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Teratoid Wilms Tumor: Case Report and Review of Literature

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Abstract

Teratoid Wilm's tumor is a rare variant of Wilm's tumor, which composed of well-differentiated epithelial cells or mesenchymal heterologous elements constituting more than 50% of the conventional wilm's tumors in pediatric group. We hereby report an additional case in a 6-year-old female along with review of literature.

Keywords: Wilms Tumor; Child; Teratoid Wilms Tumor

Conflict of interest: The authors declare no conflict of interest.
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Introduction

Teratoid Wilm's tumor (TWT) is a rare variant of Wilm's tumor composed of well-differentiated epithelial and/or mesenchymal heterologous cells presenting as more than 50% of the conventional wilm's tumors in children (1). The teratoid histologic variant of Wilms' tumor is rare; with only 33 prior reported cases of Renal Teratoid Wilms tumor and 5 cases of extra renal Teratoid wilms tumor (1-26).

Literature has revealed 33 previously reported cases of the renal teratoid variant of Wilms' tumor. We have summarized the characteristics of these cases with respect to age, location, histology and follow up. Among the 33 reported cases, the age ranged from 3 month to 7 years, locations of tumors in these reports are limited to the renal region. Histologically the appearance varied from predominant mesenchymal component to heterologous epithelial components which show a mixed pattern.

Usually a Teratoid Wilms' tumors appear to present at a high stage.

Treatment strategies should focus on wide total surgical resection due to this entity's poor response to chemotherapy. We hereby report an additional case in a 6-year-old female along with review of literature.

Case Report

A 6-year-old girl, presented with a gradually increasing abdominal mass in right flank for 6 months. She complained of abdominal pain and discomfort. However, there was no history of nausea or vomiting. Past history of the patient was uneventful; she was a term normal vaginal delivery baby, with no significant family history.

General Physical Examination revealed a large abdominal mass measuring 10×4 cm in the right lumbar region. A clinical impression of Wilm's tumor or a neuroblastoma was considered at first. The patient was taken up for radiological investigations. Computed tomography (CT) of the whole abdomen showed a well-defined heterogeneously enhancing mass arising from the upper and lower pole of the kidney extending from T9 to L4. No evidence of metastatic deposits was noted. A radiological diagnosis of Wilm's tumor was given. The patient was started on preoperative chemotherapy of vincristine was administered for 7 weeks. No response to chemotherapy was seen, and the tumor size increased to 13×6 cm over a period of 2 months.

Hence, Right radical nephrectomy along with part of ureter and lymph nodes including paracervical, paraaortic, aorto caval, iliac and mesenteric lymph nodes was done. On gross examination, the nephrectomy specimen weighed 800gms and

measured 16×8×10 cm along with an attached ureter. The external surface of the kidney was covered by a capsule, which was thinned out. At few foci breech in the capsule was also identified (Figure 1). On cut section, the entire kidney was replaced by a tumor, covering upper pole, pelvis and lower pole.

Posteriorly compressed renal parenchyma was seen. The tumor had a variegated appearance with few areas of hemorrhage and necrosis (Figure 1). The tumor was grossly given a provisional diagnosis of Wilm's tumor.

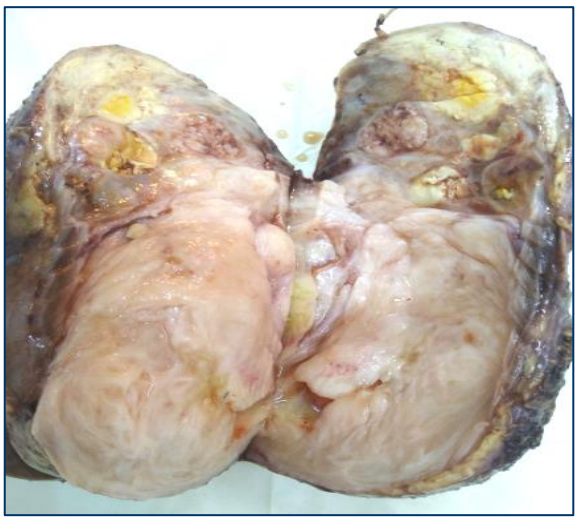

Figure 1. External surface of the kidney covered by a capsule, entire kidney replaced by a tumor, showing white firm growth, with variegated appearance and few areas of hemorrhage and necrosis.

