Teratoid Wilms Tumor and Classical Wilms Tumor: A Retrospective Ten-year Single-center Study

wei wu
Shanghai Jiaotong University Children's Hospital: Children's Hospital of Shanghai

yibo wu
Shanghai Jiaotong University Children's Hospital: Children's Hospital of Shanghai

weijue xu
Shanghai Jiaotong University Children's Hospital: Children's Hospital of Shanghai

jiangbin liu
Shanghai Jiaotong University Children's Hospital: Children's Hospital of Shanghai

zhibao lv (lvzhibao@yeah.net)
Shanghai Jiaotong University Children's Hospital: Children's Hospital of Shanghai

Research

Keywords: Wilms tumor, Teratoid, Nephroblastoma, Prognosis

Posted Date: October 4th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-942102/v1

License: © This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Background

Wilms tumor (WT) is the most common renal tumor in the pediatric population. Nevertheless, teratoid Wilms tumor (TWT) is a rare category of WT characterized by different tissue types, and fewer than 40 cases have been reported in the literature to date. Methods A total of 67 WT patients admitted in our hospital from 2010 to 2020, including 5 patients with TWT, were enrolled in this study. The clinical features, preoperative and postoperative chemotherapeutic regimens, intraoperative findings, histopathological information, as well as prognoses of the WT patients were evaluated.

Results

TWT cases were matched to classical WT cases at 1:3 for the comparison of various variables. 7.46% (5/67) of WT patients were diagnosed with TWT. The tumor volume was dramatically larger for patients with TWT than for those with classical WT (203.30 ± 109.89 cm$^3$ vs. 104.30 ± 66.97 cm$^3$). However, the tumor weight of the two groups was similar (471.00 ± 80.65 vs. 432.67 ± 109.25).

Conclusions

Our data with the first reported Chinese children with TWT, preliminarily demonstrated that chemotherapy combined with surgery might be the appropriate treatment option for patients with WT, and prognoses of these patients differed sharply due to various stages. The density of TWT might be lower than that of classical WT. Future studies with more basic research to understand the biologic nature and theranostic markers of teratoid WT, may help us optimize the patient-tailored therapy of this rare type of WT.

Introduction

Wilms tumor is the most common renal tumor of childhood [1]. Wilms’ tumor accounts for 6% of all pediatric cancers and more than 95% of all kidney tumors in children [2]. Tumor stage and histologic subtype have long been realized as important prognostic factors in Wilms’ tumor [3]. However, the clinical presentations of rare renal tumors are similar to that of Wilms’ tumor. Thus, diagnosis and treatment is not the same when we faced different subtype Wilm’s tumor [4–5].

Teratoid Wilms tumor (TWT) is a type of nephroblastoma with significant heterologous components first reported by Variend et al. in 1984. [6] TWT is classically triphasic tumor, with the combination of blastemal, stromal, and epithelial cell types observed. Other elements such as squamous, mucusin epithelium, smooth muscle, adipose tissue cartilage, osteoid, and neurogenic tissue are also occasionally found. It was proposed by Fernandes et al [7] in 1988 that the presence of more than 50% heterogeneous component is an essential criterion for the diagnosis of teratoid WT. According to Beckwith criteria, a renal teratoma should be entirely within the renal capsule, and there should be clear evidence of renal component and other tissues. The pathogenesis of this rare condition is debatable and most probably the heterologous tissue components arise from primitive metanephric blastoma [8].

Up to date, only 34 cases of teratoid Wilms tumor have been reported in English literature, and there are no related cases reported in China. In this study, in order to deepen our understanding of TWT and unveil the difference between this infrequent condition with classical types of WT, a total of 67 WT patients admitted in our hospital from 2010 to 2020, including 5 patients with TWT, were enrolled in this study. The clinical features, preoperative and postoperative chemotherapeutic regimens, intraoperative findings, histopathological information, as well as prognoses of the WT patients were evaluated. Our data with the first reported Chinese children with TWT, preliminarily demonstrated that chemotherapy combined with surgery might be the appropriate treatment option for patients with WT, and prognoses of these patients differed sharply due to various stages. The density of TWT might be lower than that of classical WT. Future studies with more basic research to understand the biologic nature and theranostic markers of teratoid WT, may help us optimize the patient-tailored therapy of this rare type of WT.

Materials And Methods
Patient enrollment

Between January 2010 and December 2020, a total of 67 patients with WT visited the general department of our hospital and were included in this study. The clinical features, preoperative and postoperative chemotherapeutic regimens, intraoperative findings, histopathological information, as well as prognoses of the WT patients were retrospectively identified and evaluated. The patients were followed up clinically every 3 months and ultrasonography abdomen in every 6 months for first 2 years.

