years and 52.6% between 10 and 15 years old.[2] RCC in children is rare, accounting for 5.9% of all paediatric malignant renal tumours,[4] but it shares equal prevalence with Wilms' tumour in the second decade of life.[5] This study showed 36% (4/11) prevalence in the first decade and 64% (7/11) prevalence in the second decade.

RCC in adults shows male to female ratio of 2:1 but in children and adolescence, no such pattern exists. Palpable mass occurs in 38%, haematuria in 38% and abdominal pain in 50%, with the classic triad being found in only 6% of cases.[6] Incidence of metastatic disease, commonly to lung and bones, in children with RCC, similar to adults with half of patients presenting with metastatic disease at the time of diagnosis has been reported. Metastases occur in lungs (40-65%), liver (35-57%), bones (10-42%) or bladder, brain or pleura (7-15%). In our study, palpable mass alone occurred in 9% (one patient), palpable mass with haematuria in 9% (one patient), haematuria alone in 36% (four patients), flank pain alone in 36% (four patients), with classical triad being reported in only 9% (one patient). In contrast to reported literature, none of our patient presented with metastatic disease.

Although paraneoplastic signs are infrequently reported in children, but Selle *et al*. reported a high frequency of general symptoms (44.5%) such as fever, nausea/vomiting, malaise, pallor and weight loss. In our series, only 2 (18%) patients (3 and 6 in series) presented with pallor and weight loss, none of our patients presented with fever.

Differentiation between RCC and Wilm's tumours pre-operatively is difficult. Wilm's tumour is diagnosed mainly in children <5 years and mostly present around 3 years whereas RCC presents around 8-9 years in most of the series. In our series, mean age of the presentation was 10.9 years. Tumour calcification on plain X-ray is more common in RCC (25%) than in Wilm's tumour (5%).

A greater incidence of papillary carcinoma in children has been previously reported[6,7] but has been refuted by others, who reported a similar distribution of histologic subtypes in children and adults (predominance of clear

Table 1: Spectrum of presentation and duration of follow-up

Age	Sex	Side	Clinical presentation	Stage on CT-scan	Duration of presentation (months)	Follow-up (months)
12	M	RT	Flank pain	1	3	60
18	M	RT	Flank pain	2	4	48
13	F	LT	Palpable mass+haematuria	3	2	60
11	F	LT	Flank pain	1	3	48
7	F	RT	Haematuria	1	2	NA
15	M	LT	Classic triad	3	3	48
5	F	LT	Haematuria	2	1	36
11	M	LT	Palpable mass	3	2	24
9	M	RT	Haematuria	1	3	30
4	F	LT	Haematuria	1	3	24
15	M	LT	Flank pain	2	6	24

CT: Computed tomography; M: Male; F: Female; RT: Right; LT: Left; NA: Not available

Table 2: Final staging and histopathology distribution

Final stage	No. of patients	Histopathology
T1N0M0	5	Papillary-3 Clear cell-1 Unclassified-1
T2N0M0	3	Papillary-1, Clear cell-2
T2N1M0	3	Papillary-1 Clear cell-2

cell carcinoma).[1,7] Papillary carcinoma in adults is relatively rare (<10%) and is more commonly associated with a familial papillary carcinoma type. Some studies showed that papillary and rarer subtypes are more frequent in paediatric age group.[8]

In our study, greater prevalence of papillary histopathology was encountered in the first decade, also associated with multifocal tumour but equal prevalence of clear and papillary histopathology was noticed in the second decade. Moreover, no patient with papillary carcinoma had a positive family history for RCC, suggesting that their papillary carcinoma was sporadic. Another useful observation was that clear cell variant was more commonly associated with advanced stage, but it is difficult to draw the conclusion whether it was statistically significant or not because of short cohort of patients.

RCC in childhood not only shows a different morphologic spectrum but also shows difference genetically. Von Hippel-Lindau alterations are uncommon in children. In adults with non-papillary histology, terminal deletion or translocation of 3p chromosome is common but this chromosomal abnormality is uncommon in children. In contrast to adults, a large proportion of children are still categorised as unclassified (24% in Bruder study while 16% in Selle *et al*. study).[2] In our study, only one patient (9%) was unclassified.

The standard cornerstone of therapy for RCC in children and adolescents remains radical nephrectomy. Nephron-sparing surgery is currently recommended in adults for selected small-volume tumours, but additional data are needed before this experience can be extensively transferred to the paediatric population. The therapeutic value of complete retroperitoneal lymph node dissection is still controversial, especially in patients without suspected nodal involvement, be they adults or children. It is important to note that most patients with RCC do not have positive nodes. Furthermore, it is important to remember that lymph node disease is known to significantly worsen the survival of patients with RCC. All patients underwent regional retroperitoneal lymph node dissection at our institution because it is our belief that lymph node dissection not only improves the survival but it guides one the exact pathological staging and one can adopt the more aggressive follow-up in advanced pathological staging.

Although immunotherapy with interferon or interleukin has been reported for advanced cases, beneficial effects of these treatment options are uncertain in children. Although rare in children and adolescents, RCCs raise important questions concerning the best treatment approach and accurate pathologic classification. The differences emerging between childhood and adulthood RCC probably prevent any direct generalised application of therapies to children that are validated for adults.

The backbone of systemic therapies for adult RCC has recently been changed by the introduction of drugs designed to target tumour-related angiogenesis and signal transduction. It is worth noting that the largest clinical efficacy trials on targeted molecules have been conducted on clear-cell RCC. While targeted drugs have become the standard of care for adult metastatic RCC, there are currently no published reports on their role in children, and their use should be considered for patients with unresectable metastatic or advanced-stage RCC. On the other hand, the utility of targeted therapies in the adjuvant setting remains to be seen for both adults and children. Unlike in other paediatric RCC series, none of our patients received neo-adjuvant chemotherapy or radiotherapy.

Five years survival for patients with stage 1 is more than 90%, is 50-80% for patients with stages 2 and 3 and <10% for stage 4.[9] Overall prognosis in children appears to be similar in adults.[10] Tumour stage appears to be the most important factor for the survival. The patients with a localised stage (stages 1 and 2) have the best prognosis.[11] Lung and liver are the sites that should receive careful monitoring. Most recurrences and deaths occur within the first 2 years after diagnosis, but late recurrences are not infrequent.[12]

Out of 11 patients, follow-up of 10 patients was available. Median duration of follow-up was 40.2 months (range: 24-60 months). In our series, five patients were stage 1, three patients were stage 2 and another three patients were stage 3. Two years survival for all stages was 100% in our series. None of the patients had a recurrence of disease with the mentioned duration of follow-up. It suggests the importance of strict follow-up.

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