

## Non-Wilms' Renal Tumors In Childhood

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### ABSTRACT

**Objective:** To determine the outcomes, demographics, clinical and surgical characteristics of NWRT in children.

**Methods:** Forty-three children who underwent surgery for NWRT between 1970 and 2016 were included. The charts and surgery notes were evaluated retrospectively and age, sex, complaints and physical findings at presentation, results of biochemical tests, details of surgery, pathologic findings, and the postoperative course were noted.

**Results:** The female to male ratio was 15:28. Distribution according to histological groups were CCSK (n=14), CMN (n=10), RCC (n=7), CN (n=4), angiomyolipoma (n=2), MRT (n=2), sclerosing nephrogenic rest (n=1), renal tubular adenoma (n=1), metanephric stromal tumor (n=1), and renal adenocarcinoma (n=1). Nephroureterectomy was the most frequently used surgical treatment (n=38) (88%). The mortality rate was 21% in malignant NWRT (3 with CCSK, 2 with MRT) and 10% in benign NWRT (2 CMN) during the five-year follow up period.

**Conclusion:** Non-Wilms renal tumors are rare in childhood. The presumptive diagnosis is usually a Wilms tumor. Hypercalcemia may be encountered. A nephroureterectomy is necessary in most cases. NSS can be performed in selected cases and under suitable conditions.

**Keywords:** Renal tumor, congenital mesoblastic nephroma, clear cell sarcoma, malignant rhabdoid tumor, cystic nephroma, multilocular cyst of the kidney

## INTRODUCTION

The Wilms tumor is the most common malignant tumor of the kidney, whereas non-Wilms' renal tumors (NWRT) are quite rare in childhood. There are several histopathological diagnoses in this group such as clear cell sarcoma of the kidney (CCSK), congenital mesoblastic nephroma (CMN), renal cell carcinoma (RCC), cystic nephroma (CN), angiomyolipoma, and other less common

tumors [1,2]. These tumors are poorly understood due to their heterogeneity and rarity. Therefore, a retrospective clinical study was conducted to present a clear picture of the entire spectrum of pediatric NWRT based on our experience and a brief literature review. The current study consists of one of the largest non-collected pediatric NWRT series treated in a single medical center.

## MATERIALS AND METHODS

The records of children treated for NWRT at our department between 1970 and 2016, inclusive, were reviewed retrospectively. Information recorded for each patient included age at admission, gender, past medical and family history, presenting signs and symptoms, clinical characteristics, results of laboratory tests (complete blood counts, serum electrolytes levels, creatinine levels, and urine tests), radiologic examination methods (US, IVP, CT, MRI), stage of the disease, preoperative chemotherapy and radiotherapy applications, preoperative biopsy results, details of surgical intervention (nephroureterectomy, partial nephrectomy, enucleation of tumor, and excision of palpable lymph nodes), early and late complications of surgery, pathologic findings, postoperative chemotherapy and radiotherapy applications, and outcomes.

Data were analyzed with SPSS 23.0 software (Macintosh, IBM Corp., Armonk, NY). Descriptive data are expressed as frequency and percentage and continuous variables as medians, interquartile ranges (IQR) and minimum and maximum values. For the survival outcomes, Kaplan–Meier method was used. This study was approved by the Institutional Ethical Committee (GO 16/745).

### Surgery details

If the excision of the tumor could be completed without a high level of risk, surgery was recommended for all patients as the initial mode of treatment. Otherwise, preoperative chemotherapy was recommended in patients whose initial imaging findings consisted of a primary malignant renal tumor. The term nephron sparing surgery (NSS) refers to a partial nephrectomy, wedge resection, or enucleation. A partial nephrectomy is performed by excision of the upper or lower pole that contains the tumor. Enucleation is performed by excision of the small lesion with a thin rim of surrounding renal parenchyma, if possible.

