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CASE REPORT

Extrarenal Wilms' Tumor of the Female Genital System: A Case Report and Literature Review[△]

Minmin Cao, Cuiping Huang, Yafen Wang, Demei Ma*

Department of Gynaecology, the Second Hospital of Shandong University,
Jinan 250000, China

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Abstract Extrarenal Wilms' Tumors (ERWTs) are rare. There have been only 25 cases of ERWT arising from the female genital system reported in the literature. In this paper, we report a 60-year-old woman with a complaint of vaginal bleeding and a polypoid mass in the uterine cavity by sonography that was demonstrated as ERWT by pathology after resection. The pathological characteristics, histological origination, diagnosis, therapy and prognosis of ERWT in female reproductive system are discussed in this paper in the purpose of improving the diagnosis and therapy of this rare tumor.

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WILMS' tumor (WT), also known as nephroblastoma, is one of the most common pediatric malignant tumor. It classically originates in the kidney in most cases. The tumors found in extrarenal organs with typically morphological features are rare. Such tumors are called extrarenal Wilms' tumors (ERWTs). In literature, it was reported to originate from retroperitoneum,¹ lumbosacral region,² prostate,³ sigmoid mesocolon,⁴ testis,⁵ inguinal canal,⁶ mediastinum,⁷ chest wall,⁸ uterus,⁹⁻²¹ ovary.^{18,22-26} Here we report a case of uterine Wilms' tumor with a comprehensive literature review of ERWTs in the female genital system.

CASE DESCRIPTION

A 60-year-old woman presented mainly complaining about vaginal bleeding for more than 20 days. She had been post-menopausal for more than 10 years. Gynecological ultrasound examination showed enlargement of the uterine cavity with a cystic solid heterogeneous mass about 6.2cm×5.3cm×3.9cm in size. Irregular anechoic fluid areas were detected inside the mass. No abnormality was found in bilateral adnexa area. Lab examination revealed slightly elevated Ca125 (43.53 U/mL). Hysteroscopy examination with low pressure showed a polypoid mass in the uterine cavity with obvious blood vessels on its surface. So uterine polyp electrocution through aspiration was performed.

Gross visualization showed the mass was extremely soft, fragile and vascularized, with internal focal hemorrhage and necrosis. The tumor presented typical pathological characteristics of WT (Fig. 1): a triphasic mixture of epithelial cells,

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*Corresponding author Tel: 86- 15153169285, E-mail: mademei65@126.com

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primitive blastematos cells and mesenchymal stroma. The nests of primitive blastema interbedded with adenoid regions were the predominant constitution. Blastomas were composed of small cells with ovoid, darkly stained nuclei, scant cytoplasm and frequently brisk irregular mitosis. Blastemal areas were separated by spindle stromal cells. No teratoid heterologous component was found. Besides, primitive glomeruloid structures and primitive epithelial tubules lined with columnar or cuboidal cells were conspicuous. The histopathological diagnosis was uterine Wilms' tumor. No anaplastic feature was identified. Immunohistochemical examinations showed strongly positive for WT-1, positive for CK and CD56, slightly positive for Vimentin, P53, CD99, and negative for ER, PR, CK20, Desmin, NSE, SMA and α -Inhibin. The positive ratio of Ki-67 was about 70%, which was consistent with the diagnosis of ERWT.

Uterine sonography was performed after the polyp electrocision, and no specific finding was found. Then the patient received laparoscopic hysterectomy and salpingo-oophorectomy, accompanied with pelvic and para-aortic lymphadenectomy. The final pathology demonstrated that the tumor was confined to the polyp without endometrial or extrauterine invasion.

Postoperatively, the patient received six cycles of chemotherapy with doxorubicin and ifosfamide. A close follow-up has been performed for one and a half years, and

there is no evidence of recurrence so far.

DISCUSSION

Wilms' tumor is a kind of malignant tumor that predominantly occurs in the kidney of children.^{18, 19} The first case of ERWT in the female genital system was described by Constanzi in 1970.⁹ Through an extensive literature review, there are 25 cases of ERWTs arising from the female genital system reported so far, including 16 cases from the uterus, 7 cases from the ovary and 1 case considered most likely from the right oviduct.²⁷ Among them, 19 cases^{9-17, 19-26, 27} were described in detail. The onset age of the disease ranged from 2 to 77 years old, with an average of 26.05 ± 21.96 years old; 45% of them were under 15 years old. McAlpine *et al*¹⁸ summarized uterine ERWT cases in 2005 in a literature review. The ovarian ERWTs reported were summarized in the Table 1.

Pathologically, ERWT has been categorized into the pure ERWT and the teratoid Wilms' tumor (TWT) that comprises teratoid elements >50% in the tumor.²¹ The latter is even rarer than the former. Diagnostic criteria for primary pure ERWT were established,¹⁷ including the presence of epithelial cells predominantly with glomeruloid structures and embryonic tubules, variably differentiated stroma and primitive metanephric blastemal components. In addition, there must be no evidence of teratoid elements

Figure 1. Micrographic findings of histopathological examination.