Assessment of TWT and classical WT

As for diagnosis of TWT, histopathologic examination shows a mixture of mature squamous and mucus-producing columnar epithelium. Presence of more than 50% heterogeneous component is an essential criterion for diagnosis of TWT. A prominent component of mature adipose tissue including the blastemal, stromal, and epithelial cell types, and other elements such as squamous, mucinous epithelium, osteoid, adipose tissue cartilage, smooth muscle, and neurogenic tissue are occasionally found. Final diagnosis would be established after an MDT discussion.

The other types of WT were treated as classical WT in this study, and experienced pathologists are responsible for the definite diagnosis of classical WT. When comparing the difference of variables between patients with TWT and those with classical WT, a 1:3 matching was performed between these patients to reduce potential bias.

Statistical Analysis

R software (version 3.6.3) was used for data analyses in this study. The results were showed using mean with SD for continuous variables or N with percentage for categorical variables. Kolmogorov–Smirnov analysis was performed for normality testing. The two groups were compared with Student’s \( t \) test for continuous variables or Fisher exact test for categorical variables. A two-sided confidence level \( P \) value < 0.05 was considered statistically significant.

Results

Demographics, clinical presentations and prognoses of the patients

In this study, up to 7.46% (5/67) of WT patients were diagnosed with TWT. The difference of the variables between TWT and classical WT patients did not reach statistical difference. Despite this, the tumor volume was dramatically larger for patients with TWT than for those with classical WT (203.30 ± 109.89 cm\(^3\) vs. 104.30 ± 66.97 cm\(^3\)), while the tumor weight of the two groups was similar (471.00 ± 80.65 vs. 432.67 ± 109.25). The comparison of demographics, clinical characteristics and prognoses between the two groups is listed in Table 1.
Table 1
The comparison of demographics, clinical characteristics and prognoses between the two groups.

|                      | TWT       | Classical WT | P value* |
|----------------------|-----------|--------------|----------|
| Number of patients   | 5         | 15           | -        |
| Age                  | 27.20 ± 13.97140 | 27.87 ± 16.91  | 0.932    |
| Sex                  |            |              |          |
| Male                 | 1          | 4            | 0.999    |
| Female               | 4          | 11           |          |
| Side                 |            |              | 0.999    |
| Left                 | 2          | 6            |          |
| Right                | 3          | 9            |          |
| Stage                |            |              | 0.106    |
| I                    | 1          | 0            |          |
| II                   | 2          | 7            |          |
| III                  | 0          | 6            |          |
| IV                   | 2          | 2            |          |
| Volume (cm³)         | 203.30 ± 109.89 | 104.30 ± 66.97 | 0.115    |
| LOH                  |            |              | 0.53     |
| Yes                  | 0          | 4            |          |
| No                   | 5          | 11           |          |
| Weight (g)           | 471.00 ± 80.65 | 432.67 ± 109.25 | 0.423    |
| WT1                  |            |              | 0.617    |
| Positive             | 3          | 6            |          |
| Negative             | 2          | 9            |          |
| Chemotherapy         |            |              | 0.140    |
| Yes                  | 3          | 14           |          |
| No                   | 2          | 1            |          |
| Survival             |            |              | 0.999    |
| Yes                  | 5          | 15           |          |
| No                   | 0          | 0            |          |
| Relapse              |            |              | 0.250    |
| Yes                  | 1          | 0            |          |
| No                   | 4          | 15           |          |

Note. *There were two kinds of P values, one for the Student’s t test for continuous variables and another for the Fisher exact test for categorical variables.
### Table 2
Specific information of patients with Teratoid Wilms tumor in our hospital

| age | sex | Side | stage | surgery                        | size  | LOH | weigh (g) | Histology | WT1 | chemo | Follow up                  |
|-----|-----|------|-------|--------------------------------|-------|-----|----------|-----------|-----|-------|---------------------------|
| 4 Months | M  | right | I     | Right radical nephrectomy     | 5X3X3 | no  | 350      | FH        | N   | No    | A&W after 3 years          |
| 3 years | F  | left  | II    | Left radical nephrectomy      | 8X7X7 | no  | 540      | FH        | N   | Yes   | A&W after 9 years          |
| 2 years | F  | right | IV (pulmonary, bone marrow) | Right radical nephrectomy     | 12X10X6 | no | 460      | FH        | P   | Yes   | Pelvic relapse at 2 years |
| 3 years | F  | right | IV (lung) | Right radical nephrectomy     | 12X7X8 | no  | 550      | FH        | P   | No    | A&W after 3 years          |
| 3 years | F  | left  | II    | Left radical nephrectomy      | 8X9X9 | no  | 455      | FH        | P   | Yes   | A&W after 6 months         |