Histopathology

Microscopically, on examination of multiple sections, there were few areas showing blastema (Figure 2) with abortive renal tubules (Figure 3).

No features of anaplasia were detected.

Most of the tumor was composed of heterologous stromal elements in the form of skeletal muscle (Figure 4).

There were many foci of mature adipose tissue (figure 5). On further sectioning many areas showing squamous (figure 6) as well as rhabdomyoblastic differentiation (figure 7).

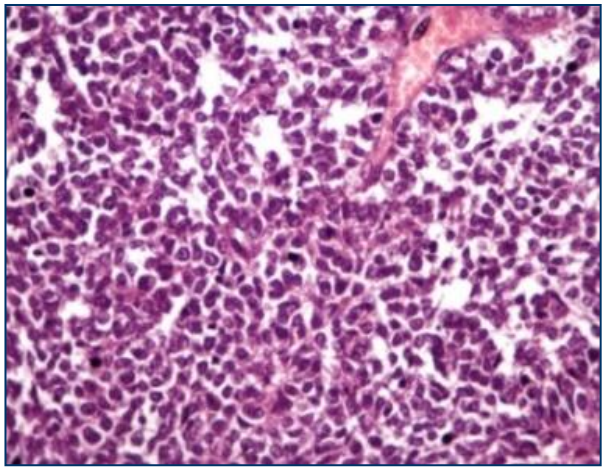

Figure 2. H&E 400x, Blastemal Component showing small round cells with minimal cytoplasm and high Nucleo-cytoplasmic ratio. Few mitosis and, few apoptotic bodies also seen.

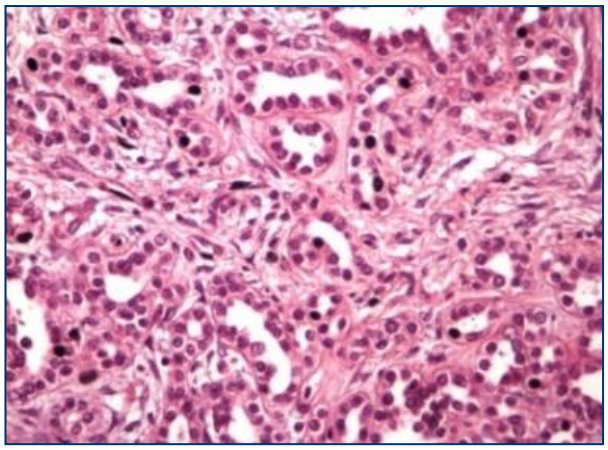

Figure 3. H&E 400x, Abortive tubules: epithelial component.

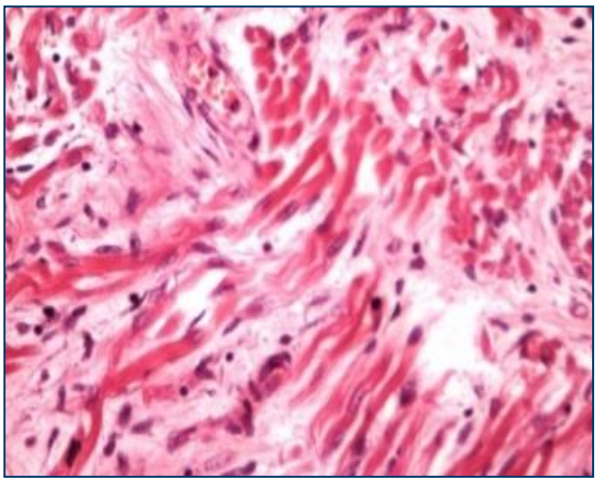

Figure 4. H&E 400x, Heterologous component: Skeletal muscle (Mesenchymal).

