

The THAI *Journal of* SURGERY

Official Publication of the Royal College of Surgeons of Thailand

Vol. 39

January - March 2018

No. 1

Original Article

Renal Tumors in Children: Outcomes of Treatment in a 10-year Period

Siripuk Sawetchaikul, MD

Suranetr Laorwong, MD

Rangsan Niramis, MD

Department of Surgery, Queen Sirikit National Institute of Child Health, Bangkok, Thailand

Abstract

Background: Renal tumors are the second most common intraabdominal tumor in children and Wilms' tumor is mostly mentioned. Other renal tumors have a small number and also have different clinical characteristics, treatment and prognosis comparing with Wilms' tumor.

Purpose: The aim of this study was to determine characteristics and outcomes of treatment of renal tumors in children.

Materials and Methods: A retrospective chart review of patients with renal tumors who were surgically treated at Queen Sirikit National Institute of Child Health from January 2006 to December 2015 was conducted. Patients' data were collected and analyzed for demonstration of treatment outcomes of the various renal tumors.

Results: Sixty-four patients, 30 males and 34 females, were available for the study. Age at diagnosis ranged from 2 months to 14.5 years (average 3.2 years). The three most common clinical manifestations were palpable abdominal mass, hematuria and abdominal pain in 47 (73.4%), 17 (26.6%) and 12 cases (18.8%), respectively. The principal preoperative imaging was computerized tomographic scan which was done in 62 cases (96.9%). Benign and malignant renal tumors were noted in 7 (10.9%) and 57 cases (89.1%). Benign renal tumors including mesoblastic nephroma (4 cases) and others (3 cases) were treated by total nephrectomy and all of the 7 cases survived. Malignant renal tumors included Wilms' tumor (42 cases), clear cell sarcoma (6 cases), renal cell carcinoma (5 cases) and others (4 cases). Primary nephrectomy could be done in 80% of all malignant renal tumors. Adjuvant chemotherapy and radiotherapy were used to treat malignant renal tumors. Four patients died in this study, Wilms' tumor (2 cases), renal cell carcinoma (1 case) and mesenchymal chondrosarcoma (1 case). There was no mortality in the benign group.

Conclusion: Wilms' tumor was the most common renal tumor in children with good prognosis. Mesoblastic nephroma was the most common benign renal tumor and had a 100% survival rate.

Keywords: Renal tumors, children, Wilms' tumor, mesoblastic nephroma, outcome

Correspondence address: Rangsan Niramis, MD, Department of Surgery, Queen Sirikit National Institute of Child Health, 420/8 Rajavithi Road, Bangkok 10400, Thailand; Telephone/Fax: +66 2354 8095; E-mail: miramis@hotmail.com

INTRODUCTION

Renal tumors are the second most common solid intraabdominal tumor in children that represent malignant more common than benign tumors. Wilms' tumor is the most common pediatric renal tumor approximately 90% of the malignant group¹⁻⁵. The other malignant renal tumors include clear cell sarcoma, malignant rhabdoid tumor and renal cell carcinoma. Benign renal tumor is the minority group including congenital mesoblastic nephroma, cystic renal tumor and angiomyolipoma. Renal tumors in children have different identities and manifestations. Prognosis of each tumor is depended on histology, stage, age of the patients, tumor weight, response to therapy and chromosomal abnormalities. However, it is not possible to definitely identify the difference between each type with clinical manifestation and preoperative imaging^{6,7}. Herein, we are interested to review our experience in management of the renal tumors in a-10-year period. The objective of the study was to determine the characteristics and outcomes of the treatment of the renal tumors in children at our institute.

MATERIALS AND METHODS

After the proposal was approved by the Ethic Committees of the institute (Document No. 59-065), medical records of children (age 0-15 years) with the diagnosis of renal tumors from January 2006 to December 2015 at Queen Sirikit National Institute of Child Health (QSNICH) were reviewed. Patients who had been surgically treated from other hospitals were excluded from this study. Data collection included demographics, clinical manifestations, underlying diseases, preoperative imaging, metastasis work up, staging, types of management and results of treatment. Follow-up time was determined by the last contact at QSNICH until December 31, 2016 by review of the medical records. We contacted some patients in order to update clinical data by telephone and letter. Patients' data were analyzed using descriptive statistic.