A&W: Alive and well. FH: Favorable Histology. N: Negative. P: Positive
| SN. | Author/Year       | Age | Sex | **Histology**                                                                 | Follow up                      |
|-----|------------------|-----|-----|--------------------------------------------------------------------------------|--------------------------------|
| 1   | Variend et al    | 3   | F   | Various epithelial and mesenchymal elements.                                  | Unknown                        |
| 2   | Fernandes et al  | 2   | M   | Not reported.                                                                  | Died, sepsis and renal failure |
| 3   | Fernandes et al  | 2   | M   | Not reported.                                                                  | NED after 7 years              |
| 4   | Fernandes et al  | 2   | M   | Not reported.                                                                  | chronic renal failure          |
| 5   | Vujanic 1991     | 1.1 | F   | Fibro adipose tissue, rhabdomyoblasts, smooth muscle, cartilage, neuroepithelium, squamous, columnar and mucinous epithelium. | NED after 2 years              |
| 6   | Magee et al      | 2.5 | M   | Epithelial cells, spindle cells, mature adipose tissue.                       | NED after 4 years              |
| 7   | Magee et al      | 0.9 | M   | Squamous, mucinous columnar epithelium, mature muscle and adipose tissue.     | NED after 1 year               |
| 8   | Kotiloglou et al | 3   | F   | Mature adipose tissue, glandular and mucinous epithelium                      | NED after 23 months            |
| 9   | Williams, et al  | 3   | F   | Skeletal muscle, adipose tissue, mucus glands.                                | Died from extensive pulmonary metastasis |
| 10  | Ashworth, et al  | 3   | F   | Mucin secreting epithelium, fibromyxoid stroma, skeletal muscle, cartilage and adipose tissue. | Relapsed at 2 months; unknown outcome |
| 11  | Paterson et al   | 2   | M   | Mature adipose tissue, skeletal muscle, connective tissue.                   | Unknown                        |
| 12  | Karaca, et al    | 2.5 | M   | Squamous epithelial component (70% tumor)                                    | Died; pulmonary relapse at 6 months |
| 13  | Bakshi et al     | 1.5 | M   | Predominantly heterologous tissues (adipose, glial, muscle, cartilage, or bone) | NED after 3 years              |
| 14  | Cacchetto et al  | 4   | F   | Cylindrical ciliated, cystic squamous epithelium with hair follicles, adipose tissue muscle fibers, rhabdomyoblasts. | NED after 32 months            |
| 15  | Inoue M 2006     | 0.4 | M   | Stratified squamous, columnar epithelium, pigmented, mature adipose, and cartilage and bone tissue. | NED after 3 years              |
| 16  | Myers JB 2007    | 4.5 | F   | Keratinized squamous and nodules resembling epidermoid cysts (> 50% of tumor volume) | NED after 4 years              |
| 17  | Koksal Y 2007    | 2.5 | M   | Mature adipose tissue, skeletal muscle, bone, cartilage and neurons.         | NED 16 months                  |
| 18  | Parikh B et al   | 1   | M   | Heterologous/ blastemal elements.                                             | Not reported                   |
| 19  | Seo J et al      | 50  | M   | Heterologous elements: skeletal muscle, cartilage, adipose Tissue, neural tissue; squamous epithelium. | Not reported                   |
| 20  | Kajbafzadeh A    | 4   | M   | Stromal elements, cartilage, calcification, smooth muscle fibers. Few squamoid areas. | NED 9.5 years                  |

