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NON-WILMS` RENAL TUMORS: DIFFICULT MANAGEMENT EXPERIENCE IN THIRD WORLD

Oncology

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ABSTRACT

Background: Renal tumors other than Wilms' tumors are infrequent in childhood and account for less than 1% of all pediatric tumors. Differentiation in these tumors is important for better outcome. Lack of awareness and resources, late presentation, difficult diagnosis, and less oncology centers/experts, made the situation unfavorable resulting in poor outcome.

Aim of this study is to present our experience with non-Wilms` malignant renal tumors resulted in fair outcome.

Method: We retrospectively reviewed all patients (n = 7) treated for non Wilms` renal tumor from January 2013 to July 2108. Data collected regarding presentations, management and follow-up with special attention on diagnostic difficulties.

Result: Seven patients were included in the study with histological diagnosis of Clear Cell Sarcoma (CCSK, 3), Rhabdoid Tumor (RTK, 2), Ewing`s/PNET Tumor (1) and Congenital Mesoblastic Nephroma (CMN, 1). Two were females and aged ranged from 7 – 96 months (median 36 months). 4 patients has left sided tumor. Four patients were already evaluated and received chemotherapy (DD4A regime) before referral (2 CCSK; 1 RTK and 1 CMN) in which 3 patients had pathology report of Wilm`s Tumor but no response to chemotherapy. All patients were evaluated and biopsy performed in 6 patients (Trucut-5; open-1). Only one patient (CCSK) had radiological evidence of metastasis (bone and lung) and died during treatment. CMN patient was operated and managed well but lost in follow-up after 3 months. Rest 5 patients were operated, received chemo-radiation and are alive without recurrence. Follow-up period ranged 12 - 56 months (median 38 months).

Conclusion: Because of similar clinical presentations, it is almost impossible to differentiate Non-Wilms` Tumor from Wilms` Tumor and lack of resources / experts further add in it. Differentiation is mandatory because of separate treatment protocols and proper diagnosis and multimodal treatment may result in favorable outcome

KEYWORDS

Non-Wilms` Tumor; Clear Cell Sarcoma, Rhabdoid Tumor, Congenital Mesoblastic Nephroma

Renal tumors other than Wilms' tumors are quite less during childhood. Wilms' tumors account for 6% to 7% of all childhood cancer, whereas the remaining renal tumors account for less than 1%. The most common non-Wilms' tumors are Clear Cell Sarcoma of the kidney (CCSK), Rhabdoid Tumor of the kidney (RTK), Renal Cell Carcinoma (RCC), Congenital Mesoblastic Nephroma (CMN), and Multilocular Cystic Nephroma. Collectively, these tumors account for less than 10% of the primary renal neoplasms in childhood **[1,2].** Differentiation is important for better outcome because each tumor has different chemotherapy protocol. Currently, histopathology, immunohistochemistry and molecular markers are used for definite tissue diagnosis and to differentiate them. In third world countries like India, lack of awareness/education resulting in late presentation. Limited resources and lack oncology centers/experts, made the situation unfavorable resulting in delayed / incorrect diagnosis and finally poor outcome.

Here, we present our experience with few patients of non-Wilms` malignant renal tumors referred late to tertiary care center with wrong diagnosis but resulted in comparably far outcome.

MATERIAL & METHOD:

We retrospectively reviewed all patients (n = 7) treated for non Wilms` renal tumor from January 2013 to July 2108. Data collected regarding presentations, management and follow-up with special attention on diagnostic difficulties. We reviewed all interventions and patient records (OT and follow-up).

RESULT:

From January 2013 to July 2108, we managed 7 non-Wilms` tumor patients. All were referred late and given some sort of therapy including chemotherapy in 4 patients **[Table: 1]**. Two patients were females. Age ranged from 7 – 96 months (median 36 months). 4 patients had left sided tumor while 3 had right sided pathology. Biopsy was performed in 6 patients (Trucut-5; open-1) while one patient with diagnosis of CMN was managed with upfront surgery. Histopathological diagnosis were Clear Cell Sarcoma (CCS, 3), Rhabdoid Tumor (RTK, 2), Ewing`s/PNET Tumor (1) and Congenital Mesoblastic Nephroma (CMN, 1). All patients were evaluated and only one patient (CCS) had radiological evidence of metastasis (bone and lung) and died during treatment (Immunosuppression with infections). Four patients were already received chemotherapy (DD4A regime) before referral (2 CCK; 1 RTK and 1 CMN) in which 3 patients already had pathology report of Wilm`s Tumor but no response to chemotherapy. CMN patient was operated and managed well but lost in follow-up after 3 months. Rest 5 patients were operated, received chemo-radiation and are alive without recurrence. Follow-up period ranged 12 - 56 months (median 38 months).

Table-1: Detail of Patients –

Diagnosis	Age / Sex	Presentation	Stage	Treatment	Follow-up
CMN	7 mth Male	Abd mass, fever, vomiting, electrolyte imbalance	III	S	Lost in follow-up
CCSK1	54 mth Female	Abd mass, pain, fever	III	C/S/R	24 mth
CCSK	28 mth Male	Abd mass, fever	III	C/S/R	12 mth
CCSK2	60 mth Male	Abd mass, fever, dehydration, vomiting, immunosupression	IV	C	Expired
RTK	36 mth Male	Abd mass	III	C/S/R	34 mth
RTK3	23 mth Male	Abd mass, fever	III	C/S/R	28 mth

Ewing`s / PNET4	96 mth Female	Gross hematuria, fever, pain, Abd mass	III	C/S/R	56 mth

- CMN- Congenital mesoblastic Nephroma; CCSK- Clear cell sarcoma of kidney; RTK- Rhabdoid tumor of kidney; PNET- primitive neuro-ectodermal tumor of kidney.
- Mth = months

[1] = Already received 2 cycle of chemotherapy before referral (DD4A-regime).

