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Extrarenal teratoma with nephroblastoma in the retroperitoneum

Case report and literature review

Yanan Li, MD[a], Chuanfen Lei, MD[b], Bo Xiang, MD, PhD[a], Fuyu Li, MD[a], Chuan Wang, MD[a], Qi Wang, MD[a], Siyuan Chen, MD, PhD[c], Yi Ji, MD, PhD[a,*]

Abstract

Rationale: Teratoma with nephroblastoma is a rare disease. The most common site at which teratoma with nephroblastoma occurs is the kidney. The mechanisms underlying the development of teratoma with nephroblastoma have not been fully elucidated.

Patient concerns: In the current report, we describe the clinical characteristics of a 3-year-old girl with a complaint of a painless abdominal mass in the upper right side of the body. Ultrasonography and computed tomography revealed a cystic-solid mass with a clear boundary.

Diagnosis: Surgical resection and a subsequent pathological examination confirmed that the mass contained teratoma tissues and renal blastemal components, which supports the diagnosis of teratoma with nephroblastoma.

Interventions: The patient underwent an exploratory laparotomy through a transverse abdominal incision. Complete resection of the mass was performed in this patient.

Outcomes: The patient's postoperative course was uneventful and she was discharged on the 8th postoperative day. The girl had no complaints during the 2 years follow-up period.

Lessons: Teratoma with nephroblastoma is a rare entity that typically presents in childhood. Due to its rarity, no standardized criteria have been established for the categorization and treatment of these lesions. However, a complete excision of this tumor allows the diagnosis to be confirmed and lowers the risk of recurrence.

Abbreviations: β-HCG = β-human chorionic gonadotropin, AFP = α-fetoprotein, CT = computed tomography, H&E = hematoxylin and eosin, TWN = teratoma with nephroblastoma.

Keywords: diagnosis, nephroblastoma, pathogenesis, retroperitoneal, teratoma

1. Introduction

Teratoma and nephroblastoma (also known as Wilms tumor) are 2 common solid tumors that typically occur during childhood. Teratomas usually appear in the gonads and along the median line of the body, such as in the sacrococcygeal region, mediastinum, and retroperitoneum.[1] Teratomas contain heterologous elements such as muscle, bone, and cartilage. Nephroblastoma, which usually occurs in children between 1 and 4 years of age, presents as an abdominal mass that originates in the kidney. Nephroblastoma is broadly considered an embryonic neoplasm that stems from the metanephric blastema. Classically, this tumor type exhibits a triphasic histological pattern with blastemal, stromal, and epithelial components.[2] Nephroblastoma occurring outside the kidney is extremely rare. Here, we describe a rare case of extrarenal teratoma with nephroblastoma (TWN) and a review of the literature.

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Ethical approval: The case reports were approved by the Ethics Committee of the West China Hospital of Sichuan University. Written informed consent was obtained for use of the images, according to the provisions of the Declaration of Helsinki.

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[a] Division of Oncology, Department of Pediatric Surgery, [b] Department of Pathology, [c] Pediatric Intensive Care Unit, West China Hospital of Sichuan University, Chengdu, China.

[*] Correspondence: Yi Ji, Division of Oncology, Department of Pediatric Surgery, West China Hospital of Sichuan University, #37 Guo-Xue-Xiang, Chengdu, 610041, China (e-mail: jijiyuanyuan@163.com).

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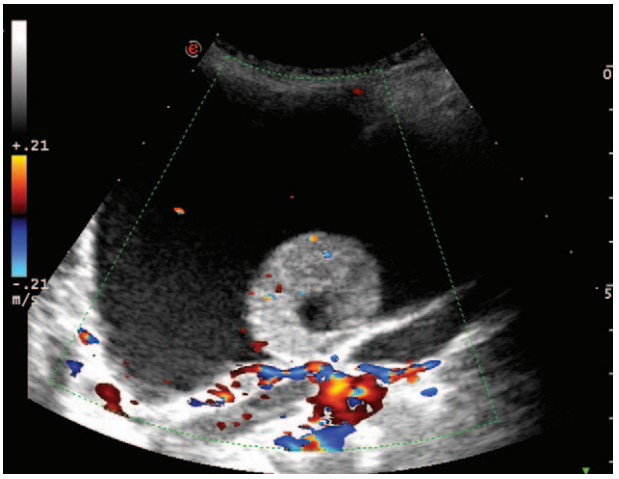

Figure 1. Ultrasound examination. An ultrasound showed a cystic-solid mass with a clear boundary in the right abdomen.

