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CASE REPORT

Adult Extrarenal Wilms' Tumor Mimicking Mixed Epithelial and Stromal Tumor in the Retroperitoneum: A Case Report with Immunohistochemical Study and Review of the Literature

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Abstract We report an extremely rare case of adult extrarenal Wilms' tumor (WT) in a 52-year-old woman who presented with fever and abdominal distension. Computed tomography revealed a well-defined mass lesion measuring 15.0 cm in the right retroperitoneum and that was in contact with the right kidney. The mass and kidney were surgically removed. Grossly, the mass was well-defined, measuring 16.3×11.0×9.8 cm, and appearing grayish-white in color. The border between the mass and the kidney was well-defined. Histologically, the tumor showed a triphasic pattern consisting of stromal, epithelial and blastemal components. The stromal component was predominant in the tumor and consisted both of spindle cells and smooth muscle cells. The epithelial component showed a mature glandular structure. Immunohistochemically, the stromal component was positive for vimentin, smooth muscle actin and desmin. The blastemal component was positive for vimentin, while the epithelial component was positive for cytokeratin (CK) 18, CK7 and vimentin. WT-1 was negative in the all three components, and the Ki-67 proliferation index was low. The postoperative histopathological diagnosis indicated extrarenal WT arising in the retroperitoneum. Although not treated by either chemotherapy or radiation therapy, she was free from disease recurrence for 30 months after surgery. To the best of our knowledge, this report is only the fourth case of adult extrarenal WT arising in the retroperitoneum. Furthermore, the present case showed predominant smooth muscle differentiation and a mature glandular structure, mimicking a mixed epithelial and stromal tumor.

Keywords Adult · Extrarenal · Retroperitoneum · Mixed epithelial and stromal tumor · Wilms' tumor

Abbreviations

WT	Wilms' tumors
MEST	mixed epithelial and stromal tumor
CK	cytokeratin
WT-1	Wilms' tumor 1

Introduction

Most of Wilms' tumors (WT) appear in the first 5 years of life, though adult WT is rare, with fewer than 300 cases having been reported in the literature [1]. Furthermore, adult extrarenal WT is extremely rare, with cases reported to arise in the uterus [2], ovary [3], retroperitoneum [4–6], and testis [7].

We report the fourth case of adult extrarenal WT arising in the retroperitoneum, a rare instance of adult WT revealing a good outcome without either chemotherapy or radiation therapy. Furthermore, in the present case, WT showed an unusual histological pattern mimicking a mixed epithelial and stromal tumor (MEST).

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Case Report

Clinical Findings

A 52-year-old Japanese woman presented with abdominal distension and fever. Physical examination confirmed the presence of a large fixed, smooth, elastic-firm mass occupying the right side of the lower abdomen. The tumor markers were within normal limits. Computed tomography revealed a well-defined and slightly enhanced mass lesion measuring 15.0 cm in the right retroperitoneum (Fig. 1). Although a retroperitoneal neoplasm was suspected, a renal neoplasm was not completely ruled out. At surgery the retroperitoneal mass in contact with the right kidney showed no adhesion to the surrounding connective tissue, and was easily dissected free. The operation culminated in the removal of the right retroperitoneal mass and kidney.

The postoperative histopathological diagnosis was adult extrarenal WT in the retroperitoneum. Following her informed consent, the patient was not treated by either adjuvant chemotherapy or radiation therapy, and remained free from disease recurrence for 30 months after surgery.

Pathological Findings

Grossly, the mass measured 16.3×11.0×9.8 cm, and weighed 101 g. The cut surface revealed a grayish-white solid mass (Fig. 2). The border between the mass and kidney was well-defined, and there was no mass lesion in the right kidney.

Histologically, the bulk of the tumor consisted of a stromal component, though blastemal and epithelial components of the mixed stromal component were observed in very small area. The stromal component consisted of both spindle cells (Fig. 3a) and smooth muscle cells (Fig. 3b), while the epithelial component showed mature glandular structures (Fig. 3c). These findings mimicked a MEST of the kidney. However, blastemal cells typical of WT, showing scanty cytoplasm and round nuclei with finely dispersed chromatin, were present (Fig. 3d). Anaplasia, such as multipolar mitotic figures or nuclear enlargement with hyperchromasia, was not observed. There were no nephrogenic rests in the kidney or perirenal fatty tissue.