All of the findings mentioned above were compatible with teratoid Wilms' tumor. A few foci of tumor necrosis were observed. The tumor was extending minimally into the renal sinus. However the gerota's fascia was uninvolved. No capsular or renal vein invasion was seen. The uninvolved part of the kidney showed no evidence of nephrogenic rests or nephroblastomatosis. Biopsied lymph nodes were negative for tumor. An Immunohistochemical (IHC) staining was considered to check for wilm's tumor gene mutation and cellular proliferation (Ki-67).

The IHC for WT1 was strongly positive, 80% of the nuclei stained positive. The Ki-67 staining was positive in 30% of the blastemal cells. A diagnosis of Teratoid Wilm's tumor (TWT) stage one was given in accordance with the children's oncology group protocol. The child was followed up for one year post surgery and was alive and doing well.

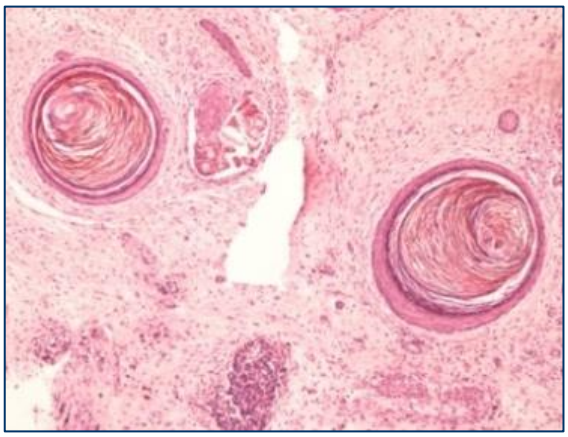

Figure 6. H&E 400x: Heterologous component: squamous differentiation (Epithelial).

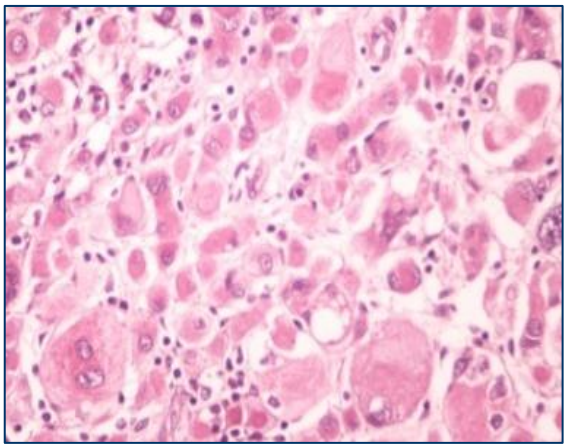

Figure 7. H&E 400x, Heterologous component: Rhabdomyoblastic differentiation (Mesenchymal).

Discussion

Wilms tumor is the most common renal tumor in childhood. It is an embryonic tumor with classically a triphasic histologic pattern represented by blastemal, stromal, and epithelial components (27). The tumor most commonly presents with a favorable histology and is characterized by its high chemo and radiosensitivity, which makes it a highly treatable entity. Interestingly, the tumor cells of Wilms tumor may differentiate into heterologous tissues, including skeletal muscle, smooth muscle, adipose tissue, cartilage, osteoid, and bone. In 1984, Variend et al. (2) reported the first incidence of a renal tumor that showed a diverse histological pattern in addition to foci of triphasic wilm's pattern. The term teratoid Wilms' tumor was therefore coined by Fernandes et al. (1) and Variend et al. (2). They defined teratoid wilm's as a tumor that contains heterologous elements comprising more than 50% of the tumor. They put forward an interesting hypothesis that the more heterologous elements seen are as a result of the totipotency of the blastemal component, which is further dependent on the stage of nephrogenesis at which the tumor induction occurs (1,2) . It was later on concluded that the origin of these diverse histological subtypes was from a totipotent primitive nephric blastema (1, 28). Teratoid Wilms' is a rare variant of Wilms' tumor with only 33 cases reported in the English literature (1-26). We present a review of previous 33 and our case in Table 1.