## RESULTS

There were 43 children who underwent surgery for NWRT during the study period. The male to female ratio was 1.8 (28 boys and 15 girls). The median age at diagnosis was 30 months (15 days–16 years). The

distribution according to histological diagnosis was CCSK (n=14, 33%), CMN (n=10, 23%), RCC (n=7, 17%), CN (n=4, 9%), angiomyolipoma (n=3, 5%), malign rhabdoid tumor (n=2, 5%), sclerosing nephrogenic rest (n=1, 2%), renal tubular adenoma (n=1, 2%), metanephric stromal tumor (n=1, 2%), and renal adenocarcinoma (n=1, 2%) (Table 1). The presenting symptoms were abdominal swelling (n=16, 37%) and abdominal pain (n=10, 23%). Other presenting symptoms included hematuria (n=7, 16%), weakness (n=2, 4%), respiratory distress (n=1, 2%), and vomiting (n=1, 2%). A tumor was detected incidentally in four (9%) and prenatally in one (2%). One patient with RCC also had tuberous sclerosis with no family history. The most common

**Table 1.** Demographics and Clinical Characteristics of Children With Non-Wilms' Renal Tumors

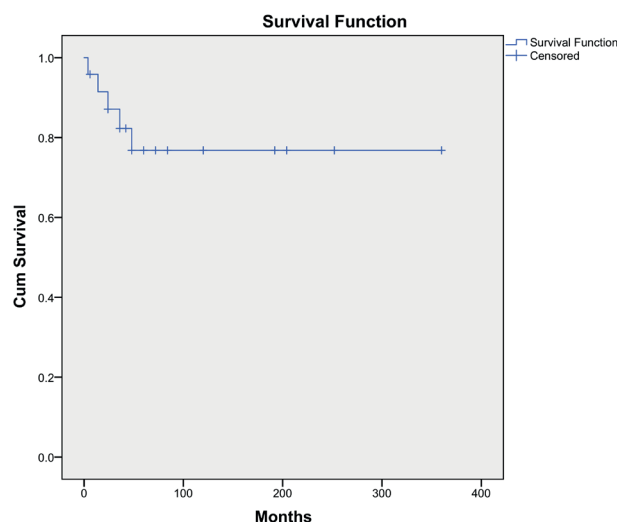
Sex	n	%
Male	28	66
Female	15	34
<b>Age (year)</b>		
0	8	18
1–4	20	46
5–9	9	20
10–14	7	16
15–19	-	-
<b>Tumor histology</b>		
Clear cell sarcoma of the kidney	14	33
Congenital mesoblastic nephroma	10	23
Renal cell carcinoma	7	17
Cystic nephroma	4	9
Angiomyolipoma	2	5
Malignant rhabdoid tumor	2	5
Sclerosing nephrogenic rest	1	2
Renal tubular adenoma	1	2
Metanephric stromal tumor	1	2
Renal adenocarcinoma	1	2
<b>Tumor stage</b>		
Local (stage1–2)	14	32
Regional (stage 3)	18	42
Distant (stage 4)	11	26
<b>Surgery approach</b>		
Nephroureterectomy	38	88
Lymph node sampling	10	23
Nephron sparing surgery	4	9
Subtotal excision	1	2
<b>Recurrence</b>	6	14
<b>Distant metastasis</b>	11	25
<b>Mortality</b>	7	16

finding upon physical examination was a palpable abdominal mass (n=37, 86%). Other findings were hypertension (n=3, 7%), paleness (n=2, 4%), tachycardia (n=2, 4%), growth retardation (n=1, 2%), and tachypnea (n=1, 2%). Preoperative laboratory investigations revealed that seven patients (16%) (4 with CCSK, 1 with CMN, and 2 with RCC) had hematuria, two patients (4%) had anemia (CMN, MRT), and three patients (7%) had hypercalcemia (2 with RCC, 1 with CMN). The tumor location on either the right or left side was 22 and 21, respectively. No bilateral tumor was identified.