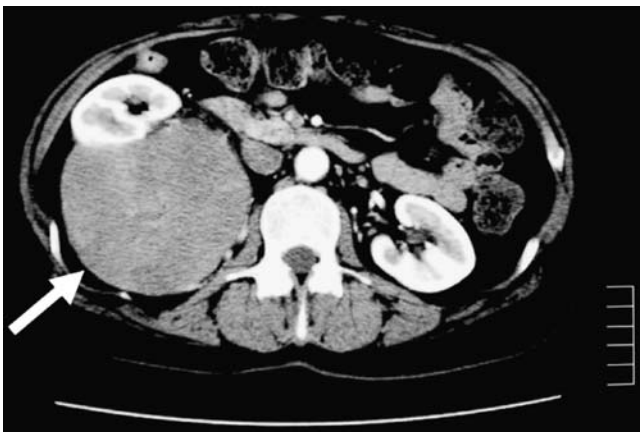

Fig. 1 Enhanced computed tomography showing a slightly enhanced mass measuring 15.0 cm in the right retroperitoneum (*arrow*)

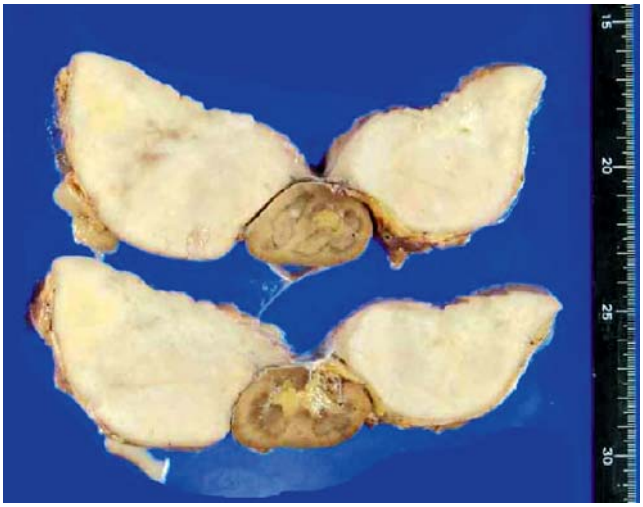

Fig. 2 Gross appearance showing grayish-white solid mass

Immunohistochemically, the stromal component consisting of spindle cells and smooth muscle cells was positive for vimentin (Dako, clone V9), smooth muscle actin (Dako, clone 1A4) (Fig. 4a), and desmin (Dako, Polyclonal), while the blastemal component was positive for vimentin. The epithelial component was positive for cytokeratin (CK) 18 (Novocastra, clone DC-10) (Fig. 4b), CK7 (Novocastra, clone OV-TL 12/30) and vimentin, whereas CD34 (Novocastra, QBEnd/10), S-100 protein (Dako, polyclonal), Melanosome (Dako, clone HMB-45), estrogen receptor (Immunotech, clone ER1D5), progesterone receptor (Immunotech, clone 1A6), and WT-1 (Dako, clone 6F-H12) were confirmed negative in all three components. The Ki-67 (Dako, clone MIB-1) proliferation index was 3% in both the blastemal and the epithelial components, and 1% in the stromal component.

Discussion

Adult extrarenal WT is extremely rare, and this report is only the fourth case arising in the retroperitoneum (Table 1 summarized those four cases) [4–6]. It has been well-known that the stromal component of WT reveals various types of differentiation, such as adipose tissue, skeletal muscle, bone, cartilage, and neuroglial tissue. However, such a case of adult extrarenal WT showing predominant smooth muscle differentiation had not been reported previously.

