ORIGINAL ARTICLE

Clinicopathological Profile of Wilms Tumor of Pediatric Patients in Dr. Sardjito General Hospital, Yogyakarta, Indonesia

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ABSTRACT

Introduction: Wilms tumor is the major kidney neoplasm in childhood. Approach to therapy gives a 90% 2-year survival rate. However, the mortality rate in developing countries is relatively still high. Research about the clinicopathological profile of Wilms tumor in Indonesia is very limited. This study aimed to investigate the Wilms tumor patients in an Indonesian setting. **Methods:** This research was a descriptive observational study using a cross-sectional design. Clinical and pathological data were collected from patients' medical records in Dr. Sardjito General Hospital, from 2011 to 2016. **Results:** Twenty-five patients were recruited with 52% female subjects. The mean age at the first diagnosis was 38 months. All patients had unilateral tumors. The tumor size was mostly (67%) equal or more than 10 cm. The most frequent symptom was abdominal mass. Ninety-two percent of patients have favorable histology. Most cases (68%) had triphasic morphology. The most common metastasis site of tumor was the liver, followed by the lung, skeletal bone, and spleen. Eighty-four percent of patients received chemotherapy, 80% received surgery, and 28% received radiotherapy. The gender distribution and the most common metastasis site in this study were different compared to previous studies. **Conclusion:** The clinicopathological profile of Wilms tumor in Yogyakarta, Indonesia, generally matches with other studies from other countries, except the gender distribution and the most common metastasis site. Further prospective studies regarding the prognosis of the patients are urgently needed.

Keywords: Clinicopathological profile, Indonesia, Pediatric patients, Wilms tumor, Yogyakarta

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INTRODUCTION

Wilms tumor is the most common primary malignant renal tumor in children with an incidence of 10 out of 100,000 newborns (1). Wilms tumor's incidence rate in Indonesia is reported lower than in developed countries. In Dr. Sardjito Hospital in 2000-2009, there were 51 children diagnosed with Wilms tumor (2). About 93-96% of Wilms tumor cases arise sporadically and unilaterally, with the peak age of presentation during the third year of life. Bilateral tumors are reported in 4-7% of cases with the mean age of 2.6 years (3).

The most common clinical presentation of Wilms tumor is abdominal enlargement due to the mass of the tumor. This mass has the tendency to expand and compress other organs around it. This compression causes obstruction of the intestines, and sometimes urinary bleeding, with respiratory suppression resulting in death (4). The presence of Wilms tumor activates the renin-angiotensin system that causes an increase in blood pressure, as found in 25-60% of cases (5). These symptoms are not pathognomonic because similar symptoms are also present in other tumors in abdominal cavities, such as neuroblastoma.

Diagnosis and degree of tumor are two important aspects to determine modality of treatment. The most common tool of diagnosis that is widely used in children suspected with Wilms tumor is ultrasound. Computed tomography (CT) and magnetic resonance imaging (MRI) are more accurate compared to ultrasonography (5). However, typically in Indonesia, these two examinations have not

been done in secondary health care centers due to limited facilities. The gold standard of Wilms tumor diagnosis is histopathologic examination of tumor tissues obtained by open biopsy. The pattern of dispersion of anaplastic cells has significance in the determination of treatment modalities. Wilms tumors with diffuse anaplastic cells that penetrate renal capsules have poor outcomes, requiring a more aggressive treatment modality than usually with Wilms tumor with focal anaplastic cell distribution (4).

Multimodality approach to therapy gives 90% 2-year survival rate, however mortality rate in developing country is still high (4,6). Research about clinicopathological profile of Wilms tumor in Indonesia is very limited. In response to this deficit, research on Wilms tumor was conducted to describe its clinicopathological profile. This study aimed to examine children with Wilms tumor in an Indonesian setting and expand the current research about this childhood illness that often results in death.

MATERIALS AND METHODS

This research was a retrospective study that was conducted to evaluate clinicopathological profiles in children with Wilms tumor. The data used were secondary data from medical records and pathological examinations in Dr. Sardjito General Hospital year 2011-2016. Data were collected from March until October 2017. Inclusion criteria were all pediatric patients aged 0-18 years, diagnosed with Wilms tumor with evidence of histopathology examination results in Dr. Sardjito General Hospital year 2011-2016. Twenty-five patients met the inclusion criteria.

RESULTS

A total of 50 pediatric patients were diagnosed with Wilms tumor in Dr. Sardjito General Hospital in 2011-2016, but only 25 patients met the inclusion and exclusion criteria such as data completeness and evidence of histopathologic examination. The data obtained were analyzed and described one by one as follows. From 25 children, it is known that the number of female patients was slightly larger than male patients. There were 13 female patients (52%). The average age of the patients at diagnosis was 3 years and 2 months (38 months) and the number of patients with Wilms tumor aged less than 6 years was 22 patients (88%) (Table I). Several radiology examinations were done to diagnose Wilms tumor of the patients. Radiological data in this study were taken from thorax X-ray examinations to observe metastasis to the lung, ultrasound to see solid / cystic mass in the abdominal cavity, and CT scan to see more clearly the mass or spread of tumor to surrounding organs and regional lymph nodes.