2. Case presentation

A 3-year-old girl was admitted to the West China Hospital of Sichuan University with a complaint of a painless abdominal mass in the right upper side of the body. Perinatal and family histories were noncontributory to the diagnosis. Upon physical examination, a well-defined, firm, round, non-tender mass was found in the upper right abdomen. Her serum β-human chorionic gonadotropin (β-HCG), α-fetoprotein (AFP), carcinoembryonic antigen (CEA), and neuron-specific enolase (NSE) levels were normal. Laboratory tests, including serum electrolyte levels, urinalysis, and complete blood counts, showed normal results. Transabdominal ultrasonography revealed a cystic-solid mass with a clear boundary in the right abdomen. The mass had multifocal solid components with variable echogenicity (Fig. 1). Contrast-enhanced computed tomography of the abdomen showed a cystic-solid mass in the upper right abdomen, with some calcification, that was $10 \times 12 \times 15$ cm (Fig. 2A and B). Hypodense areas of fat density were seen within the mass. Other symptoms such as lymph node enlargement, ascites, vascular invasion, or obstruction of the collecting system were not found.

Under general anesthesia, the patient underwent an exploratory laparotomy through a transverse abdominal incision. The operative finding was a large and well-defined retroperitoneal mass with a clear boundary and no invasion of the surrounding organs and vital vessels. The resected specimen was a well-encapsulated multinodular soft mass, which was $10 \times 13 \times 14$ cm with mostly solid areas and some focal cystic areas. The outer surface was covered by a thin fibrous capsule. On a cut section, the mass was composed of yellow adipose tissue, bone, cartilage, and abundant mucoid contents. The remainder consisted of several nodules of a solid, fleshy tumor that were yellow-gray in color and that occasionally exhibited a variegated appearance with hemorrhage and necrosis.

Microscopic examination of the lobulated adipose tissue portion of the mass revealed a mature teratoma composed of fibrovascular septa, adipose tissue, skeletal and smooth muscles, bone, cartilage, and cystic structures. The solid area revealed a diffuse proliferation of immature tumor cells, which resembled renal blastemal components; these were separated by mature fibrous, fatty, and glial tissues (Fig. 3A–C). Anaplasia was not present.

The solid area of this tumor was strongly positive for Wilms tumor antigen 1 (WT1), transducing-like enhancer of split 1 (TLE-1), and Antigen Ki-67 (Fig. 4A–C) but was diffusely negative for Sal-like protein 4 (SALL4), chromogranin A (CgA), Syn, EMA, S-100, glial fibrillary acidic protein (GFAP), desmin, Lens culinaris agglutinin (LCA), oligo-2. These findings are consistent with the diagnosis of TWN (stage I).

The patient was discharged home on the 8th day after surgery because of her high therapeutic compliance. The girl had no complaints during the 2 years follow-up period, and her serum β-HCG, AFP, CEA, and NSE values were all within the normal ranges.

2.1. Literature review

A literature search was conducted using PubMed/NCBI. The selected keywords were "teratoid Wilms tumor," "teratoma with nephroblastic tissue," or "teratoma with nephroblastoma." We were able to identify 53 previously reported cases in addition to our case.[1–46] The cases involved 31 boys and 23 girls, with a male-to-female ratio of 1.35:1. Almost all patients were young children, except for a 62-year-old woman and 6 adult men. The mean age at diagnosis was 80 months (range, 0–744 months).

The locations of these 54 tumors were the kidney (31), retroperitoneum (7), sacrococcyx (4), testis (3), mediastinum (2), abdomen (the specific location is unknown, 2), thoracic cavity (1), stomach (1), neck region (1), uterus (1), and vagina (1). At presentation, 12 patients had stage I disease, 6 had stage II disease, 5 had stage III disease, 2 had stage IV disease, and 5 had stage V disease; the stages of the other 24 cases were unknown.