RESULTS

Sixty-six patients were treated with renal tumors during the study period. Two patients with Wilms' tumor were excluded from this study. One was sent

from the other hospital after tumor recurrence and the other was transferred after primary surgery from the rural hospital to continue chemotherapy. Therefore, 64 patients were available for the study.

Pathological diagnosis

Malignant renal tumors were identified in 57 of the 64 patients (89.1%) and Wilms' tumor had the most common incidence (42 cases or 65.5% of all renal tumors and 73.8% of malignant renal tumors). The other malignant renal tumors were clear cell sarcoma (6 cases or 9.4% of all renal tumors), renal cell carcinoma (5 cases or 7.8% of all renal tumors), rhabdoid tumor (2 cases) and others (mesenchymal chondrosarcoma and malignant round cell tumor in one case, each). The remaining 7 patients (10.9%) had benign renal tumors including mesoblastic nephroma (4 cases) and others (metanephric adenoma, cystic partial differentiated nephroblastoma and angiomyolipoma in one case, each).

Demographic data

Of the 64 patients with renal tumor there was no difference of sex incidence between male and female (30 vs 34) (Table 1). For analysis of each type of the tumors, male was more common than female in malignant non-Wilms' tumor (2:1) and benign renal tumor (2.5:1), whereas female are more predominant than male in Wilms' tumor (1:1.8).

Age of the patients with renal tumor ranged from 2 months to 14 years. Each type of tumor was found in different age groups (Figure 1). Median age of rhabdoid tumor, mesoblastic nephroma and Wilms' tumor was 1.08, 1.12 and 1.45 years, where as median age of clear cell sarcoma and renal cell carcinoma was 4.58 and 7.83 years, respectively.

Associated anomalies

Four patients had associated anomalies. Three patients with Wilms' tumor were noted to have association with Denys-Drash syndrome, autosomal recessive polycystic kidney disease and hypospadias with bilateral undescended testes. One patient with angiomyolipoma was previously diagnosed with tuberous sclerosis.

Clinical manifestations

The most common presentation of these patients

Table 1 Gender and type of renal tumors

| Gender | Wilms' tumor (n=42) | Malignant non -Wilms' tumors (n=15) | Benign renal tumor (n=7) | Total (N=64) (%) |
|--------------|------------------------|--|-----------------------------|---------------------|
| Male | 15 | 10 | 5 | 30 (46.9) |
| Female | 27 | 5 | 2 | 34 (53.1) |
| Male: Female | 1:1.8 | 2:1 | 2.5:1 | 1:1.1 |

Table 2 Clinical manifestations of patient with renal tumors

| Type of renal tumors | Abdominal mass | Abdominal pain | Hematuria | Fever | Weight loss | Hypertension |
|--------------------------------|-------------------|----------------|-----------|----------|-------------|--------------|
| Wilms' tumor (n=42) (%) | 32 (76.2) | 9 (21.4) | 11 (26.2) | 4 (9.5) | 2 (4.8) | 6 (14.3) |
| Clear cell sarcoma (n=6) (%) | 5 (83.3) | - | 2 (33.3) | - | - | - |
| Renal cell carcinoma (n=5) (%) | 2 (40) | 1 (20) | 2 (40) | 2 (40) | 2 (40) | - |
| Rhabdoid tumor (n=2) (%) | 1 (50) | - | 2 (100) | 1 (50) | - | - |
| Mesoblastic nephroma (n=4) (%) | 4 (100) | - | - | - | - | - |
| Other (n=5) (%) | 3 (60) | 2 (40) | - | 2 (40) | - | - |
| Overall (N=64) (%) | 47 (73.4) | 12 (18.8) | 17 (26.6) | 9 (14.1) | 4 (6.3) | 6 (9.4) |

with renal tumor was palpable abdominal mass (Table 2). Gross hematuria was found in every type of malignant renal tumors. Only 6 patients (14.3%) with Wilms' tumor developed hypertension. There were two patients who did not have any symptoms. One patient with angiomyolipoma was found during screening ultrasonography of tuberous sclerosis. One with Wilms' tumor was incidental finding during exploratory laparotomy due to splenic injury.