From medical records' data in Dr. Sardjito General Hospital in 2014-2016, it is known that 13 patients underwent radiological examination, all patients were examined with X-ray (100%), 11 patients (84.62%) underwent CT scan, and 6 patients (46.15%) received ultrasound examination (Table I).

Based on historical data, there were 23 patients (92%) who presented with a complaint of abdominal mass. Other symptoms found were fever (24%), weight loss (16%), hematuria (12%), abdominal pain (12%), nausea vomiting (8%), and other symptoms such as weakness (4%), dizziness (4%), and diarrhea (4%) (Table I).

Table I: Demographic characteristics, sign, and symptoms of Wilms tumor patients

Characteristics	Number of cases (n= 25)	Percentage (%)
Gender		
Female	13	52
Male	12	48
Age (year)		
< 6	22	88
≥ 6	3	12
Radiology examination		
X-ray	13	52
CT scan	11	44
Signs and symptoms		
Abdominal mass	23	92
Fever	6	24
Weight loss	4	16
Hematuria	3	12
Abdominal pain	2	12
Nausea, vomiting	2	8
Weakness	1	4
Dizziness	1	4
Diarrhea	1	4

All patients (100%) had unilateral tumors, most of which were located on the left kidney. From supporting examination data (radiological examination, especially the results of CT scan and histopathology examination) which were obtained, we could evaluate the size of 12 tumors. There were 8 tumors (67%) with diameter greater than or equal to 10 cm, and 4 tumors (33%) had diameter less than 10 cm. Classification of tumor histopathologic examination results based on the presence or absence of anaplastic features were divided into favorable (absence of anaplastic features) and unfavorable. There were 23 patients (92%) with favorable features and the remaining 2 patients (4%) had unfavorable histopathological features (Table II).

Histopathologic results were grouped into triphasic, biphasic, and monophasic based on the components of the tumor encountered, i.e. blastemal, stromal, and epithelial. Triphasic features were present in 68% of cases, followed by biphasic images of 16% and

Table II: Tumor location, histopathologic finding, size and spreading of the Wilms tumor

Tumor Characteristic	Number of cases (n)	Percentage (%)
Location		
Right	11	44
Left	14	56
Histopathologic findings		
Favorable	23	92
Unfavorable	2	8
Size of tumor		
≥ 10 cm	8	32
<10 cm	4	16
Tumor Spread Towards one organ	4	57,1
Lung	1	14,3
Hepar	2	28,6
Bone	1	14,3
Towards > one organ	3	42,9
Lung and liver	1	14,3
Lung and bone	1	14,3
Liver and spleen	1	14,3

monophasic at 16% (Table III).

From 13 patients who underwent radiological examination, there were 7 patients (53.85%) with metastasis based on X-ray radiography, ultrasound, and CT scan examinations. From these 7 patients there were 3 tumors (30%) which spread to the lungs, 4 tumors (40%) metastasized to the liver, 2 tumors (20%) metastasized to the bone, and 1 tumor (10%) metastasized to the spleen. There were 4 cases (57.14%) of metastasis to a single organ (lung, hepatic, or bone), and 3 cases (42.86%) of metastasis that occurred to more than 1 organ (Table II).

Nine patients (36%) received one type of therapy (chemotherapy, surgery or radiotherapy), 9 patients (36%) received two types of therapy, and 7 patients (28%) received three types of therapy. Five patients (20%) received chemotherapy, 4 patients (16%) received surgical treatment, 9 patients (36%) underwent chemotherapy and surgery, and 7 patients (28%) received chemotherapy, surgery and radiotherapy (Table IV).

Table III: Histological subtypes of the Wilms tumor

Histological subtype	Number of cases (n = 25)	Percentage (%)
Triphasic	17	68
Biphasic	4	16
Blastemal and epithelial	2	8
Blastemal and stromal	1	4
Stromal and epithelial	1	4
Monophasic	4	16
Blastemal	3	12
Epithelial	1	4
Stromal	0	0

From 16 patients who underwent chemotherapy and surgery, 3 patients received preoperative chemotherapy, 12 patients received chemotherapy treatment after surgery (postoperative), and 1 patient received both chemotherapy and surgery with unknown sequence of treatment procedures because medical treatment with time data was incomplete in the patient's medical records (Table V).