[2] = Already received 5 cycle of chemotherapy before referral (DD4A-regime).

[3] = Already received 3 cycle of chemotherapy before referral (DD4A-regime).

[4] = Already received 1 cycle of chemotherapy before referral (DD4A-regime).

We followed the guideline of National Wilms` Tumor Study Group (NWTSG-5) and used the I-regime for CCS, RTK-regime for Rhabdoid tumor and VDC-IE regime 3 weekly in Ewing's/PNET tumor. All patients received neoadjuvant chemotherapy followed by surgery and adjuvant chemo-radiation.

DISCUSSION:

Renal mass is the most common retroperitoneal mass in children and Wilms` tumor accounts for almost 85% while other rare renal tumors including stromal tumors constitute only 15% of all pediatric renal masses **[3-5].** CSSK, RTK, Ewing`s/PNET tumor of kidney are rare tumors and known to have poor prognosis while CMN have good prognosis after complete excision. RTK is most aggressive and lethal tumor characterized by early onset of local and distant metastases, usually resistance to chemotherapy. Overall survival rate is only 20-25% (Wilms` tumors >85%). Histogenetic origin remains obscure and 10-15% of patients have synchronous or metachronous brain tumors. Most patients present with stage III or IV disease but not associated with the WAGR or Beckwith-Wiedemann`syndrome **[6-8].**

CCSK is Uncommon tumor and constitutes <3% of all renal tumors. NWTSG labeled it "unfavorable histology" in clinical protocols. It has poor outcome and has tendency to "Metastasize to bone" (Marsden, *et al*) **[9,10].** Approximately 5% of patients have metastatic disease at presentation. It has sarcomatous nonepithelial nature and not associated with intralobar nephrogenic rests. Overall survival was 87.5%, for patient receiving 15 months of chemotherapy. Four independent prognostic factors are described by Argani, *et al* – stage; age of diagnosis; tumor necrosis and treatment with doxorubicin **[11,12].**

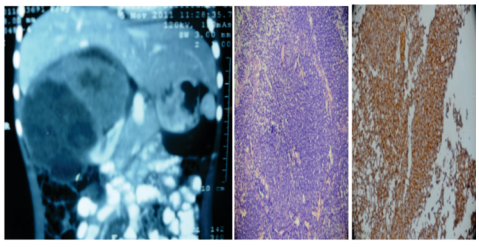
Ewing`s/PNET tumor is extraordinarily rare primary tumor in kidney and usually seen in young adults. It is an aggressive tumor and has high local recurrence and early metastases. 5 year survival rate is < 10% without chemotherapy. Aggressive Surgery and chemo-radiation is the mainstay of therapy. CMN is the most common renal tumor in newborn and infancy. Bolande *et al*. were the first to describe this tumor as a separate entity from Wilms' tumor **[13].** Classic CMN reflects intrarenal fibromatosis and cellular CMN is intrarenal infantile fibrosarcoma. Most cases of CMN are cured with radical nephrectomy with lymph nodes sampling. Metastasis to lung, liver, brain, and heart have been reported **[14,15,16].**

These rare tumors have similar clinical and radiological characteristics to Wilms` tumor and usually present late because of their aggressive nature. Preoperative diagnosis is almost impossible without histopathology and immunohistochemistry, even with modern imaging techniques.

They should be treated promptly. Differentiation is important for better outcome because each tumor has different chemotherapy protocol. In third world countries like India has limited resources in form of cancer expert practitioners, cancer hospitals, etc. Lack of awareness about pediatric malignancies, illiteracy, financial problems and unethical practices delayed the early referral of patients. Non-availability of quality computed tomography and pathology labs either could not diagnose or leads to incorrect diagnosis and treatment.

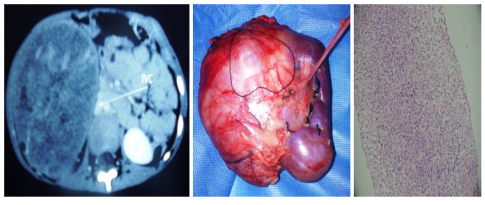
In our cohort, 3 patients had a pathology report of Wilms` tumor and got correct chemotherapy for that but when biopsied again, was diagnosed to have non-Wilms` renal tumor. CMN patient was treated for peri-renal abscess and referred late. After Computed tomography, he underwent upfront surgery and complete excision was achieved but he was discharged due to lack of finances and finally lost in follow-up. One patient presented in low general condition with severe immunosuppression due to chemotherapy for Wilms` tumor (DD4A-regime) but final diagnosis was CCSK and finally died due to sepsis. None of the patient had proper documentation of previous treatment. It is advisable to ignore all previous reports in such cases and should re-evaluate the patient from beginning as we did.

In conclusion, non-Wilms` tumors are rare and need tissue diagnosis before treatment. In third world countries like India, it is very difficult to get early referral but proper diagnosis and multimodal treatment may result in favorable outcome.



A: Right renal mass after chemotherapy before Surgery (Ewing`s/PNET tumor of kidney).

B &C: IHC strongly positive for vimentin, Cd99.



A: Right renal mass after chemotherapy before Surgery (CCSK).
B: Excised mass with Kidney.
C: Histopathology showing clear cells.

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