NED: No evidence of disease.
| SN. | Author/Year                | Age | Sex | Histology                                                                 | Follow up                      |
|-----|----------------------------|-----|-----|---------------------------------------------------------------------------|--------------------------------|
| 21  | Gupta R 2009               | 4   | M   | Cystic wall with colon type muscular wall                                 | NED 5 months                   |
| 22  | Sultan I 2010              | 2   | M   | Skeletal muscles and mature fat (85% of the tumor)                        | NED 20 months                  |
| 23  | Sultan I 2010              | 5   | F   | Rhabdomyoblastic, mature adipose tissue, mucin producing columnar epithelium | Relapse followed by remission; no evidence of disease |
| 24  | Sultan I 2010              | 1.1 | F   | Skeletal muscles, mature adipose tissue and osteoid. Glandular, squamous epithelial with focal pilosebaceous | NED 9 months                   |
| 25  | Mukhopadhyay 2011          | 4   | F   | Mature mucous epithelium and rhabdomyoblasts.                           | Unknown                        |
| 26  | Treetipastit 2011          | 0.9 | M   | Skeletal muscle, mature adipose tissue, bone, small islands of odontogenic epithelium | Unknown                        |
| 27  | Yadav 2012                 | 2   | M   | Squamous with keratin pearls (~75%); adipose and glial tissue            | Unknown                        |
| 28  | Bardesi 2012               | 4   | M   | Cysts lined by flattened, stratified squamous epithelium, keratin flakes. Focal spindle cells / smooth muscle differentiation | NED 21 months                  |
| 29  | Sinha A 2013               | 2   | M   | Squamous epithelium; abundant keratin pearls (~75%)                      | NED 21 months                  |
| 30  | Ramani M 2013              | 0.3 | M   | Skeletal muscle; stratified squamous epithelium with keratinization      | Unknown                        |
| 31  | Mohammed Akhta 2016        | 2   | M   | multiple foci of squamous epithelium and mature adipose tissue           | NED                            |
| 32  | Mohammed Akhta 2016        | 1.8 | M   | foci with a triphasic pattern consisting of blastemal, epithelial and mesenchymal components | NED                            |
| 33  | Mohammed Akhta 2016        | 11  | F   | smooth muscle elements and extensive mature epithelial glandular elements with squamous and goblet cell differentiation | NED                            |
| 34  | Santosh G. Rathod 2019     | 4   | F   | classic triphasic combination of blastemal, stromal, and epithelial cell types | NED 1 year                     |

NED: No evidence of disease.

**Detailed information of patients with teratoid WT**

**Case 1**

A 4-month-old male presented with a right sided abdominal mass for 1 month and came to the department of surgery in our hospital. Preoperative routine investigations, including serum urea, creatinine, and the blood urea nitrogen were within normal range. Besides, serum alpha feto-protein levels were also within normal limits. Later, the patient underwent nephrectomy. Histologically, a stage I tumor (favorable histology) weighing less than 350g (specimen weighed 100 g). Immunohistochemical results showed that tumor cells were negative for WT suppressor gene (WT1). Concerning the effect from postoperative therapy, this baby was discharged from hospital without receiving neither preoperative nor postoperative chemotherapy. He currently remains alive and well, without evidence of disease recurrence, 9 years from her initial presentation.

**Case 2**

A 26-month-old male presented with abdominal distension for two weeks due to a large abdominal mass. Physical examination revealed a hard mass without tenderness at the right flank of the abdomen. Chest and brain CT, one marrow puncture found nothing. Intraoperatively, we observed that most of the right kidney was replaced by the tumor, which was enveloped by a smooth,
glistening capsule. The inferior vena cava and vascular invasion was not observed. The nephrectomy specimen weighed 540 g and measured 9×7×5 cm³. Histologically, specimen consisted of smooth muscle elements and extensive mature epithelial glandular elements with squamous and goblet cell differentiation. Scattered islands of the usual embryonal epithelial, stromal and blastemal elements were identified. The tumor cells were positive for WT1. She had received treatment with 3 drugs (Ifosfamide, Etoposide, and Vincristine) for 4 cycles of postoperative chemotherapy. The patient is alive and free of disease 9 years after surgery.

Case 3

A 20-month-old girl with a right renal tumor presented to our hospital with a history of anemia (hemoglobin 95g/L). The patient had been diagnosed with a needle biopsy in another hospital. At the meantime, she had pulmonary and bone marrow metastasis at diagnosis (stage IV). She had received treatment with 3 drugs (Ifosfamide, Etoposide, and Vincristine) for 4 cycles of preoperative chemotherapy. After 8 weeks, abdominal CT showed 50% reduction in the renal tumor. Four weeks later, the patient underwent nephrectomy, and tumors in intrarenal vessels were not observed. There was no lymph node metastasis. An oval cystic-solid mass measuring 9×10×9 cm³ with adherent parts of renal tissue from either side was seen. Histologically, the tumor consisted predominantly of heterologous tissues (lack of kerator, adipose, muscle, cartilage, or lace-like osteoid) and islands of classic WT three components (blastemal, primitive tubuli and stromal). Immunohistochemical study showed that tumor cells were positive for WT1. Postoperatively the patient began adjuvant treatment consisting of 3 drugs (Ifosfamide, Etoposide, and Vincristine) for 4 cycles of chemotherapy. Unfortunately, abdominal CT revealed pelvic implantation after 6 months. She currently remains alive.