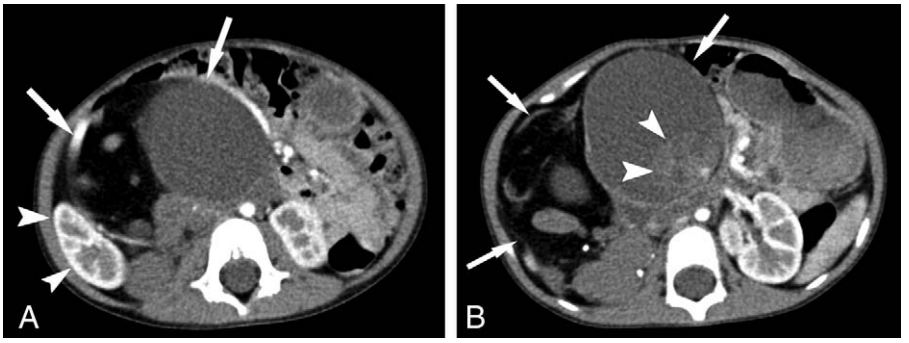

Figure 2. CT scan. (A), A CT scan demonstrated a mass (arrowhead) of fatty and solid densities in the upper right side of the abdomen, located anterior to the right kidney (arrow). (B), Focal calcification (arrow) can be seen within the mass (arrowhead). CT = computed tomography.

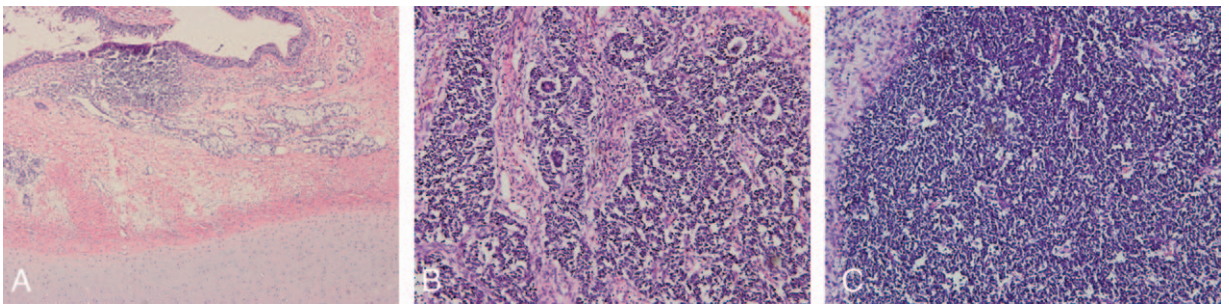

Figure 3. Histopathological examination. Histologic examination showed (A), skeletal muscles and epithelial components (H&E, original magnification ×100). (B), The solid areas demonstrated islands of blastemal elements, abortive glomeruli and primitive tubules (H&E, original magnification ×200). (C), Undifferentiated blastema components showed increased cellularity and scanty cytoplasm, with few mitoses (H&E, original magnification ×200).

Three patients presented with pulmonary metastasis at diagnosis, 2 had lymph node metastasis, and 1 had brain metastasis. Abdominal pain and distension were the most common presenting symptoms. In all cases, microscopic studies showed that the tumors were largely composed of heterogeneous tissues, including adipose tissue, skeletal and smooth muscles, fibrovascular septa, cartilage, immature glomeruloid elements, and tubular structures. The masses in the majority of cases were composed mainly of adipose tissue, and the next most common component was epithelial tissue.

The chemotherapy protocols that were utilized were not uniform. Chemotherapy was administered in 38 cases. However, only 1 patient (2.6%) demonstrated sensitivity to chemotherapy. In 19 cases, chemotherapy was administered preoperatively, and the sole responder was in this group. Thirty patients were administered postoperative chemotherapy, and 11 patients received both preoperative and postoperative chemotherapy. Six patients received both preoperative whole-body external-beam radiotherapy and chemotherapy, but none of those patients responded to treatment. Twelve patients were administered postoperative radiotherapy.

The mean length of the follow-up period for all cases was 23 months (range, 0–7 years). Moreover, 49 of the 54 cases (90.7%) were alive and healthy at the last follow-up time point, although 1 patient developed chronic renal insufficiency. Five deaths (9.3%) occurred as follows: 1 from primary tumor, 2 from tumor recurrence, 1 from postoperative sepsis, and 1 from pulmonary relapse at 6 months.

3. Discussion

TWN is an extremely rare condition: fewer than 53 cases have been described thus far in the literature worldwide. We have summarized the various sites at which TWN has been observed and details pertaining to the development of TWN outside the kidney (Table 1). The true incidence and prognosis of TWN are difficult to determine for several reasons. First, no standardized definitions of these lesions have been established, and the case reports on these rare lesions, which have detailed their occurrences, have not been consistent over the past 50 years.