Table IV: Several types of therapy for Wilms tumor patients

Type of therapy	Number of cases (n = 25)	Percentage (%)
One type of therapy	9	36
Chemotherapy	5	20
Surgery	4	16
Radiotherapy	0	0
Two types of therapy	9	36
Chemotherapy + Surgery	9	36
Chemotherapy + Radiotherapy	0	0
Surgery + Radiotherapy	0	0
Three types of therapy	7	28
Chemotherapy + Surgery + Radiotherapy	7	8

Table V: Onset of chemotherapy pre and post-surgery treatment

Onset	Number of cases (n = 16)	Percentage (%)
Preoperative	3	18.75
Postoperative	12	75
Unknown	1	6.25

DISCUSSION

From the data recorded in the Yogyakarta Pediatric Cancer Registry (YPCR), the number of pediatric patients with Wilms tumor in 2000-2009 was ranked fifth after acute lymphoblastic leukemia, acute myeloid leukemia, retinoblastoma and neuroblastoma. Wilms tumor's incidence rate in Indonesia is reported to be lower than in developed countries. There were 51 children with Wilms tumor who presented to Dr. Sardjito General Hospital, Yogyakarta in the years between 2000-2009.

In this study, female patients were predominant, with as many as 13 patients (52%). This finding is not in accordance with research conducted at the University of Texas Southwestern Medical Center 2000-2008 where the percentage of male patients was higher (54%) (7). Another study also stated that the number of male patients was larger (56%)(8). However, one study mentioned that gender does not affect the incidence of Wilms tumor with a gender ratio of pediatric patients with Wilms tumors close to one (9). In our study, the male to female ratio was 0.92 which is consistent with

various studies that range from 0.8 to 0.95(9).

In previous study, the age range at diagnosis of patient was 2 to 120 months with median age of 45.2 months (8). Another study mentioned the age range at diagnosis was 2-144 months with median 39 months (10). Approximately 80% of patients were under 6 years old (11), while in this study the number of patients aged less than 6 years was 22 patients (88%). Based on studies conducted by SIOP and NWTS, patients with older age at diagnosis have greater risk of non-metastatic Wilms tumor recurrence (12). Age of patient also affects location of the tumor. Unilateral tumors are usually found in patients with an average age of 3.3 years, while bilateral masses generally occur at younger ages (about 2.6 years old) (3). Bilateral tumors are common in children with congenital anomalies such as WAGR, Denys-Drash, and Beckwith Wiedemann syndromes. This pattern of pathology occurs as a result of germinal mutation (pre-zygote) or before the incorporation of sperm and ovum, which is either inherited or genetic (13).

In another study, the number of bilateral Wilms tumor cases was higher than that obtained in this study. Wilms tumors occur more often unilaterally, but have occurred bilaterally (14) in 3.2% of Wilms tumor cases. Another study also mentioned that there were 1.8% bilateral Wilms tumors (8). In this study, more tumors occurred in the left kidney in 14 patients (56%). Two other studies have also mentioned that Wilms tumor is more common in the left kidney with a majority of patients presenting with an enlarged renal mass (8, 15).

The most common clinical presentation is abdominal mass. Other studies have shown that the common sign of Wilms tumors is the abdominal mass. The majority of patients (92%) had symptoms of abdominal mass, while other symptoms were abdominal pain (30%), hematuria (8%), and other non-pathognomonic symptoms (16). Although most Wilms tumors have symptoms of abdominal enlargement, further investigation is necessary to confirm the diagnosis.

In 25 patients with histopathologic examination, 92% patients have favorable histology. This result is comparable with the research conducted by Yildiz et al. in which from 102 cases, 88.2% (90 cases) had favorable histopathologic features (10). Another study also mentioned that only 5.6% of cases were found with unfavorable histology (17). In this study, there were 17 tumors (68%) triphasic, 4 tumors (16%) biphasic and 4 tumors (16%) monophasic. The three histological components have different potentials of proliferation and responses to therapies. The stromal component has the lowest proliferation index, and usually does not respond to chemotherapy (18).

Research by Guruprasad et al. mentioned that the most common site of tumor spread is the lungs (16). One study also mentioned that the most common site of tumor metastasis is the lungs, with as much as 43% of cases, and the second most common organ is the liver (8). The spreading of tumor may occur directly, hematogenously through renal vein or vena cava, or lymphogenically through the aortic lymph nodes. Pulmonary route of spreading is the most common site of metastasis because the lungs receive systemic venous blood from most organs directly. Venous blood from the gastrointestinal tract and pancreas also flows to the liver via the hepatic portal blood flow system, so the liver also often becomes the primary site of metastasis (19).

In other studies, it is known that the number of tumors with diameters greater than or equal to 10 cm was greater. The size of tumor affects the outcome of surgical therapy. About 65% of tumors with sizes greater than or equal to 10 cm are associated with an increased risk of complications in surgery (20). Multimodality approach to therapy gives 90% 2-year survival rate, even for tumors that spread out from the kidneys. A 2-year survival rate usually implies good treatment progress and successful healing (4).

CONCLUSION

The clinicopathological profile of Wilms tumor in Dr. Sardjito General Hospital Yogyakarta, Indonesia, generally is similar with other studies from other countries. However, in this study the gender distribution and the most common metastasis site were different than other studies. Further prospective studies regarding the prognosis of the patients are urgently needed.

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