Case 4

A 38-month-old girl presented with abdominal pain for one week, then abdominal ultrasound showed a 7×5×9 cm³, solid tumor in right renal with microcalcification. An abdominal CT scan revealed large heterogeneous soft tissue mass in the posterior aspect of the right kidney, measuring 7×6×8 cm³, and extending beyond the cortex but not crossing the midline. Fortunately, there was no evidence for abdominal node /lung/bone marrow metastasis. The patient underwent right nephrectomy. The specimen weighed 350 g. Histologic examination found areas of classic Wilms’ architecture admixed with keratinized squamous cells, in discrete nodules resembling epidermoid cysts, which occupied greater than 70% of the tumor volume. She had received 4 cycles of postoperative chemotherapy. She has been out of our hospital for 10 years. She is doing well with no evidence of relapse.

Case 5

A 3-year-old girl presented with a mass in the left side of the abdomen present since 2 months old, and had low fever for 2 weeks. Her blood pressure was normal. A left-sided abdominal mass measuring 8cm×9cm×9cm was palpable in the left lumbar region. It did not cross the midline. There were no associated anomalies. Urine examination showed microscopic hematuria and culture was sterile. Hemoglobin was 8.7 gm/dl. Renal, Chest radiograph, and liver function tests were normal limit. Ultrasonography of the abdomen showed a large heteroechoic mass measuring 10cm×10cm×9cm, arising from the lower pole of the left kidney. The right kidney was normal. There was no involvement of the blood vessels. Contrast-enhanced computed tomography (CT) of the abdomen showed heterogeneous mass in the mid and lower pole of the left kidney and measured 10×10×9 cm³. Good excretion of contrast with splaying of pelvicalyceal system was seen. There was no enlargement of local lymph nodes. Laparotomy was done through a supraumbilical transverse transperitoneal incision. Left radical nephrectomy was done. The contralateral kidney was examined and found to be normal. On 6 months follow-up, the patient was doing well.

Literature review

A literature search was conducted using PubMed/NCBI. The selected keywords were “teratoid Wilms tumor” and “teratoid nephroblastoma.” We were able to identify 34 previously reported cases [6–41] in addition to our 5 cases. The age and clinical features of patients with teratoid WT are similar to those of patients with classic WT. male and female with a median age of 2.9 years(3m-11y) at diagnosis. Initial signs and symptoms are an abdominal mass and abdominal pain. At presentation, 18 patients had stage I and stage II, 5 had stage III (regional lymph node involvement), 4 had stage IV (pulmonary metastasis), and 7 had stage V (bilateral disease). 5 patients had hypertension at presentation. 8 patients had congenital abnormalities including
inguinal hernia, club feet, Beckwith-Wiedemann syndrome, horseshoe kidney and bilateral cryptorchidism, ectopic ureteropelvic system. Almost all the teratoid WT demonstrated favorable histology as reported. (Table 4)

| Total No. | 34 |
|-----------|----|
| Age       | 2.9 years (3m-11y) |
| Gender    | Male 16 (47.0%) |
|           | Female 18 (52.9%) |
| Stage     | I and/or II 18 (52.9%) |
|           | III 5 (14.7%) |
|           | IV 4 (11.7%) |
|           | V 7 (20.7%) |
| Histology | Favorable 33 (97.1%) |
|           | Unfavorable 1 (2.9%) |
| Survival  | alive 31 (91.2%) |
|           | dead 3 (8.8)* |
| Congenital abnormalities | Hypertension; bilateral cryptorchidism; club feet; Beckwith-Wiedemann syndrome; horseshoe kidney; inguinal hernia; ectopic ureteropelvic system |

*3 died of sepsis and renal failure, and/or extensive pulmonary metastasis.