Preoperative imaging

Plain film of abdomen was done in 41 patients (64.1%) and mostly revealed soft tissue mass density in the kidney. Abdominal ultrasound was done in 42 patients (65.6%) and could differentiate between solid and cystic renal tumors. Computerized tomographic (CT) scan was done in 62 patients (96.9%). Two patients was not investigated with the CT scan because of incidental diagnosis of Wilms' tumor during operation of ruptured appendicitis (one case) and using intravenous pyelography (IVP) instead of the CT scan (one case). The CT scan could not differentiate the definite type of renal tumors.

Location of the renal tumors

Table 3 showed the renal sides involved by primary renal tumors. Tumors originated more often in the

right kidney than the left one, both benign and malignant tumors (56.3% vs 40.6%). Only two cases with Wilms' tumor involved bilaterally.

Operative procedures

All of the patients were treated along with National Wilms' Tumor Study Group-5 (NWTSG-5)² and Thai Pediatric Oncology Group 2014 (Thai POG 2014)⁸. Primary nephrectomy was the recommended procedure. If nephrectomy was not possible, tumor biopsy for tissue diagnosis should be done. All of 7 patients with benign renal tumor (100%) and approximately 80% of the malignant renal tumors could undergo primary nephrectomy (Table 4). Nine malignant renal tumors were primarily treated with open tissue biopsies. Needle biopsy was performed in one case and open biopsy was repeated after pathological report of inadequate tissue. Eight of 10 patients with primary tumor biopsy underwent nephrectomy after treatment with chemotherapy and radiation. Other two patients were lost to follow-up, one with renal cell carcinoma and one with undifferentiated malignant round cell tumor.

Chemotherapy and radiation

All of the patients with benign tumor underwent only nephrectomy, no other additional treatment. All

Table 3 Location of the primary renal tumors (n=42)

| Type of renal tumor | Right kidney | Left kidney | Bilateral kidneys |
|-------------------------------|------------------|------------------|-------------------|
| Malignant renal tumors | | | |
| Wilms' tumor | 25 | 15 | 2 |
| Renal cell carcinoma | 2 | 3 | 0 |
| Clear cell sarcoma | 3 | 3 | 0 |
| Rhabdoid tumor | 0 | 2 | 0 |
| Mesenchymal chondrosarcoma | 1 | 0 | 0 |
| Malignant round cell tumor | 0 | 1 | 0 |
| Benign renal tumors | | | |
| Mesoblastic nephroma | 3 | 1 | 0 |
| Metanephric adenoma | 0 | 1 | 0 |
| Angiomyolipoma | 1 | 0 | 0 |
| Cystic partial differentiated | | | |
| Nephroblastoma | 1 | 0 | 0 |
| Total (%) | 36 (56.3) | 26 (40.6) | 2 (3.1) |

Table 4 The first operative procedure

| Operative procedures | Wilms' tumor (n=42) | Malignant Non-Wilms' tumors(n=15) | Benign renal tumors (n=7) | Total (N=64) |
|-------------------------|---------------------|-----------------------------------|---------------------------|--------------|
| Primary nephrectomy (%) | 35 (83.3) | 12 (80) | 7 (100) | 54 (84.4) |
| Tumor biopsy | | | | |
| Open (%) | 7 * (16.7) | 3 (20) | - | 10 (15.6) |

*Initial needle biopsy in one case and open biopsy later because of inadequate tissue in the first procedure