A Tru-Cut needle biopsy was used in seven patients because either the radiological findings were not suggestive of a Wilms tumor, or there was no response to neoadjuvant chemotherapy for a Wilms tumor. Histopathological findings were suggestive for RCC (n=3), CCSK (n=2), neuroblastoma (n=1), MRT (n=1), and mesenchymal tumor (n=1). The final diagnose changed to CCSK in two patients (one with neuroblastoma and the other with a mesenchymal tumor diagnosis) after nephroureterectomy. Frozen biopsies were performed in 7 (16%) to determine if NSS could be performed. These biopsies were reported as malignant renal tumors in five children (final diagnoses were RCC in 2, CMN in 1, CCSK in 1, and angiomyolipoma in 1). The remaining two biopsies revealed benign or equivocal findings, which were subsequently reported as RCC and sclerosing nephrogenic rest, respectively. Therefore, the patient with RCC experienced reoperation for complementary nephroureterectomy.

Distant metastases were detected in 10 patients (23%) having CMN (n=4), CCSK (n=4), RCC (n=1), and renal adenocarcinoma (n=1). Bone metastases were detected in 7 (4 with CCSK, 2 with CMN, and 1 with renal adenocarcinoma), lung metastases in two children (RCC and CMN) who also underwent metastasectomy, and liver metastases in 2 (renal adenocarcinoma and CMN).

The postoperative period was uneventful in all. Seven patients (16%) died and five patients (11%) were lost to follow up. One of the patients with CCSK was operated on for an adhesive intestinal obstruction. Two patients with CCSK (n=2) were reoperated on due to local recurrence. Patients with MRT had the highest mortality rate. Multiple metastases were the cause of death in four children. The five-year OS were 76% in malignant NWRT (Fig. 1).



**Figure 1.** Overall survival for patients operated with malignant NWRT

### Clear cell sarcoma

Fourteen patients were diagnosed with CCSK. The male to female ratio was 3.6. The median age at diagnosis was 30 months (18-72). The presenting symptoms were abdominal pain (n=5, 35%), abdominal swelling (n=4, 28%), hematuria (n=4, 28%), and malnutrition (n=1, 7%). A palpable abdominal mass was encountered in all. The median size of the mass was 128mm (IQR, 105–150). The tumor was located in the right kidney in most (n=8, 57%). No familial or syndrome-associated CCSK was identified. The tumor stages were as follows: stage 1 (n=1, 7%), stage 2 (n=8, 58%), stage 3 (n=3, 21%), and stage 4 (n=2, 14%). Preoperative Tru-Cut biopsies were performed in three and the presumptive diagnoses were CCSK, neuroblastoma, and malignant round cell tumor. All patients underwent a nephroureterectomy (Table 2). Excisions of lymph nodes were performed in five and the lymph nodes were positive for metastasis in one. This patient had local recurrence one year later. A frozen biopsy was performed in one. Distant metastases were detected in four (28%) and bone was the target tissue in all. Local recurrence was seen in two having bone metastases at the time of diagnosis and these patients underwent reoperation 6 months and 1 year after the first operation. Neoadjuvant chemotherapy was given to five patients (Adriamycin was included in three cases) and adjuvant chemotherapy was used in eight. Eight patients were treated with adjuvant radiotherapy. The median follow up duration was 48 months (IQR, 36-84). Three patients (2 with stage 4, 1 with stage 2) died within two years (Table 3).