Discussion and Review of Literature

A compilation of 33 cases (including present case) shows the age ranged from 3 months to 7 years, in addition, one case of TWT in an adult patient (19 years) has been recorded. A review of the literature revealed only five reported cases of extra renal wilms tumor limiting not only to pelvicalyceal junction but including sacrococcygeal region, vagina and abdomen (Table 2).

19 cases of TWT were less than the age of 2 years of age, 13 cases ranged between 3-7 years, and one case was of an adult (19years) TWT. The present case was a 6-year-old female. Age has been seen as a prognostic factor according to the Children's Oncology Group (COG), United Kingdom (UK), and International Society of Pediatric Oncology (SIOP) (33). The explanation for the higher risk of with increasing age was the higher frequency of anaplasia at higher age. Other suggested reasons

were delay in diagnosis, advanced tumor stage, and different biological behaviors (33). However, no anaplastic morphology was seen in the reported 34 cases of TWT and correlation of age with prognosis was not very significant.

Among these 33 cases, males seemed to be affected more (24/34) than females. Most of the cases were limited to one kidney. Bi-laterality was seen in 30% cases (10/33). The present case was in a female and the mass was located in the right kidney.

18 of these reported cases received pre-operative neo-adjuvant chemotherapy. Myers et al. (13) have stated in their previous findings that resistance to chemotherapy and radiotherapy is thought due to the presence of well-differentiated histologic appearance (13). Ghamdi et al. (26) further stated that resistance to chemotherapy is attributed to the presence of a high proportion of relatively mature heterologous tissues within the tumor. These findings are in concurrence with the review which showed that 83% patients (15/18) showed no response to pre-operative chemotherapy one patient showed a partial response and only two patients showed a cytoreductive response. These findings depict a resistance in response to chemotherapy in a TWT. Our case received 6 cycles of pre-operative chemotherapy but no response in the tumor size was seen. However, presently the patient is alive and well.

Most of these patients underwent a complete surgical removal with wide margins (26/33 cases). Upon the histological examination, the cases of Teratoid Wilms Tumor were divided into three morphologic patterns depending upon the predominant histologic type. Tumors containing a predominant mesenchymal component such as smooth muscle or rhabdomyomatous elements were categorized as mesenchymal predominant (27). Tumors in which heterologous epithelial components were predominant, most commonly abundant squamous epithelium are called epithelial or squamous predominant (27). The third type of a TWT was composed of heterogeneous epithelial and mesenchymal elements without major predominancy in any of these components. This type of TWT is known as a mixed pattern (27).The presenting case also showed a mixed pattern.

Diverse differentiation in histology was seen in these 33 cases. The epithelial elements included squamous epithelium with keratinization and columnar epithelium with mucin production, glandular elements of salivary gland, intestine and respiratory tract, and odontogenic epithelium. The mesenchymal heterologous elements consisted of skeletal muscle, smooth muscle, bone, cartilage, adipose tissue and differentiated neural tissue (27). The present case revealed a mixed pattern consisting of mature squamous epithelium, skeletal muscle, rhabdomyoblastic differentitation with adipose tissue.

Based on the histological assessment, the most important differential diagnosis for TWT is intra renal teratoma. Many cases of TWT have been regarded as an intra-renal teratoma and vice versa. However, a criterion was proposed by Yaqoob et al. (35) which was later on accepted and defined by beckwith (27). They suggested that for a tumor to be termed a renal teratoma it should meet two criteria: (a) the primary tumor should be of intra-renal origin and should be well encapsulated. There should be no teratomas in any other site which could have metastasized to the kidney. (b) The tumor should have an unequivocal heterotopic organogenesis (27, 34).