Table 5 Outcome of patients with Wilms' tumor (n =42)

| Patients' data | Follow-up time after nephrectomy | | | | |
|-------------------|----------------------------------|----------|--------|---------|---------|
| | 3 months | 6 months | 1 year | 2 years | 3 years |
| Follow-up | 39 | 39 | 38 | 34 | 33 |
| Lost to follow-up | 3 | 3 | 4 | 7 | 7* |
| Death | 0 | 0 | 0 | 1 | 2* |
| Tumor recurrence | 0 | 2 | 2 | 3 | 4* |

*accumulative number

of the patients with malignant tumor were treated by chemotherapy and radiation after nephrectomy or tumor biopsy, based on the guideline of NWTSG-5² and Thai POG 2014⁸.

Outcomes

Mean follow-up time was four years. Of the total 64 patients, 42 cases (65.6%) had contact with the hospital over 3 years after nephrectomy.

Malignant renal tumors

Wilms' tumor: Table 5 showed patients' data of Wilms' tumor after surgical treatment in a 3-year period. Tumors recurred after nephrectomy in 4 cases (9.5%) within 6 months (2 cases), 2 years (1 case) and 3 years (1 case), respectively. All of the recurrence cases were treated with chemotherapy and tumor resection. Two cases died after nephrectomy within one and three years in one case, each. Therefore, the patients were

alive more than 2 years in at least 34 cases (81.0%) and more than 3 years in at least 33 cases (78.6%) of the total 42 cases after nephrectomy.

Clear cell sarcoma: Four of the 6 patients were doing well after 3-year follow-up. Other two patients had recurrence diseases at one and two years after nephrectomy. One case was in the process of treatment and another case received a palliative care.

Renal cell carcinoma: Two of the 5 patients were doing well without any recurrence after 3-year follow-up. Two patients were transferred to the rural hospital after surgical treatment, one case died a few weeks later and there was no information on another case. The remaining one case was lost to follow-up six months after tumor biopsy.

Rhabdoid tumor: All of the two patients were lost to follow-up within one year after nephrectomy and chemotherapy.

Other malignant renal tumors: One case with chondrosarcoma had recurred within 1.5 years and died within 3 years after primary nephrectomy. One patient with undifferentiated malignant round cell tumor was lost to follow-up within three months after tumor biopsy.

Benign renal tumors

Mesoblastic nephroma: Four patients were alive over 3-year follow-up. One of the 4 patients had recurrence at 1.5 years after nephrectomy. He underwent tumor resection once again and was doing well after that.

Other benign renal tumors: Three patients with

angiomyolipoma, cystic partial differentiated nephroblastoma and metanephric adenoma were alive over 3-year follow-up without any recurrence.

DISCUSSION

Wilms' tumor is the most common renal tumor in children. Approximately 94% of childhood renal tumors was reported in the United States^{7,9,10}. Our experience from the present study revealed that Wilms' tumor was found in only 65.6% of all renal tumors. Rhabdoid tumor and clear cell sarcoma of the kidney were previously classified in a variant of Wilms' tumor. Clear cell sarcoma and renal cell carcinoma in this study were found to have a higher incidence than those in the report of Ying¹¹ (9.4% vs 2.8% and 7.8% vs 2.5%). In other previous study, there is no sexual predominance in any group of the renal tumor, except slightly higher of female in Wilms' tumor^{9,12,13}, whereas our present study revealed female predominance in Wilms' tumor and male predominance in malignant non-Wilms' tumor and benign renal tumors. Age group of each renal tumor is different but overlapped in some types. Wilms' tumor, rhabdoid tumor and mesoblastic nephroma were present in infant and early childhood, but renal cell carcinoma was commonly found in adolescent. Clear cell sarcoma was present in early childhood period (Figure 1). Regarding associated abnormality, although tuberous sclerosis is found in angiomyolipoma, it may be associated with renal cell carcinoma as the report of Kida et al.¹⁴. Asymptomatic abdominal mass is the main problem to seek for