3.1. Nomenclature

Variend et al[42] first used the term "teratoid Wilms tumor" in 1984 to describe a Wilms tumor with extensive heterologous elements. They further defined the teratoid Wilms tumor as one with a clear predominance of teratoid elements that comprise more than 50% of the tumor. Approximately, 31 teratoid Wilms tumors, manifested as heterogeneous solid masses, have been described in the literature. Interestingly, other groups have also reported occurrences of TWN or teratoma with nephroblastic tissue.[3,12] Until now, the association of teratoma and nephroblastoma has not been well understood. We categorized our lesion as a mature teratoma with nephroblastoma. We initially presumed that mature teratoma with nephroblastoma might be classified separately because the origin of this tumor might differ from that of a true TWN. However, after a review of the literature, we found that the masses in all 54 cases were composed of heterogeneous tissues, including adipose tissue, skeletal and smooth muscles, fibrovascular septa, cartilage, immature glomeruloid elements, and tubular structures. It is possible that these masses are different manifestations of the same disease. Unfortunately, no direct evidence supports this hypothesis. Therefore, further studies are needed to verify this hypothesis and define standardized criteria for the categorization of this tumor.

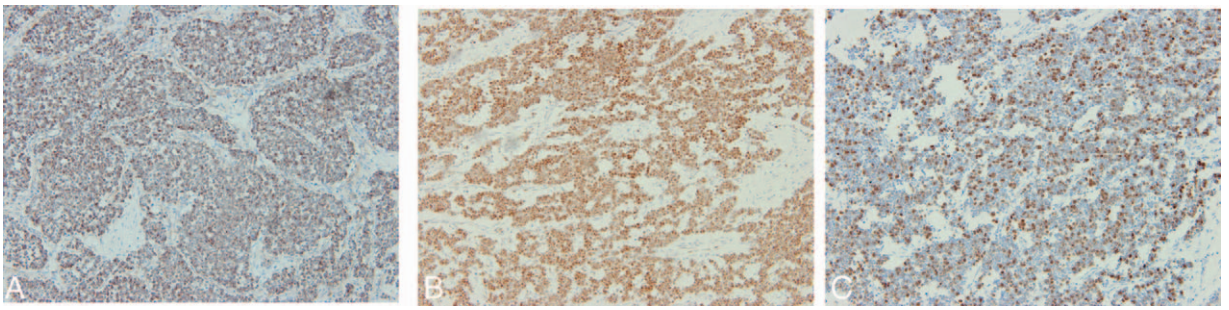

Figure 4. Immunohistochemical findings. The epithelial component displayed positive expression for WT1 (A, magnification ×400), TLE-1 (B, magnification ×400), and Antigen Ki-67 (C, magnification ×400). WT1 = Wilms tumor antigen 1, TLE-1 = transducing-like enhancer of split 1.

Table 1

Published cases of teratoma with nephroblastoma.