**Discussion**

WT is the most common primary tumor of the kidney in children. It is characterized by recognizable attempts to recapitulate different stages of nephrogenesis. The classic triphasic combination of blastemal, stromal, and epithelial cell types is found. Heterotopic mesodermal elements may be seen but they usually involve a minor part of the neoplasm. Unusual renal tumors like clear cell sarcoma kidney, rhabdoid tumor kidney, multilocular cystic nephroma, teratoid WT, and renal teratomas are found infrequently [35]. TWT as a renal tumor having a different of cell types and tissues in a neoplasm, where areas of classic nephroblastoma tissue existed. A teratoid WT was diagnosed as having a clear predominance of teratoid elements comprising >50% of the solid tumor. The published papers reported that TWT have contained a variety of elements including adipose tissue, skeletal muscle, cartilage, squamous epithelial cysts, neurological tissue, and mucinous epithelium [27, 28]. In the present study, the group differences of tumor volume did not reach significance, in substantial part due to the TWT group's small sample size and large standard deviations. On the other hand, the tumor volume was dramatically larger for patients with TWT than for those with classical WT, while the tumor weight of the two groups was similar. Therefore, it seems that the density of TWT might be lower than that of classical WT, which could be explained by the unique characteristic of adipose tissue and squamous epithelial cysts in the TWT.

WT may manifest genetic abnormalities in one of the two regions in the short arm of chromosome 11 namely 11p13 (WT1) and 11p15 (WT2). Cytogenetic studies in nine reported cases of TWT have revealed 11p deletion or monosomy 11 [35]. The WT1 gene is located on the short arm of chromosome 11 (11p13). It spans approximately 50 kb and includes 10 exons, encoding a 3 kb mRNA. The carboxyl-terminal portion (Exon 7-10) contains 4 zinc finger motifs, which form the DNA-binding domain. WT1 can bind, through its zinc fingers, to the promoter regions of a multitude of putative downstream target genes. All mutations in WT1 alter the structure of the DNA binding domain, which changes its ability to bind to DNA, resulting in loss of function [40]. Al
Ghamdi D et al described although germline mutations of WT1 gene have been detected in children with genetic predisposition to WT mutational analysis of their cases was limited to tumor tissue only. Similar to the reported incidence (~20%) of WT1 mutations in sporadic WT only one of their three cases showed WT1 mutation. Data on WT1 gene mutation in TWT is sparse and their study indicates that they are similar to classic cases of WT with mutation being present in only a small minority [36]. Interestingly, 3 of our patients had positive WT1 in immunohistochemistry tests, dose this means WT1 have potential research value to this higher proportion. We need more genetic level to make sure.

As far as we concerned, teratoid WT is a non-aggressive and this tumor comparison with classical WT, the teratoid variant was reported to be resistant to chemotherapy and radiotherapy due to the well-differentiated nature of the teratomatous element. Is that true? we may underestimate that malignant solid tumor. Treatment of teratoid WT has not yet been established because of its rarity and presence of varying tumor components. So far, 3 patients with teratoid WT, who died, have been reported. One of them died due to renal failure and sepsis with no evidence of disease, the other two died due to metastatic disease [7]. As to our patients, two of them have metastases and one of the tumors pelvic recurred postoperative, which may be related to needle biops. The tumor may show aggressive features including anaplasia and regional and distant spread, its accompanying anaplastic elements may increase the likelihood of metastases, leading to death. We appeal malignant tumor is malignant tumor, protocols designed for WT is still needed. Further research and association should be pay more attentions to establishing the treatment guideline.

Conclusion

Our WT patients with the first reported Chinese children with TWT, preliminarily demonstrated that the density of TWT might be lower than that of classical WT. We recommend treating this rare tumor with protocols designed for TWT and to conduct more basic research to understand its biologic nature. Future studies with more basic research to understand the biologic nature and theranostic markers of teratoid WT, may help us optimize the patient-tailored therapy of this rare type of WT. At the same time more additional studies are needed at the genetic level to diagnose whether there are specific and unique markers for the rare subtype of WT. Ultimately, though due to the high proportion of differentiated tissue elements, chemotherapy may not be useful in reducing tumor volume, in our opinion surgical treatment alone is unsatisfactory in treating this rare tumor.

Declarations

Ethics approval and consent to participate

All therapeutic methods were carried out in accordance with relevant guidelines and regulations. This study was approved by Ethical Committee of Shanghai Children's Hospital and the study methodology conformed to Helsinki Declaration standards as revised in 2000. The Ethical Committee of Shanghai Children's Hospital granted permission to access and use the medical records of participants of the study. All data remained confidential, the legal guardians of all participants signed the informed contents. Appropriate measures were applied to ensure the confidentiality of the data.

Consent for publication

Written parental consents for the publication have been obtained.

Competing interests

The authors have no financial and non-financial conflicts of interest.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.
Funding
No funding.

References

1. Hol Janna A, Jewell Rosalyn, Chowdhury Tanzina et al. Wilms tumour surveillance in at-risk children: Literature review and recommendations from the SIOP-Europe Host Genome Working Group and SIOP Renal Tumour Study Group. [J]. Eur J Cancer, 2021, 153: 51-63.