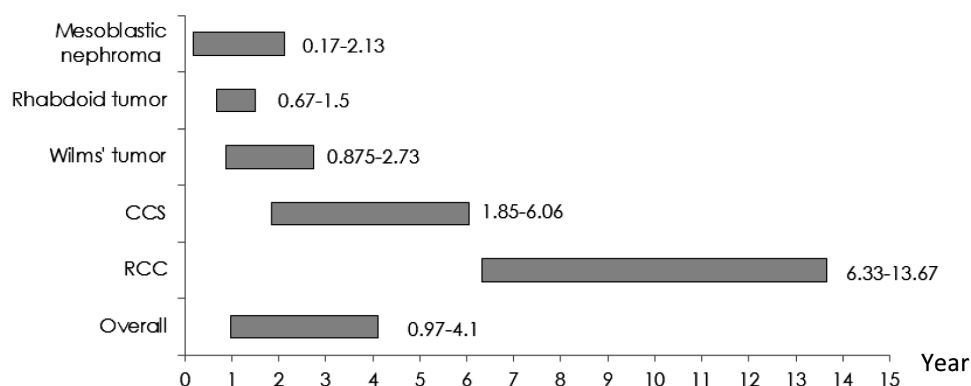


Figure 1 Age distribution of renal tumors (25th -75th percentile)

Abbreviation: CCS = clear cell sarcoma

RCC = renal cell carcinoma

medical service. Preoperative imaging by a CT scan has unique features but limited value in differentiate type of the renal tumors^{6,7}. Previously an IVP was done for demonstration of renal tumors¹⁵. One patient in our study was investigated by an IVP instead of a CT scan to differentiate renal tumor and hydronephrosis.

Management of renal tumors at our institute was based on NWTSG-5² and Thai POG 2014⁸. Primary nephrectomy could be performed in 100% of benign renal tumors and approximately 80% of malignant renal tumors. There was no difference in primary nephrectomy between Wilms' and malignant non-Wilms' tumor (83.3% vs 80%). In the patients with initial treatment by tumor biopsy, every case with Wilms' tumor underwent nephrectomy after chemotherapy, whereas nephrectomy was not done in two of three cases with malignant non-Wilms' tumor because of loss to follow-up.

Improved outcomes of Wilms' tumor management in our institute revealed from the previous studies in two periods of time. The first period was between 1986 and 1995 with the 2-year survival rate of 50%¹⁶. The second one was between 1999 and 2009 with the 2-year survival rate of approximately 90%¹⁷. Five-year overall survival rate in the United States^{18,19}, Siriraj Hospital²⁰ and 4-year overall survival rate at Songklanagarind Hospital²¹ were 95%, 77.40% and 65.20%, respectively. Malignant-non Wilms' tumor group had poorer prognosis than Wilms' tumor. Clear cell sarcoma had better prognosis than renal cell carcinoma and rhabdoid tumor¹¹. There were more recurrences in clear cell sarcoma but the patients survived. All of rhabdoid tumor was lost to follow-up within one year with unknown reason. Benign renal tumor had good prognosis. It might recur in the case with remaining residual tumor and successfully treated by redo-surgical resection.

The present study had some limitations because it was a retrospective review and had a short time for clinical follow-up of the patients. We could not compare a long-term outcome with other institutes.

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บทคัดย่อ **เนื้องอกของไตในเด็ก: ผลของการรักษาในระยะเวลา 10 ปี**

ศิริพักตร์ เสวตชัยกุล, พ.บ.*, สุรเนตร ลอวงศ์, พ.บ.*, รั้งสรรค์ นิรามิษ, พ.บ.*

*กลุ่มงานศัลยศาสตร์ สถาบันสุขภาพเด็กแห่งชาติมหาราชินี กรุงเทพฯ

ความเป็นมา: เนื้องอกของไตพบได้บ่อยเป็นอันดับที่สองของเนื้องอกในช่องท้องในเด็ก และส่วนใหญ่จะกล่าวถึงแต่ Wilms' tumor เนื้องอกของไตชนิดอื่นๆ พบเป็นจำนวนน้อย และมีคุณลักษณะแตกต่างกันในแต่ละชนิด รวมทั้งการรักษาและการพยากรณ์โรครก็แตกต่างกัน เมื่อเทียบกับ Wilms' tumor