Authors and year	Age	Sex	Location	Stage	Preoperative chemotherapy	Preoperative radiotherapy	Response	Surgery	Postoperative chemotherapy	Postoperative radiotherapy	Metastasis	Follow-up
Moyson (1961)	3 y	F	Mediastinum	Unknown	+	–	–	+	+	–	–	Unknown
Malik (1967)	6 y	F	Retroperitoneum	Unknown	–	–		–	–	–	–	Unknown
Kamran (1974)	3 y	F	Sacrococcygeal region	Unknown	–	–		+	+	+	–	46 m
Samuel (1974)	3 y	F	Sacrococcygeal region	Unknown	–	–		+	+	+	–	12 m
Aidancarne (1975)	41 y	M	Retroperitoneum	2	–	–		+	–	+	–	Died after 4 m
Sadick (1984)	3 y	F	Left kidney	Unknown	+	–	+	+	–	–	–	Unknown
Fernandes (1988)	2 y	M	Bilateral kidney	5	+	+	–	–	–	–	–	Died
	2 y	M	Bilateral kidney	5	–	–		+	+	+	–	7 y
	2 y	M	Bilateral kidney	5	+	+	–	+	+	+	–	Unknown
Youn (1990)	10 m	F	Retroperitoneum	Unknown	–	–		+	+	–	–	4 m
Hye (1991)	4 y	F	Retroperitoneum	Unknown	–	–		+	+	–	–	Recurrence after three m
Vujanic (1991)	13 m	F	Right kidney	1	+	–	–	+	–	–	–	2 y
Magee (1991)	2.5 y	M	Left kidney	Unknown	–	–		+	+	–	–	4 y
	9 m	M	Right kidney	Unknown	–	–		+	+	–	–	1 y
Williams (1994)	3 y	F	Bilateral kidney	5	+	–	–	–	–	–	–	Unknown
Kotiloglu (1994)	3 y	F	Right kidney	1	+	–	–	+	–	–	–	23 m
Ashworth (1996)	3 y	F	Left kidney	3	+	+	–	+	+	+	–	Unknown
Henk (1997)	6 m	F	Left abdomen	3	+	–	–	+	+	–	–	11 m
Pawel (1998)	7 y	M	Right kidney	1	–	–		+	+	–	–	18 m
Govender (1999)	2 y	M	Left kidney	3	+	+	–	+	+	+	–	9 m
Paterson (2000)	2 y	M	Left kidney	5	+	–	–	+	–	–	–	Unknown
Karaca (2000)	2.5 y	M	Right kidney	3	–	–		+	–	–	–	Died
Nasir (2003)	1.5 y	F	Left kidney	1	–	–		+	+	+	–	3 y
Park (2003)	4 y	F	Left kidney	Unknown	–	–		+	–	–	–	Unknown
Giovanni (2003)	4 y	F	Right kidney	Unknown	+	+	–	+	+	+	–	32 m
Robert (2004)	22 y	M	Left testis	Unknown	–	–		+	+	–	+	21 m
Mikihiro (2006)	4 m	M	Right kidney	1	–	–	–	+	–	–	–	3 y
Andrea (2006)	18 y	M	Mediastinum	2	–	–		+	+	–	–	Recurrence
Bill (2007)	18 y	M	Right testis	3	–	–		+	–	–	–	4 m
Eremy (2007)	4.5 y	F	Right kidney	4	–	–		+	+	+	+	4 y
Yavuz (2007)	2.5 y	M	Right kidney	Unknown	+	–	–	+	+	–	–	16 m
Jinwon (2009)	50 y	M	Right kidney	1	–	–		+	–	–	–	2 w
Ruchika (2009)	4 y	M	Right kidney	Low	–	–		+	–	–	–	5 m
Olga (2009)	62 y	F	Uterus	Unknown	–	–		+	+	+	–	14 m
Motita (2010)	20 d	M	Stomach	2	–	–		+	–	–	–	6 m
Joonseon (2010)	13 d	F	Vagina	Unknown	–	–		+	+	–	–	7 y
	New born	M	Sacrococcygeal region	Unknown	–	–		+	+	–	–	2.5 y
Sultan (2010)	2 y	M	Left kidney	1	+	+	–	+	–	–	–	20 m
	5 y	F	Thorax	4	+	–	–	+	+	–	+	20 m
	11 m	F	Bilateral kidney	1	–	–	–	+	+	–	–	9 m
Serkan (2011)	19 y	M	Testis	2	+	–	–	–	–	–	–	Died after 18 m
Jitsupa (2011)	9 m	M	Bilateral kidney	Unknown	+	–	–	+	+	–	–	82 w
Chowhan (2011)	15 m	M	Retroperitoneum	2	–	–		+	+	–	–	6 m
Mukthopadhyayb (2011)	4 y	F	Right kidney	2	–	–		+	+	–	–	7 y
Kajbafzadeh (2011)	4 y	M	Left kidney	1	–	–		+	+	–	–	Unknown
Yogesh (2012)	2 y	M	Right kidney	Unknown	–	–		+	–	–	+	Unknown
Okur (2012)	10 m	M	Bilateral kidney	Unknown	+	–	–	+	+	+	–	Unknown
Anuradha (2012)	2 y	M	Right kidney	Unknown	–	–		+	–	–	–	1 y
Mitsuaki (2012)	2 m	F	Retroperitoneum	Unknown	–	–		+	–	–	–	3 m
Zeynep (2013)	New born	M	Neck	Unknown	–	–		+	–	–	–	50 d
Indian (2013)	3 y	M	Horseshoe kidney	Unknown	–	–		+	–	–	–	1 y
Yangyang (2014)	24 w	M	Sacrococcygeal region	1	–	–		+	–	–	–	8 w
Esra (2015)	8 y	M	Left kidney	1	+	–	–	+	+	–	–	Unknown

d = days, F = female, FM = male, Fm = months, Fw = weeks, Fy = years.