2. Cone EB, Dalton SS, Van Noord M, Tracy ET, Rice HE, Routh JC. Biomarkers for Wilms Tumor: A Systematic Review. J Urol. 2016 Nov;196(5):1530-1535.

3. Friedman AD. Wilms tumor. Pediatr Rev. 2013 Jul;34(7):328-30;

4. Dome JS, Perlman EJ, Graf N. Risk stratification for Wilms tumor: current approach and future directions. Am Soc Clin Oncol Educ Book. 2014:215-23.

5. Treger T, Chowdhury T, Pritchard-Jones K, Behjati S. The genetic changes of Wilms tumour. Nat Rev Nephrol. 2019 Apr;15(4):240-251.

6. Variend S, Spicer RD, Mackinnon AE. Teratoid WT. Cancer. 1984;53:1936-42.

7. Fernandes ET, Parham DM, Ribeiro RC, Douglass EC, Kumar AP, Wilimas J. Teratoid Wilms tumor: The St Jude experience. J Pediatr Surg. 1988;23:1131-4.

8. Beckwith JB. Wilms' tumor and other renal tumors of childhood: A selective review from the National Wilms' Tumor Study Pathology Center. Hum Pathol. 1983;14:481-92.

9. Vujanic GM. Renal tumours of childhood: An overview. Diagn Histopathol. 2009;15:5019.

10. Al-Hussain T, Ali A, Akhtar M. Wilms tumor: An update. Adv Anat Pathol. 2014, 21:166-73.

11. Vujanic GM. Teratoid WT: Report of a unilateral case. Pediatr Pathol. 1991;11:303-9.

12. Magee JF, Ansari S, McFadden DE, Dimmick J. Teratoid Wilms’ tumour: A report of two cases. Histopathology. 1992;20:427-31.

13. Kotiloğlu E, Kale G, Sevinir B, Hiçsönmez A, Akçören Z. Teratoid WT. A unilateral case. Tumori. 1994;80:61-3.

14. Williams MA, Schropp KP, Noe HN. Fat containing renal mass in childhood: A case report of teratoid Wilms tumor. J Uro. 1994;151:1662-3.

15. Ashworth MT, Pizer BL, Oakhill A, Spicer RD, Berry PJ. A teratoid WT with raised serum alpha-fetoprotein level. Pediatr Pathol Lab Med. 1996;16:853-9.

16. Paterson A, Sweeney LE. Teratoid Wilms’ tumour occurring synchronously with classical Wilms’ tumour in Beckwith Wiedemann syndrome. Pediatr Radiol. 2000;30:656-7.

17. Karaca I, Sencan A, Ortaç R, Bostanci-Sencan A, Mir E. Teratoid WT: A case report. Turk J Pediatr. 2000;42:242-5.

18. Bakshi N, Mansoor I, Venkataramu NK, Katariya S. An unusual renal malignancy of childhood: Unilateral teratoid WT. Pediatr Pathol Mol Med. 2003;22:435-41.

19. Inoue M, Uchida K, Kohei O, Nashida Y, Deguchi T, Komada Y, Kusonoki M. Teratoid WT: A case report with literature review. J Pediatr Surg. 2006;41:1759-63.
20. Cecchetto G, Alaggio R, Scarzello G, Dall’Igna P, Martino A, Bisogno G, Guglielmi M. Teratoid WT: Report of a unilateral case. J Pediatr Surg. 2003;38:259-61.

21. Myers JB, Dall’Era J, Odom LF, McGavran L, Lovell MA. Furness P 3RD. Teratoid WT, an important variant of nephroblastoma. J Pediatr Urol. 2007;3:282-6.

22. Koksal Y, Varan A, Akyuz C, Kale G, Buyukpamukcu N, Buyukpamukcu M. Teratoid WT in a child. Pediatr Int. 2007;49:414-7.

23. Gupta DK, Sharma S, Agarwal S, Carachi R. Saga of Wilms’ tumor: Lessons learnt from the past. J Indian Assoc Pediatr Surg. 2005;10:217-28.

24. Myers JB, Dall’Era J, Odom LF, McGavran L, Lovell MA, Furness P. Teratoid WT, an important variant of nephroblastoma. J Pediatr Urol. 2007;3:282–6

25. Seo J, Yeon-Lim Suh YL, Choi HY. Adult teratoid WT with prominent neuroepithelial differentiation. Pathol Int. 2009;59:44-8.