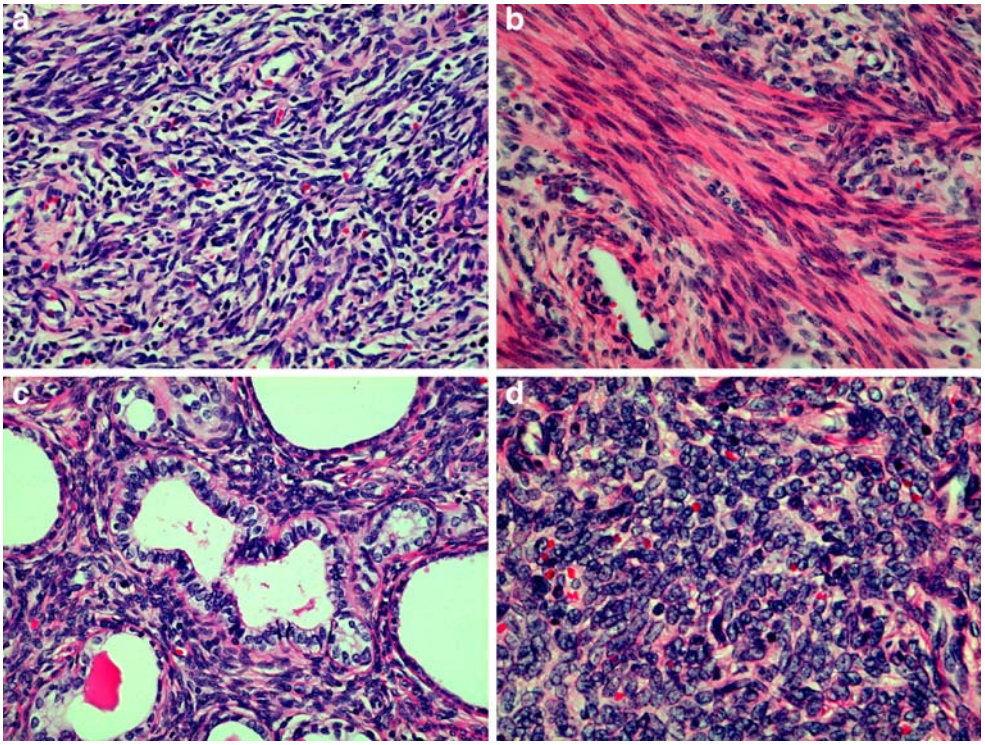

Fig. 3 Microscopic appearance (hematoxylin-eosin stain, magnification 400×). **a** Stromal component consisting of spindle cells. **b** Stromal component consisting of smooth muscle cells. **c** Epithelial component showing glandular structure. **d** Blastemal component showing scanty cytoplasm and round nuclei

The following criteria have been proposed for a case to be considered one of adult WT: primary neoplasm in the extrarenal region, a primitive blastematous spindle or round cell component, formation of abortive or embryonal tubular or glomeruloid structures, no area of the tumor diagnostic of hypernephroma or teratoma, microscopic confirmation of histological characteristics, and a patient age greater than 15 years [5]. The present case fulfills all those criteria.

In extrarenal WT, it may be necessary to take into account the possibility of a metastasis from renal WT for a differential diagnosis; a metastatic WT is excluded by confirmation of the absence of WT in the kidney. As noted above, the present case showed a predominant smooth muscle differentiation and mature glandular structure, mimicking MEST, thus making it necessary to take MEST into account for a differential diagnosis. Grossly, such a tumor is well-circumscribed and consists of both solid and cystic components, most often in equal proportions but varying in distribution. Microscopically, a mixture of epithelial and stromal components, with no blastemal component, characterizes MEST [8]. The epithelial component, which is scattered throughout the stromal component, consists of a collection of small glands focally transformed into large cysts. The stromal component consists of spindle cells ranging from paucicellular to densely cellular with a smooth muscle appearance. Immunohistochemically, estrogen receptor is detectable in the nuclei of spindle cells. Muscle makers, such as smooth muscle actin, are diffusely and strongly positive in the spindle cells. In the present case, MEST is excluded via confirmation of the absence of cystic change, a blastemal component, and estrogen receptor expression. Moreover, MEST is recognized to be a distinctive tumor arising in the kidney, whereas any extrarenal lesion has yet to be reliably reported.

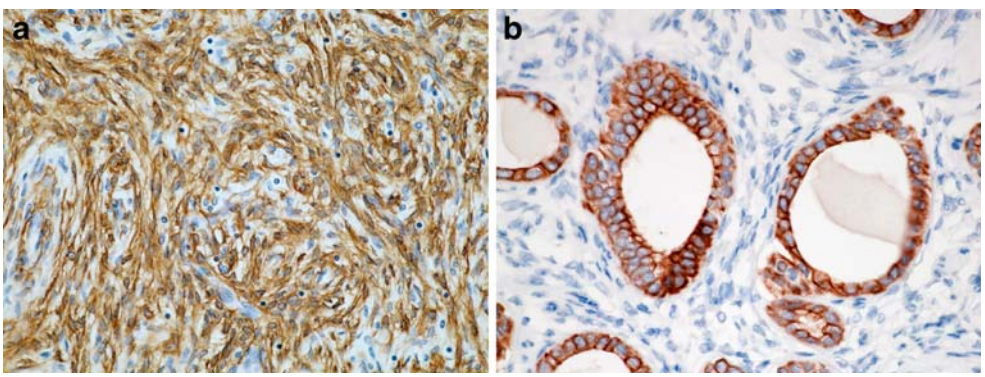

Fig. 4 Immunohistochemical findings (magnification 400×). **a** Stromal component showing positive reaction for smooth muscle actin. **b** Epithelial component showing positive reaction for cytokeratin 18