3.2. Pathogenesis

Currently, the pathogenesis of TWN is unknown, and the origin of TWN is still controversial. Some investigators believe that most of these tumors are pure tumors but that only a small fraction originates from teratomas or germ cell neoplasms.[1] An alternative explanation, which some authors favor, is that TWN arises from extensive metaplasia of metanephric blastema.[12,32,39] They believe that it is unlikely that TWN is

derived from a renal teratoma, given the rarity of renal teratomas and the absence of organogenesis in teratoid Wilms tumors. In addition, extrarenal TWN has been identified in various locations. The presence of nephroblastoma-like tissue in germ cell tumors outside the kidney has suggested that the combination of TWN might be a hybrid of 2 different neoplasms that originate from pluripotent cells.[40] Therefore, the concept of neometaplasia from a stem cell population, which is distinguished from a renal phenotype, would be a more attractive alternative. Early molecular and genetic events that regulate embryogenesis and organogenesis may modulate the pathogenesis of TWN. Further studies are needed to evaluate and verify these mechanisms to gain a greater understanding of the pathogenesis and the development of TWN.

3.3. Presentation

Remarkably, our data showed a male predominance among patients with TWN, especially in the predominance of men among adults (6:1). However, we found no explanation for the increased incidence of TWN in male patients. The most common site of TWN is the kidney (57.4%). Atypical locations include the retroperitoneum (13.0%), testis (5.6%), mediastinum (3.7%), abdomen (3.7%, the specific location is unknown), thoracic cavity (1.9%), stomach (1.9%), neck (1.9%), vagina (1.9%), and uterus (1.9%). In retroperitoneal TWN, the most common symptom is the presence of an abdominal mass, which occasionally presents with abdominal distension and/or abdominal pain.

3.4. Diagnosis

Both ultrasonography and contrast-enhanced computed tomography may be useful in identifying the features of TWN.[26] However, despite these imaging tests, a confident preoperative diagnosis of TWN is impossible. This may be due to the variable presentation of TWN and the lack of awareness of TWN. In the literature, the accurate diagnoses of TWN in identified cases have all been based on biopsy. Therefore, biopsy is the only option for establishing a definitive diagnosis and excluding the possibility of other tumors.[10] Different heterogeneous tissues may be observed within a TWN, including adipose tissue, fibrovascular, cartilage, skeletal, glomeruloid elements, and tubular structures. Differential diagnoses of TWN include neuroblastoma, teratoma, and nephroblastoma.[4,47–49]

3.5. Management

Because of its rarity, no standardized criteria have been defined for the treatment of these lesions.[20] Although the prognosis of TWN is generally good, patients in later stages who have experienced metastasis and mortality have been described. Because the final diagnosis of TWN is not made until pathological analysis, all parts of the mass should be removed to prevent malignant recurrence. The histology of the lesion and the extent of disease may be the main clinical factors that determine treatment regimens and prognosis. However, according to published reports, the treatment regimens for TWN may be quite different, especially in terms of chemotherapy protocols. Clinically, the decision to administer chemotherapy and/or radiotherapy, or the decision to perform only a surgical resection is often left to the judgment of the clinicians. However, in contrast to typical nephroblastoma, TWN may be somewhat resistant to chemotherapy and radiotherapy.[50] This resistance to chemotherapy and radiotherapy may be due to the mature, well-differentiated heterologous elements that form a large part of the tumor.[8,26] Therefore, TWN should be recognized such that the use of potentially toxic chemotherapy can be avoided because such tumors usually do not respond to preoperative chemotherapy.[18] In the present report, no radiotherapy or chemotherapy regimen was administered to our patient. Remarkably, chemotherapy with 4 cycles of cisplatin (20 mg/m^2) and ifosfamide (4.5 g/m^2) has been successfully employed for the treatment of adult patient with TWN.[1] Six months treatment of newly diagnosed TWN using vincristine, cyclophosphamide, and actinomycin-D has also been reported.[13]

Postoperative follow-up that consists of the detection of the tumor markers β-HCG and AFP is often used and is further supported based on the malignant recurrence of TWN. The increased level of AFP in tumors generally indicates advanced malignant disease. Generally, the prognosis is relatively good if the tumor is completely excised. In the present report, the prognosis and outcome of our patient were promising after complete resection. However, insufficient experience was noted both at our institution and in the literature in the reporting of long-term follow-up data regarding the management of TWN.

4. Conclusion

TWN is a rare entity that occurs in childhood. The clinical features of TWN are variable and can be non-specific. Current imaging modalities are unable to accurately delineate the differences between TWN and other tumors. The treatment of choice for TWN is complete resection. Although the prognosis of TWN is usually good, metastasis and death have been reported in some cases. Therefore, outpatient follow-up of these patients is recommended. Future research efforts should seek to establish the intrinsic quality of TWN and a normalized standard for its treatment.

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