วัตถุประสงค์และวิธีการ: เป็นการศึกษาย้อนหลังจากการทบทวนเวชระเบียนของผู้ป่วยที่เป็นโรคเนื้องอกของไตที่ได้รับการรักษาโดยการผ่าตัดที่สถาบันสุขภาพเด็กแห่งชาติมหาราชินี ตั้งแต่เดือนมกราคม 2549 ถึง เดือนธันวาคม 2558 ข้อมูลของผู้ป่วยถูกรวบรวมและวิเคราะห์ เพื่อแสดงถึงผลของการรักษาของเนื้องอกของไตแต่ละชนิด

ผล: ผู้ป่วย 64 ราย (เพศชาย 30 ราย เพศหญิง 34 ราย) ที่มีข้อมูลเหมาะสมในการศึกษา อายุเมื่อทำการวินิจฉัย ตั้งแต่ 2 เดือน ถึง 14.5 ปี (อายุเฉลี่ย 3.2 ปี) ลักษณะทางคลินิกที่สำคัญ 3 อย่างที่พบในผู้ป่วยได้แก่ ก้อนที่คลำได้ในท้อง ถ่ายปัสสาวะเป็นเลือดสีแดง และปวดท้อง พบในผู้ป่วย 47 ราย (ร้อยละ 73.4), 17 ราย (ร้อยละ 26.6) และ 12 ราย (ร้อยละ 18.8) ตามลำดับ ภาพรังสีที่สำคัญตรวจก่อนการผ่าตัดคือ การสแกนด้วยคอมพิวเตอร์ (CT scan) ทำในผู้ป่วย 62 ราย (ร้อยละ 96.9) เนื้องอกของไตชนิดไม่ร้ายแรงและเนื้องอกชนิดร้ายแรงหรือมะเร็ง พบได้ 7 ราย (ร้อยละ 10.9) และ 57 ราย (ร้อยละ 89.1) เนื้องอกของไตชนิดไม่ร้ายแรง ได้แก่ mesoblastic nephroma (4 ราย) และเนื้องอกไม่ร้ายแรงชนิดอื่นๆ (3 ราย) เนื้องอกของไตชนิดร้ายแรงประกอบด้วย Wilms' tumor (42 ราย), clear cell sarcoma (6 ราย), renal cell carcinoma (5 ราย) และเนื้องอกร้ายแรงอื่นๆ (4 ราย) การรักษาครั้งแรกโดยการผ่าตัดเอาไตออก สามารถทำได้ร้อยละ 100 ในผู้ป่วยเนื้องอกของไตชนิดไม่ร้ายแรง และสามารถตัดไตออกได้ประมาณร้อยละ 80 ในเนื้องอกของไตชนิดร้ายแรง การรักษาด้วยเคมีบำบัดและการฉายแสงร่วมด้วยใช้ในเนื้องอกไตชนิดร้ายแรง ในการศึกษาครั้งนี้มีผู้ป่วยเสียชีวิต 4 ราย จาก Wilms' tumor 2 ราย, renal cell carcinoma และ mesenchymal chondrosarcoma อย่างละ 1 ราย ไม่มีผู้ป่วยเสียชีวิตในกลุ่มเนื้องอกของไตชนิดไม่ร้ายแรง

สรุป: Wilms' tumor เป็นเนื้องอกของไตชนิดร้ายแรงที่พบได้บ่อยที่สุดในเด็ก และมีการพยากรณ์โรครที่ดี mesoblastic nephroma เนื้องอกของไตชนิดไม่ร้ายแรงที่พบได้บ่อยที่สุด และมีอัตราการมีชีวิตรอดร้อยละ 100