Another important differential that comes in the picture is a Germ Cell Tumor arising in another location which has metastasized to the kidney. However, this tumor will lack an embryonic cellular element of a blastema that is usually present in TWT. A complete histological examination with extensive grossing should be attempted in order to correctly diagnose a case as a TWT.

The literature demonstrates that for diagnosis a preoperative imaging, with a CT scan or magnetic resonance imaging exam, along with a renal biopsy may be adequate in preoperative staging of Wilms' tumor. Although Teratoid Wilms' tumors present with a high stage, they appear to be generally of a low grade. The presence of differentiated stromal elements in this subtype of Wilms' tumor might explain the generally favorable outcome, although it does cause a resistence to chemotherapy (35).

Park et al. (36) have previously described the utility of CT and US findings from a cystic renal mass with multifocal solid components containing fatty elements in children. In other reports, CT of the abdomen showed renal masses that contained areas of density and calcification (37). In the present case, abdominal US and CT showed a large mass 14 cm in diameter with mixed density and echogenicity. Treatment guidelines for TWT are not completely defined, more so due to the rarity of the lesion. A

complete surgical resection appears to be the treatment of choice. Pre or post-operative chemotherapy and radiotherapy have been added in many protocols, but have not shown promising results. Ironically an increase in size post-chemotherapy has been noted in few cases. It could be due to the differentiated tissue. In the 34 cases studied, data on follow up is available for 30 cases. Maximum of these cases have been shown to be free of recurrence or metastasis. This is because the neoplastic tissues continue to differentiate; thus giving a false impression of an anaplastic biology (27). Genetics of Wilms Tumor remains multifold. WT1, WT2, CTNNB1, WTX, TP53 and few syndromic conditions such as WAGR, DDS, and BWS have also been implicated in various stages of tumorigenesis of WT (38-40). However, data on genetic abnormalities in TWT is sparse, which needs more research. The mutational analysis in a TWT, its driving mutations can help us explore the pathogenesis of this entity which is rarely seen and may also help in targeted treatment modalities.

Table 1. Reported cases of Teratoid Wilms Tumor (TWT) in literature

No.	Author/ Year	No. of cases	Age /Sex	Laterality	Pre-operative chemo	Complete tumor resection	Histology of tumor	Radio therapy	Survival
1	Variend et al. (2) 1984	Case 1	3y/F	Bilateral	Yes, Effective	yes	Mixed histology	No	Unknown
		Case 2	2y/ M	Bilateral	Yes, Not effective	Yes	Not reported.	Yes	Died, sepsis and renal failure
		Case 3	2y/ M	Bilateral	Not given	Yes	Not reported.	No	Alive and Well (7yrs follow up)
		Case 4	2y/ M	Bilateral	Yes, Not effective	No	Not reported	Yes	Post-op course complicated by chronic renal failure
3	Vujanic et al. (3) 1991	Case 5	1y/ M	Bilateral	Yes, Not Effective	Yes	Fibro adipose tissue, rhabdomyoblasts, smooth muscle, cartilage, neuroepithelium, squamous, columnar and mucinous epithelium.	No	Alive and Well (2yrs followup)
		Case 6	2y/ M	Left kidney	Not given	Yes	Epithelial cells, spindle cells, mature adipose tissue	No	Alive and Well (4yrs followup)
		Case 7	9mo /M	Right Kidney	Not given	Yes	Squamous, mucinous columnar epithelium, mature muscle and adipose tissue.	No	Alive and Well (4yrs followup)
5	Kotilogelu et al. (5) 1994	Case 8	3y/F	Right Kidney	Yes, Not Effective	Yes	Mature adipose tissue, glandular and mucinous epithelium.	No	Alive and Well (2yrs follow up)
6	William et al. (6) 1994	Case 9	3y/F	Bilateral	Yes, Not Effective	No	Skeletal muscle, adipose tissue, mucus glands.	yes	Died from extensive pulmonary metastasis
7	Ashworth et al. (7) 1996	Case 10	3y/F	Left Kidney	Yes, Not Effective	No	Mucin-secreting epithelium, myxoid stroma, skeletal muscle, cartilage and adipose tissue.	yes	Relapsed at 2 months; unknown outcome
8	Paterson et al. (8) 1998	Case 11	7y/ M	Right Kidney	Not given	Yes	Mature adipose tissue, skeletal muscle, connective tissue.	No	Unknown
9	Karaca et al. (9) 2000	Case 12	2y/ M	Bilateral	Yes, Not Effective	Yes	Squamous epithelial component (~70% tumor).	No	Died; pulmonary relapse at 6 months