**Table 2.** Summary of The Management of Patients

	CCSK (n)	CMN (n)	RCC (n)	CN (n)	Angiomyolipoma (n)	MRT (n)	Others (n)
	14	10	7	4	2	2	4
<b>Neoadjuvant chemotherapy</b>	5	3	1	1	-	1	-
<b>Surgery</b>							
Nephroureterectomy + Lymph node sampling	5	2	1	-	1	1	-
Nephroureterectomy	9	8	5*	4	-	-	1
Subtotal nephrectomy	-	-	-	-	-	1	-
Partial nephrectomy	-	-	1†	-	-	-	1
Enucleation	-	-	-	-	1	-	1
Complementary nephroureterectomy	-	-	1†	-	-	-	-
<b>Adjuvant chemotherapy</b>	14	4	4	-	-	2	1
<b>Adjuvant radiotherapy</b>	8	1	1	-	-	1	-
<b>Palliative chemotherapy</b>	3	2	-	-	-	2	-

Note: CCSK, clear cell sarcoma of the kidney; CMN, congenital mesoblastic nephroma; RCC, renal cell carcinoma; CN, cystic nephroma; MRT, malignant rhabdoid tumor; \*Frozen biopsy in 2 cases, †Complementary nephroureterectomy after partial nephrectomy.

**Table 3.** Characteristics of Patients Who Died of Disease

Case no	Sex	Age (years)	Metastasis and recurrence	Surgical intervention	Pathology	Follow up (year)
1	M	2.5	Bone, local recurrence	Nephroureterectomy (complementary*)	CCSK	4
2	M	1	Bone	Nephroureterectomy + LN sampling	CCSK, renal sinus invasion (+), LN (-)	5
3	M	3	Local recurrence	Nephroureterectomy	CCSK, capsule invasion (+)	2
4	F	15 days	Liver, lung, recurrence in the liver	Nephroureterectomy + adrenalectomy + tumor enucleation from liver + LN sampling	Cellular CMN, adrenal (+), liver (+), LN (-)	3
5	M	4	Bone, local recurrence	Nephroureterectomy	Cellular and spindle cell CMN, capsule invasion (-)	2
6	M	5.5	Local recurrence	Nephroureterectomy	MRT, capsule invasion (+), LN (+)	1
7	M	1.2	-	Subtotal nephrectomy	MRT, capsule invasion(+)	1 month

Note: CCSK, clear cell sarcoma of the kidney; LN, lymph node; CMN, congenital mesoblastic nephroma; MRT, malignant rhabdoid tumor; \*Underwent incisional biopsy previously at another center.

### Congenital mesoblastic nephroma

Ten patients were diagnosed with CMN. The male to female ratio was 2.3 with the median age of 6 months (IQR, 1-36) at diagnosis. The presenting symptoms were abdominal swelling (n=4, 40%), vomiting (n=1, 10%), anemia (n=1, 10%), prenatally detected abdominal mass (n=1, 10%), respiratory distress (n=1, 10%), and hematuria (n=1, 10%). The diagnosis was made incidentally in two (20%). The findings on physical examination were abdominal mass (n=10) and hypertension (n=3). One patient had hypercalcemia. The median size of the mass was 92 mm (IQR, 62-135). The tumor was predominantly located in the right kidney (n=7, 70%). No familial or syndrome-associated CMNs were identified. Distant metastases were detected in five at the time of diagnosis, bone

(n=2), lung (n=2), and liver (n=1). The tumor stages were as follows: stage 1 (n=4, 40%), stage 2 (n=1, 10%), stage 3 (n=1, 10%), and stage 4 (n=3, 30%). An incisional biopsy had been performed before admission on one patient at another center. No Tru-Cut biopsy was performed in the CMN. All patients underwent nephroureterectomy and excision of palpable lymph nodes was performed in two (Table 2). A perioperative frozen biopsy was used in one. An adrenalectomy and enucleation of hepatic metastasis were performed in one. Histopathological evaluation revealed cellular type in 8 and classic in two. Local recurrence occurred in two. One of these patients had undergone hepatic enucleation and also had a relapse in the liver. The other patient had bone metastasis at the time of diagnosis. The patient was reoperated

on for local recurrence and given chemotherapy and radiotherapy. However, the patient died after two years. Neoadjuvant chemotherapy was used in three and adjuvant chemotherapy was given to four. Adjuvant radiotherapy was given in two having tumor invasion of the renal capsule and lymph node. The other had a local recurrence during follow up without treatment in the postoperative fifth month. The histopathological features of the recurrent lesion were cellular CMN. Both patients died within two years (Table 3). The mean follow-up duration was 48 months (IQR, 24-156) in all CMN patients.