Table 1 Summary of adult extrarenal Wilms' tumor in the retroperitoneum

Case	Age (years)	Sex	Symptoms	Size (cm)	Treatment	Stromal component	Reference
1	36	M	Right lower quadrant pain	12.0	surgical removal + chemotherapy	fibrous tissue	4
2	49	M	Painless mass in left upper quadrant	15.0	surgical removal	sarcomatous lesion with fatty cells, smooth muscles, mixomatous tissues, blood vessels, and fibrous connective tissue	5
3	21	F	Severe abdominal pain Abdominal distension Loss of appetite	15.0	surgical removal + chemotherapy	fibroblast-like bland spindle-cells type with focal myxoid changes	6
4	52	F	Abdominal distension Fever	16.3	surgical removal	predominant smooth muscles	present case

WT occurring in the kidney is thought to arise from the aberrant differentiation of a persistent metanephric mesenchyme. Although the exact histogenesis of extrarenal WT is unclear, its origin from persistent embryonic nests of a primitive renal anlage is favored. Mesonephric remnants may give rise to a tumor occurring in the retroperitoneum [2, 6]. The present case would suggest that retroperitoneal mesonephric remnants have revealed a malignant transformation, and have differentiated from immature stromal cells into smooth muscle cells, and from immature epithelial components into a mature glandular structure.

The Wilms' tumor 1 (WT-1) protein has been implicated in many processes, such as proliferation, differentiation, and apoptosis [9]. Previously, no expression of WT-1 protein in extrarenal WT had been investigated, making this the first report of a case in which WT-1 immunostaining was examined in extrarenal WT. Ghanem et al. reported that WT-1 immunoreactive blastemal and epithelial cells in 59 and 57% of patients, respectively, whereas no expression was found in the stromal component [9]. It is suggested that the present case was negative for WT-1, since the stromal component was predominant in the tumor. These results indicate that, though about half the WTs show WT-1 protein expression, WT-1 immunoreactivity may not be detected in all renal WT. Furthermore, it is well-known that WT-1 is expressed in several human tumors other than WT [9]. Therefore, it is generally accepted that WT-1 expression cannot be recognized as the only reliable marker for extrarenal WT. A recent report on the immunohistochemical features of WT suggests that expressions of CD56, CD57, CK22, CK18, CK8, EMA and smooth muscle actin constitute one of the findings proven useful for an accurate diagnosis of WT in small biopsy samples [10].

Roberts et al. [11] have reported that *WT-1* mRNA expression in childhood was detected in 5 of 5 (100%) renal WT and 2 of 8 (25%) extrarenal WTs. Both *WT-1*-positive extrarenal WTs were endometrial primary cases, whereas the retroperitoneal primary cases exhibited no *WT-1* mRNA expression. Although the present case of a retroperitoneal primary was not specifically examined for *WT-1* mRNA expression, WT-1 protein expression was not detected immunohistochemically. These findings suggest that some cases of extrarenal WT, especially in the endometrial primary, may be related to *WT-1* mRNA expression, but that extrarenal WT in the retroperitoneum may produce different molecular abnormalities.

As stated in a study by the Society of Pediatric Oncology 93-01/Society for Pediatric Oncology and Hematology, a multimodal treatment administered according to a pediatric protocol, including surgical standards, chemotherapy, and radiation therapy, is recommended for adult WT [12]. Moreover, it has been stated that adult WT, if treated according to a pediatric strategy, is a curable disease with an overall survival of 83%. The general clinical course of extrarenal WT remains unclear, given that extrarenal WTs have mainly been the subject of isolated case reports. However, Coppes et al. [13] have suggested that retrospective evaluation of 34 extrarenal WT patients shows a clinical course very similar to that of renal WT, and reported an estimated overall 2-year survival rate of 82% in 34 patients. Most cases reviewed were treated by chemotherapy with or without radiation therapy. Their results supported the conclusion that ours is indeed a rare case of adult WT revealing a good outcome without either chemotherapy or radiation therapy. Moreover, the patient who has remained free from disease recurrence for 30 months after surgery.

In order to evaluate its prognostic value in WT, a blastemal WT-1 expression was reported to be indicative of clinical progression and tumor-specific survival, whereas epithelial staining proved to be of no prognostic value [9]. Moreover, the blastemal Ki-67 proliferation index, at a cutoff value of 5%, was also reported to be a prognostic marker for clinical progression and tumor-specific survival [14]. Additional factors helping to explain why the present case revealed a good outcome without chemotherapy or radiation therapy include: the tumor indicated no anaplasia, was negative for WT-1, showed a low Ki-67 proliferation

index, and differentiated from immature cells into smooth muscle cells or a mature glandular structure.

In conclusion extrarenal WT should be taken into account in any differential diagnosis of adult retroperitoneal tumors.

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