10	Bakshi et al. (10) 2000	Case 13	2y/ M	Right Kidney	Not given	No	Predominantly heterologous tissues (adipose, glial, muscle, cartilage, or bone.	Yes	Alive and Well (3yrs follow up)
11	Cecchetto et al. (11) 2003	Case 14	4y/F	Left Kidey	Unknown	Yes	Cylindrical ciliated, cystic squamous epithelium with hair follicles, adipose tissue muscle, rhabdomyoblasts.	Unkno wn	Alive and Well (32 months follow up)
12	Inoue M et al. (2) 2003	Case 15	4y/F	Right Kidney	Yes, Not Effective	Yes	Stratified squamous, columnar epithelium, pigmented, mature adipose, and cartilage and bone tissue.	Yes	Alive and Well (3yrs follow up)
13	Myers Jb et al. (13) 2007	Case 16	4mo /M	Right Kidney	Not given	Yes	Stratified squamous, columnar epithelium, pigmented, mature adipose, and cartilage and bone tissue.	No	Alive and Well (4yrs follow up)
14	Koksal y et al. (14) 2007	Case 17	2.5y /M	Right Kidney	Yes, effective	yes	Mature adipose tissue, skeletal muscle, bone, cartilage and neurons.	Unkno wn	Alive and Well (1yr 4 months follow up)
15	Parikh b et al. (15) 2007	Case 18	1y/ M	Right Kidney	unknown	yes	Heterologous/ blastemal elements.	No	Alive and Well (1yr 4 months follow up)
16	Seo J et al. (16) 2008	Case 19	5y/ M	Right Kidney	Not given	yes	Heterologous elements: skeletal muscle, cartilage, adipose Tissue, neural tissue; squamous epithelium.	No	2 weeks after surgery that showed no evidence of metastatic lesions.
17	Kajbafzade h A et al. (17) 2009	Case 20	4y/ M	Left Kidney	Not given	Yes	Stromal elements, cartilage, calci cation, smooth muscle bers. Few squamoid areas.	No	Alive and Well (9.5yrs follow up)
18	Gupta R et al. (18) 2009	Case 21	4y/ M	Right Kidney	unknown	yes	Cystic wall with colon-type muscular wall	Unkno wn	Alive and Well (5 months follow up)
		Case 22	2y/ M	Left Kidney	Yes, Not Effective	Yes	Skeletal muscles and mature fat (~85% of the tumor)	No	Alive and Well (20 months follow up)
		Case 23	5y/ M	Bilateral	Yes, Effective	Yes	Rhabdomyoblastic, mature adipose tissue, mucin producing columnar epithelium	No	Relapse followed by remission, no evidence of disease
		Case 24	1mo /F	Bilateral	Yes, Not Effective	Yes	Skeletal muscle, mature adipose tissue and osteoid. Glandular, squamous epithelium with focal piloscebaceous unit	Unkno wn	Alive and Well (9 months follow up)
20	Mukhopad-hyay b et al. (20) 2011	Case 25	4y/F	Right Kidney	Yes, Not Effective	Yes	Mature mucous epithelium and rhabdomyoblasts.	No	The patient had a smooth recovery
21	Treetipsatit et al. (21) 2011	Case 26	9m/ M	bilateral	Yes, Not Effective	No, inoperabl e	Skeletal muscle, mature adipose tissue, bone, small islands of odontogenic epithelium	Unkno wn	Unknown
22	yadav yk et al. (22) 2012	Case 27	2y/ M	Right Kidney	Yes, Not Effective	Yes	Squamous with keratin pearls (~75%); adipose and glial tissue	Unkno wn	Unknown