### Renal cell carcinoma

RCC was diagnosed in seven. The male to female ratio was 0.75 and median age at diagnosis was 108 months (60-156). The presenting symptoms were abdominal pain (n=3, 42%), hematuria (n=2, 28%), and abdominal swelling (n=1, 14), and the diagnosis was incidental in one (14%). The patient with the incidental diagnosis also had tuberous sclerosis complex. The abdominal mass was detected during physical examination in four (57%). Two patients had hypercalcemia. The median size of the tumor was 59 mm (IQR, 57-60) and the tumor was located in the left kidney in five. The distribution of patients according to stages were stage 1 (n=3), stage 3 (n=3), and stage 4 (n=1, lung). A preoperative Tru-Cut biopsy was performed in two. A frozen biopsy was performed in three who had a mass on only one pole of the kidney. Frozen biopsies revealed RCC (n=2) and benign pathology (n=1). After evaluation of the permanent sections, the patient with benign pathology was found to be RCC. A complementary nephrectomy was performed in the patient. With the exception of this patient, all others underwent a nephroureterectomy at initial surgery and a lymph node excision was performed in only one (Table 2). The histopathological diagnoses were papillary RCC (n=5), clear cell tumor (n=1), and chromophobe RCC (30%)+oncocytoma (70%) (n=1). Distant metastasis to the lung was detected in one and treated with a metastasectomy. Chemotherapy was given in five and radiotherapy was given in one. No recurrence was seen. Three patients were lost on follow up. The median follow up duration was 60 months (IQR, 60-120) for four patients. They are still under follow up and disease free.

### Cystic nephroma

Four patients were diagnosed with CN. The male to female ratio was 1. The median age at diagnosis was 15 months (IQR, 12-19). The presenting symptom was abdominal swelling in three (75%) and one was diagnosed incidentally (25%). A palpable abdominal mass was encountered in all patients as the sole finding. The median size of the lesion was 100mm (IQR, 30-120). The right kidney was predominantly affected (75%). Nephroureterectomy was performed in all patients (Table 2). The median duration of follow up was 96 months (IQR, 60-132). All are still disease free and being followed up.

### Angiomyolipoma

There were two patients with angiomyolipoma, one male and one female aged 6.5 and 10 years, respectively. The presenting symptoms were abdominal pain (n=1) and enuresis (n=1). Physical examination revealed an abdominal mass in both cases. The sizes of the lesions were 200mm and 130mm in the right and left kidney, respectively. A partial nephrectomy with a frozen biopsy was performed in one (Table 2). A Tru-Cut biopsy was performed in the other patient, who had a 130 mm mass found to be a mesenchymal tumor. Therefore, a nephroureterectomy and excision of the palpable lymph nodes were performed in this patient (Table 2). The final diagnosis was angiomyolipoma. The patients are still disease free after 7 years and 11 years of follow up.

### Malignant rhabdoid tumor

MRT was diagnosed in two male patients 1.2 and 5.6 years of age. The presenting symptoms were abdominal pain and swelling. The physical examination revealed abdominal distension and abdominal mass. The size of both left-side lesions was 120 mm. No distant metastasis was detected. A Tru-Cut biopsy had been performed on one (5.6 years old) at another center and was reported as MRT. Neoadjuvant chemotherapy was given to the patient. A nephroureterectomy was performed on this patient. In the other patient, a subtotal nephrectomy could be performed due to dense adhesions (or local invasion) (Table 3). Only the patient who underwent the nephroureterectomy received adjuvant chemotherapy. However, a

recurrent lesion of 7 cm in size was detected in the left paravertebral region during chemotherapy in the postoperative 7<sup>th</sup> month. A Tru-Cut biopsy of the recurrent lesion was reported as MRT. The patient died in the postoperative 12<sup>th</sup> month. The other patient developed sepsis and died in the pediatric intensive care unit on the postoperative 21<sup>st</sup> day (Table 3).