26. Kajbafzadeh A, Tourchi A, Elmi A, Sadeghi Z, Ramayar A, Mahjoub F. Teratoid WT with hypertension treated with partial nephrectomy: Case report with literature review. Eur J Pediatr Surg. 2010;20:270-2.

27. Parikh B, Trivedi P, Shukla K. A unilateral teratoid WT with raised serum alpha-fetoprotein level. Indian J Pathol Microbiol. 2007;50:317-9.

28. Sultan I, Ajlouni F, Al-Jumaily U, Al-Ashhab M, Hashem H, Ghandour K, Masarweh M, Al-Hussaini M. Distinct features of teratoid Wilms tumor. J Pediatr Surg. 2010;45:e13-9.

29. Mukhopadhyay B, Shukla RM, Mukhopadhyay M, Mandi S, Roy D, Bhattacharya MK. Teratoid Wilms'tumor -A rare renaltumor. Urol Ann. 2011; 3:155-7.

30. Treetipsatit J, Raveesunthornkiet M, Ruangtrakool R, Sanpaki K, Thormer PS. Teratoid Wilms’tumor: Case report of a rare variant that can mimic aggressive biology during chemotherapy. J Pediatr Surg. 2011;46:e1-6.

31. Bardesi JH, Al-Sayyad AJ. Teratoid Wilms tumor in a child: A case report. Uro Today International Journal. 2012;5:5-7

32. Yadav YK, Sharma U, Gupta K, Arora R. Squamous predominant Wilms'tumor. J Lab Physicians. 2012;4:50-2.

33. Ramani M, Geetha K, Ramesh Reddy K, Ramsha Tahoor A, Sandhya Rani C. A rare Wilms'tumor with teratoid differentiation in a 3 month old male child -a case report. J Evol Med Denta Sci. 2013;2:4161-5.

34. Pawel BR, Chadsrevian JP, Smergel EM, Weintraub WH. Teratoid wilms tumor arising as a botryoid growth within a supernumerary ureteropelvic structure. Arch Pathol Lab Med. 1998;122:925-8.

35. Mandal Kartik Chandra, Mukhopadhyay Madhumita, Barman Shibankar et al. Uncommon renal tumors in children: A single center experience.[J]. J Indian Assoc Pediatr Surg, 2016, 21: 61-5.

36. Ghamdi Doaa Al, Bakshi Nasir, Akhtar Mohammed, Teratoid Wilms Tumor: Report of Three Cases and Review of the Literature.[J]. Turk Patoloji Derg, 2019, 35: 61-68.

37. D’Hooghe Ellen, Mifsud William, Vujanić Gordan M, “Teratoid’ Wilms Tumor: The Extreme End of Heterologous Element Differentiation, Not a Separate Entity.[J]. Am J Surg Pathol, 2019, 43: 1583-1590.

38. Rathod Santosh G, Garje Mahesh U, Sakhivel Vinayagapandian et al. Teratoid WT of kidney with neural tissue predominant: Case report with review of literature.[J]. J Family Med Prim Care, 2019, 8: 3447-3449.

39. Green DM. The treatment of stages I-IV favorable histology WT. J Clin Oncol 2004;22:1366-72.

40. Al-Hussain Turki, Ali Afshan, Akhtar Mohammed, Wilms tumor: an update.[J]. Adv Anat Pathol, 2014, 21: 166-73.
A 20-month-old girl with a right renal tumor presented to our hospital with a history of anemia. 1. CT scan of abdomen revealing a large mass (arrowheads) almost completely replacing the right kidney; 2. Nephrectomy specimen revealing a large mass replacing the kidney; histologic examination; 3,4,5 showed heterologous epithelium with Squamous epithelium, fat, calcified beads, respectively (H&E, original magnification ×40); 6. WT-1 immunostain is positive in tubules within tumor.
Figure 2

A 38-month-old girl presented with abdominal pain for one week. CT scan of abdomen revealing a large mass almost completely replacing the right kidney. Lung metastasis with a large lesion in the right lung. Cut surface of the kidney revealing a large mass partly replacing the kidney. Photomicrograph showing prominent heterologous components which includes squamous epithelial cells. WT-1 immunostain is positive in tubules within tumor.

Figure 3

A 38-month-old girl presented with abdominal pain for one week. Contrast-enhanced computed tomography (CT) of the abdomen showed heterogeneous mass in the mid and lower pole of the right kidney and measured 8 cm × 9 cm × 9 cm, and the appearance of fat or hair in CT imaging.