23	bardesi JH et al. (23) 2012	Case 28	4y/ M	Left kidney	Yes, limited response	Yes	Cysts lined by attened, strati ed squamous epithelium, keratin akes. Focal spindle cells /smooth-muscle di erentiation	Yes	Alive and Well (21months follow up)
24	Sinha A et al. (24) 2013	Case 29	2y/ M	Right Kidney	Not given	Yes	Squamous epithelium; abundant keratin pearls (~75%)	No	Alive and Well (1yr follow up)
25	Ramani M et al. (25) 2013	Case 30	3mo /M	Right Kidney	Not given	Yes	Skeletal muscle; stratied squamous epithelium with keratinization	Yes	Alive and Well (1yr follow up)
		Case 31	Cas e one: 2y/ M	Right Kidney	Unknown	Yes	Rhabdomyomatous differentiation ~90%. Multiple foci of squamous differentiation and mature adipose tissue.	Unkno wn	Alive and Well (7 months follow up)
		Case 32	1.8y /M	Right Kidney	Unknown	Yes	Rhabdomyomatous differentiation ~90%. Focal smooth muscle differentiation	Unkno wn	Alive and Well (2 months follow up)
		Case 33	1mo /F	Right Kidney	Unknown	Yes	Mature Squamous epithelium, skeletal muscle, rhabdomyoblastic differentiation	Unkno wn	Alive and Well (12 months follow up)
27	Kiran A et al	Prese nt case 34	6y/F	Right Kidney	Yes, Not Effective	Yes	Mature squamous spithelium, skeletal muscle, rhabdomyoblastic differentitation with adipose tissue	No	Alive and Well

Table 2. Extra Renal Teratoid Wilm's Tumor

No	Author/ Year	Age/ Sex	Location	Histology	Follow up
1	Pawel et al. (29) 1998	7y/M	Ureteropelvic mass	Extensive squamous and columnar cell elements with areas of classic WT	Alive and Well (18 months follow up)
2	Song (30) 2010	13y/F	Vagina	Spindle cells with rhabdomyomatous differentiation in a myxoid background. Variably sized tubular structures lined by pseudostratified columnar or cuboidal cells	Alive and Well (97 months follow up)
3	Song (30) 2010	1day/F	Sacrococcygeal mass	Skeletal muscle, bone cartilage, squamous epithelium, ciliated mucinous; blastemal/ nodular blastemal.	No follow up done
4	Chowhan et al. (31) 2011	1.3y /M	Retroperitoneal mass	Predominantly glandular epithelium with skeletal adipose tissue and glial tissue	Alive and Well (6 months follow up)
5	Baskaran D et al. (32) 2013	3/M	Abdominal mass	Undifferentiated blastemal, adipose tissue, skeletal Muscle, cartilage, myxoid broblasts	Alive and Well (12 months follow up)

Conclusion

A child presenting with a renal mass suspected to be nephroblastoma, and radiologic findings, such as multiple calcifications and/or reduced attenuation are suggested a diagnosis of teratoid Wilms' tumor should be considered. On Histologic examination, supporting heterologous tissue must be identified within the tumor. Teratoid Wilms' tumor presents usually with a high stage, but most are of a low grade and respond very well to surgical therapy. The diagnosis, preoperatively, of this histologic variant is very important as it treatment strategies should

focus on early surgical exploration, along with complete resection of metastatic lesions, as the response to neoadjuvant chemotherapy appears to be limited. Moreover data should be collected and research should be done on cytogenetic abnormality and driver mutations to decipher a targeted treatment.

Conflict of Interest

The author declares no conflicts of interest.

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