### Renal tubular adenoma

A 14-year-old boy presented with abdominal pain. The physical examination was normal. A mass of 27 mm in diameter in the left kidney was detected by US. A partial nephrectomy was performed and the histopathological examination revealed renal tubular adenoma. The patient was lost to follow up.

### Sclerosing nephrogenic rest

A 6-year-old girl presented with enuresis. A mass originating in the left kidney was detected by US. The size of the mass was 25mm and contained cysts and calcification. Enucleation with a frozen biopsy was performed. The histopathological examination revealed a sclerosing nephrogenic rest. The follow up duration has been 10 years and the patient is still being followed without disease.

### Metanephric stromal tumor

A 3.5-month-old boy had been admitted to another center with abdominal pain and swelling. The physical examination showed an abdominal mass and CT revealed a lesion (120 mm) located in the left kidney. He was operated on and an incisional biopsy previously revealed a spindle cell tumor. A nephroureterectomy was performed after neoadjuvant chemotherapy at our center. A histopathological examination revealed a metanephric stromal tumor. The follow up duration was 120 months and he is still being followed without disease.

### Renal adenocarcinoma

A 3-month-old boy presented with abdominal swelling due to an abdominal mass. Ultrasonography and IVP revealed a lesion in the right kidney (120 mm). A nephroureterectomy and liver wedge biopsy were performed. The histopathological examination revealed renal adenocarcinoma. Distant metastases were detected in the bones and

liver, and the patient was evaluated as stage 4. The patient received adjuvant chemotherapy and was followed up for 180 months. He is still under follow up and disease free.

## DISCUSSION

Although non-Wilms' renal tumors are rare in childhood, they present a large spectrum of pathologic diagnoses and have various histological subtypes which closely relate to associated morbidities and mortality [3,4].

These patients presented with abdominal swelling, abdominal pain, and hematuria. None of these signs and symptoms is specific or helpful in the differential diagnosis of a renal mass. Therefore, the surgeon must take into consideration the findings on physical examination and results of the radiological examination to evaluate the resectability of the tumor.

About two-thirds of infantile abdominal masses are of renal origin. CMN is the most common renal tumor in infants. In the present series, the most common diagnosis was CMN in patients both until 12 months of age and under 5 years of age, 87.5%-35%, respectively. On the other hand, almost half of the patients with NWRT are under 5 years of age (Table 1). With regard to the age distribution of diagnosis, our findings are in agreement with the figures reported in the literature [5-7]. There were no patients over 15 years of age in the present series.

Hypercalcemia is a rare metabolic disorder associated with childhood cancers. Hypercalcemia was detected in two patients with RCC and one with CMN. A study of 2400 solid tumors showed only 17 cases with hypercalcemia (0.7%). Of the 325 children with renal tumors in the same study, only four (1.2%) had hypercalcemia (MRT, CMN) [8]. Another study showed that parathormone levels are high in approximately half of the NWRT patients having hypercalcemia. However, CCSK with bone metastases shows no association with hypercalcemia [9]. Therefore, hypercalcemia associated with RCC and CMN might be a kind of paraneoplastic syndrome in which the mechanism is not clearly understood.

Distant metastasis was detected in 32% of malignant NWRT. The most common metastasis site was bone (63%), and half the patients with bone metastasis had CCSK. On the other hand, patients with CCSK (71%) or RCC (14%) in local stages, cellular CMN (50%), and MRT (50%) presented distant metastases. Except for CMN, our findings were in agreement with the figures reported in the literature [7,10]. CMN is usually a benign tumor, but distant metastases have been reported in cellular CMN where local recurrence occasionally occurs, and the main site of the metastasis is the lung. In addition, other studies suggested positive surgical margins as the only parameter that predicts recurrence [11,12]. Most of the CMN patients had a cellular subtype and two had a recurrence due to local spillage. A high rate of cellular subtype histology and incomplete eradication of the tumor may explain the high rate of metastasis and local recurrences, respectively, in the present series.