A. Triphasic mixture of epithelial cell, primitive blastematos cells and mesenchymal stroma (HE staining, $\times 200$); B. WT-1 expression was strongly positive in the tumor (immunohistochemical staining, $\times 100$); C. Ki-67 expression was positive (immunohistochemical staining, $\times 200$); D. CK expression was positive in the primitive epithelial tubules lined with columnar or cuboidal cells (immunohistochemical staining, $\times 100$).

Table 1. Presentation, clinical, pathologic characteristics and the outcome of extrarenal Wilms' tumor of ovary

Author publish year	Age (y/d)	Presenting symptoms	Tumor charac- teristics	Treatments	Chemotherapeutic regimens	Follow-up	Recurrence
Sahin <i>et al</i> ²⁵ 1988	56	Bilateral calf pain, pelvic mass	12cm×11cm×7cm, solid ovoid mass	TAH, BSO, XRT, chemotherapy	Vincristine, dactinomycin, and cyclophosphamide	9 years	NED
Pereira <i>et al</i> ²³ 2000	3.5	Abdominal pain, distension	13cm×10cm× 10cm lobulated mass confined to the right ovary	Right oophorectomy, chemotherapy	Vincristine and actinomycin D	6.5 years	NED
Isaac <i>et al</i> ²⁴ 2000	21	Menorrhagia, abd- ominal symptoms, palpable pelvic mass	Right ovarian mul- tilocular mass, in diameter of 19 cm	RSO, wedge resection of the left ovary, che- motherapy	Bleomycin, etoposide, cisplatin, vincristine and actinomycin D	6 months	NED
Oner <i>et al</i> ²² 2002	3.5	Abdominal pain and vomiting	13cm×10cm× 6.5cm tuboovarian mass	Debulking, LSO, appendectomy and partial omentectomy, chemotherapy	Vincristine and actinomycin D	7 months	NED
Li <i>et al</i> ²⁶ 2008	22	Abdominal disten- tion, abdominal pain, fever	Ovarian cystic mass, 18cm×14cm×3cm	Not stated	Not stated	Not stated	Not stated

TAH, total abdominal hysterectomy; BSO, bilateral salpingo-oophorectomy; LSO, left salpingo-oophorectomy; RSO, right salpingo-oophorectomy; XRT, external radiotherapy; NED, no evidence of disease.

and primary renal neoplasm. The present case we report fulfills all these criteria for primary pure ERWT of adults. Histologic examination confirmed a triphasic mixture of epithelial cells, primitive blastematos cells and mesenchymal stroma. The epithelium was represented by primitive glomeruloid structures and the primitive epithelial tubules. Gross appearance of the tumor in our case was much more soft and fragile compared with former reported cases.

ERWTs closely resemble other rare mixed-type tumors in female genital system, so differential diagnosis is important. Presence of glomeruloid bodies and typical pathological characteristic of triphasic mixture consisting of epithelial cells, primitive blastematos cells and mesenchymal stroma, distinguish ERWT from malignant mixed mullerian tumor (MMMT), adenosarcoma, embryonal rhabdomyosarcoma and teratoma. Negative expression of ER on immunohistochemical examination assisted the differential diagnosis of ERWT from MMMT and adenosarcoma, where the ER expression is generally positive. Neural-type rosettes of epithelial components, small closely packed primitive blastemal cells and positive expression of CD99 and CD56 are the characteristic immunohistochemical markers of peripheral neuroectodermal tumor (PNET)²⁸ that may raise suspicion of PNET. The primitive glomeruli closely resembling those

in the kidney, together with positive expression of WT-1 in the nuclei, finally led to the diagnosis of uterine WT. According to our investigation, the true primitive glomeruli in our case have never been reported in primitive neuroectodermal tumor before.

Renal WTs are thought to originate from the aberrant differentiation of persistent metanephric mesenchyme or metanephric blastema.²⁹ However, the origin of ERWTs remains unclear. The origination of TWTs is thought to be from the rare indwelling metanephric blastemal foci in immature teratomas.^{21,30} There are several hypotheses about the origin of pure ERWTs. A favored hypothesis is that ERWTs may originate from the persistent embryonic nest of renal anlage through an ultimate malignant transformation of genetic event.¹⁷

There is no standard therapy for ERWTs in female genital system because of rarity of the tumor. Most scholars and specialists concur that its' treatment should parallel the treatment of classic WTs in the kidney.³¹ McAlpine *et al* suggested that surgery for the uterine ERWTs should at least include hysterectomy. The significance for further surgical staging remains unclear.¹⁸ Three cases of uterine ERWT who only received polypectomy all had recurrence of the disease. This indicated that conservative

surgery for uterine ERWT may have high risk of recurrence, and should be taken very cautiously.¹⁶

ERWTs, similar to intrarenal WT, have a favorable overall prognosis, especially when the tumor is confined to the uterus and adequate surgery is performed.¹⁹ However, WT in adults tend to be more aggressive than those in children.¹⁷

In conclusion, because of rarity of this special variant of WT, there is no conclusive opinion about treatment and prognosis of this disease. However, in the case of a mass found in female genital system, ERWTs should be included as a differential diagnosis. More reports of ERWTs from female genital system are expected for further investigation.

Compliance with ethical standards

All the authors declared they had no conflicts of interest to disclose. Informed consent was obtained from the patient reported in this study.

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