Clear cell sarcoma of the kidney had previously been considered an unfavorable histological variant of the Wilms tumor. However, it has been evaluated as a separate tumor other than Wilms tumor [6,13,14]. CCSK comprises 2%–5% of all primary renal malignancies in children [15]. Of the patients with localized disease, metastatic disease is encountered in 6%–7% of patients at diagnosis [15,16]. CCSK is the most common tumor in this series with a presenting mean age of 3.8 years and with a male gender predominance. All patients presented with a large abdominal mass, half also had hematuria, and one third had bone metastasis similar to previously reported rates [2,6,7,17]. Although hypertension had been reported in 40%–65% of patients with CCSK, none of the patients had hypertension in the present series [17,18]. Preoperative Tru-Cut biopsy results may not be confirmative and the initial diagnosis may be different than CCSK. Nephroureterectomy and lymph node sampling is the primary surgical treatment [15]. The Children's Oncology Group (COG) recommends immediate surgical excision if it can be performed safely. SIOP recommends preoperative chemotherapy with actinomycin and vincristine in local disease and three drugs (including doxorubicin) in metastatic disease for children between 6 months and 16 years [15,16,19]. However, its effect cannot be predicted and the

size of lesion may not change after Adriamycin-containing chemotherapy.

Congenital mesoblastic nephroma is the most common renal neoplasm in the first year of life, particularly in neonates [2,20]. The age at the time of diagnosis was less than one year in 87.5% in NWRT in our series. CMN composed 70% of the NWRT diagnosed at less than 1 year of age and more than half the patients were diagnosed in the neonatal period. In spite of adverse reports, the review of several patients has suggested a male predominance in our series [21–24]. Presenting signs and symptoms and their proportional frequency, such as abdominal mass (100%), hypertension (30%), hypercalcemia (10%), and hematuria (10%) did not differ from previous reports [24–26]. Recurrence and/or metastatic disease can occur in cellular CMN and cause a high mortality rate. The patients require close follow up for 12 months after surgery [27]. Surgery is the mainstay treatment of recurrent and metastatic lesions and chemotherapy may not affect the outcome. The most frequent sites of metastasis are the lung and the liver. About half of patients with recurrence and/or metastasis die of the disease [27]. A higher rate of recurrence and mortality (20%) occurred in our two patients.

Renal cell carcinoma is an unusual tumor in childhood, presenting at 9–15 years of age [28]. RCC can be seen in childhood cancer survivors and genetic syndromes such as tuberous sclerosis, von Hippel-Lindau disease, familial clear cell renal cancer, hereditary papillary renal carcinoma, hereditary leiomyomatosis, and in patients with end-stage or cystic renal diseases, sickle cell hemoglobinopathies, and child kidney transplant recipients [29]. There were two patients, one with tuberous sclerosis complex (TSC), under the age of five in our series. The others were over the age of nine. Tuberous sclerosis complex is an autosomal dominant disorder with characteristic tumors involving multiple organ systems. Angiomyolipoma is common in TSC, however RCC can also be encountered in the kidney rarely. On the other hand, TSC associated RCC are diagnosed at a younger age, as seen in our series [30]. No gender dominance was observed in children, but male predominance was encountered in the present series, as in adults [10,31–33]. The usual triad of hematuria (28%), abdominal pain (42%), and palpable mass (57%)

were seen in two patients (28%) in the present series as in previous reports [15]. Paraneoplastic manifestations can be seen in RCC such as hypercalcemia, hyperglycemia, renin production, prolactin production, hepatic syndromes, hematologic syndromes, and neuromuscular syndromes, and the clinical implications of these RCC-related paraneoplastic syndromes are not well established [34]. Hypercalcemia is present in up to 20% of patients [35]. Hypercalcemia was encountered in two cases (28%) in the present series. The main treatment is radical nephrectomy with the excision of regional lymph nodes. The need for a complete retroperitoneal lymph node dissection is controversial [29]. The rate of metastatic disease at the time of RCC diagnosis is approximately 20%, and similarly one patient with pulmonary metastasis was encountered in the present series [15]. All but one of our patients with RCC underwent a nephroureterectomy. A complementary nephroureterectomy was performed following the histopathological diagnosis of RCC in one patient undergone a partial nephrectomy during surgery. Although a partial nephrectomy has been recommended for RCC lesions smaller than 4 cm, a nephroureterectomy seems much safer due to the possibility of a multifocal tumor [2]. Immunological therapy and radiotherapy were given in three patients (with stage 3 and 4). Although four patients are still under follow up and disease free, discussion on the survival rate in RCC could not be included in this series due to the loss of follow up of others.

The malignant rhabdoid tumor is a malignant childhood renal tumor and is associated with a poor prognosis [36]. Unfortunately, both patients with MRT died in the present series, one with late postoperative sepsis and the other with recurrent disease.

The term cystic renal tumor covers cystic nephroma (CN) or multilocular cysts of the kidney, localized renal cystic disease, cystic partially differentiated nephroblastoma (CPDN) or cystic WT in childhood. The distinguishing characteristics of CN are a fully cystic mass and numerous thin-walled septa covered by epithelium without blastemal and other embryonic elements [2,37]. A nephrectomy

is the surgery of choice in large CNs. However, if the radiological data suggest a CN in a small-sized renal cystic mass, NSS may be an option after confirmation of the benign nature of the lesion with a frozen histopathological examination, if suitable. Otherwise, a nephrectomy would be curative.

Renal angiomyolipoma is a benign renal tumor. This tumor may be associated with TSC or can occur as a component of sporadic lymphangioliomyomatosis [38]. Asymptomatic small angiomyolipomas (<4cm) can be followed up with US, CT, or MRI, while symptomatic or large lesions should be treated with NSS or embolization [29]. The rate of angiomyolipoma is 4% in our series without association with TSC.

A nephrogenic rest that is persistent metanephric blastemal tissue in the kidney after the 36<sup>th</sup> week of gestation associates with the Wilms tumor. The majority of nephrogenic rests disappear spontaneously as the incidence of nephrogenic rest is about 100 times greater than the Wilms tumor. Nephrogenic rests are histologically classified as incipient nephrogenic rests, sclerosing nephrogenic rests, and hyperplastic nephrogenic rests. In addition, when most nephrogenic rests are defined, sclerosis develops [2]. In the present series, one patient had a sclerosing nephrogenic rest.

Metanephric stromal tumor (MST) is a benign stromal tumor of the kidney, and the most common presentation was an abdominal mass. MST is thought to be a biphasic tumor that can be merged with Wilms tumor histology. A relationship with papillary renal cell carcinoma has been reported [39]. A nephrectomy is usually curative [29].

## CONCLUSION

Non-Wilms' renal tumors are rare in childhood and half are malignant. Presumptive diagnosis is usually the Wilms tumor. Hypercalcemia may be encountered in patients with CMN and RCC. Nephroureterectomy is necessary in most cases. NSS can be performed in selected cases and under suitable conditions. The OS rate is 76% in malignant NWRT.



### Author contribution

Study conception and design: BA, SE, and İK; data collection: BA and SE; analysis and interpretation of results: BA, SE, and DO; draft manuscript preparation: BA, SE, AOC, FCT, DO, and İK. All authors reviewed the results and approved the final version of the manuscript.

### Ethical approval

The study was approved by the Institutional Ethical Committee (Protocol no. GO 745/2016).

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### Conflict of interest

The authors declare that there is no conflict of interest.

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