Extrarenal Wilms’ tumor: A report of two cases and review of literature

Departments of Medical Oncology, *Surgical Oncology, **Pediatric Oncology, ***Radiation Oncology, and ****Pathology, Kidwai Memorial Institute of Oncology, Bangalore - 560 029, India

Correspondence: Dr. A. V. S. Suresh, Department of Medical Oncology, Kidwai Memorial Institute of Oncology, Bangalore - 560 029, India. E-mail: sureshattili@yahoo.com

ABSTRACT
Wilms’ tumors is a renal malignancy commonly occurring in childhood with classic histopathological features. While the majority of the tumors present as renal masses, atypical presentations like extrarenal masses have also been known. However, the exact natural course of the disease and its outcome is not known. Here, we present two cases of extrarenal Wilms’ tumor, discuss the pathophysiology and review the literature for the prognostic factors and the treatment outcome.

KEY WORDS: Extrarenal, clinical features, treatment, Wilms’ tumor

INTRODUCTION
Occurrence of extrarenal Wilms’ tumour (ERWT) is very exceptional and the diagnosis is almost always made after surgical intervention. The tumor can be located in the retroperitoneum, uterus, cervix, testes, skin and even in the thorax. The exact mechanism whereby a WT occurs in extrarenal tissues is not known.[1] Even if the histological characteristics are the same as in intrarenal WT, a retroperitoneal teratoma should be investigated for a possible admixture of WT cells. Our literature search suggests a similar course for ERWT as that of the renal counterpart, therefore, similar staging and treatment protocols can be followed.[2-4]

CASE REPORTS
Case 1
A four year-old boy was admitted at our hospital with the chief complaint of a mass in the lower abdomen. He was apparently asymptomatic two months prior to presentation when the mother noticed a gradual increase in the lower abdominal region, poor appetite and severe weight loss. His family history was negative. Examination revealed an emaciated, malnourished patient with a palpable fixed smooth mass of 6 x 8 cm size occupying the umbilical and right pelvic regions. Other systemic examinations were normal. Laboratory investigations were as follows: hemoglobin 9.5 g/100 ml, microcytic hypochromic picture with white blood cell count 9000/mm³. His biochemical (renal and hepatic function) tests and the urine analysis were normal. Radiology (computerized tomography, CT) of the patient revealed normal findings in the thorax. Scan of the abdomen showed a mass in the lower abdomen with foci of hypodensity in the center suggestive of necrosis. No abnormality was detected inside the kidneys. Tumor markers (α-fetoprotein, AFP and β-human chorionic gonadotropin, β HCG) were within the normal range. The patient was taken for explorative laparotomy, which revealed a mass located in the retroperitoneum starting from the right lumbar region occupying the pelvic and the umbilical regions. The tumor had invaded the surrounding structures But was easily separable from the kidney. Thus, the criterion of sparing the kidney was met and as the tumor involved the surrounding structures, it was considered as stage III. Only debulking of the mass could be performed with gross evidence of residual tumor tissue remaining in the region. Histopathological examination showed features of WT exhibiting both epithelial and mesenchymal differentiation. The features of anaplasia were not appreciated. Resected lymph nodes showed benign lymphoid hyperplasia. Patient received therapy as per the National Wilms’ tumor study (NWTS) IV protocol which included combination chemotherapy and local radiation to the abdomen. The patient is alive and disease-free at the end of 12 months of follow-up.
**Case 2**

A three year-old girl presented to our department with the chief complaint of a mass in the abdomen. Systemic review for involvement of other systems was normal. Family history was negative. Examination revealed a normal-built patient with a palpable smooth mass of 5.6 x 7.4 cm occupying the right pelvic region. Systemic examination did not reveal any other abnormality. Laboratory investigations including the routine hematological and biochemical parameters and the urine analysis were normal. CT scan of abdomen showed a heterogeneous mass in the lower abdomen with variable signal intensity with absolutely normal kidneys bilaterally. Metastatic work-up including bone scan, CT of the thorax was normal. Tumor markers (AFP and β HCG) were within the normal range. This patient was also taken for explorative laparotomy. Intraoperative findings showed a mass located in the retroperitoneal region, easily separable from the kidney and invading the surrounding structures. Thus a final diagnosis of extra renal Wilms’ tumor stage II was made. Only debulking of the mass could be performed. Patient received therapy as per the NWTS IV protocol, which included combination chemotherapy and local radiation to abdomen. The patient is alive and disease-free at the end of 16 months of follow-up.

**DISCUSSION**

**Epidemiology**

ERWT by definition excludes those primary neoplasms arising from the kidney. It is extremely rare and while the exact incidence is not known, a literature search (English) until September 2003 showed only 72 reported cases. Medline and Google searches from then added only three new cases including the last reported by the authors. There is a slight male preponderance with an M: F ratio of 56:44. The age at presentation usually ranges from two months to ten years, although exceptionally young (an eight day-old child) and old (77 year-old female) cases have been reported. Both the cases presented in the current series are in the typical age group of the WT. It is usually associated with other neoplasms such as teratoma in many instances. The non neoplastic association of this tumor is with horse-shoe kidney reported in six patients and spinal dysraphism in two cases. However, in both our cases, we could not find any such associations.

**Clinical presentation**

Both of our cases presented as solid abdominal masses, the most commonly reported form so far. Consistent with current literature, constitutional symptoms are typically absent in both of our cases, due to which, they usually present at an advanced stage.

**Pathogenesis, staging and prognosis**

The exact mechanism is not clear as this disease is very rare. However, there are some popular hypotheses regarding the origin such as:

A. From ectopic metanephric blastema: this hypothesis is supported by the fact that the majority of the tumors occur in the retroperitoneal region. However the presence of extra-renal Wilms’ tumor cephalad to kidney argues against it.

B. From primitive mesodermal tissue: This hypothesis is based on the occurrence of ERWT in the cervix, vagina and inguinal canal, where there is a persistent mesonephric duct remnant.

C. Connheim’s cell rest theory: This is a common hypothesis where cells with persistent embryonal potential undergo malignant transformation at any point of time.

The staging systems used in literature while describing the above two cases are either NWTS or TNM (tumor, nodes and metastases). When matched with the appropriate stage, the prognosis of ERWT is similar to its renal counterparts. The cystic variant is reported to have a slightly better prognosis than the solid ones. The tumor has a potential for local recurrences as well as distant metastases, the incidence of which is similar to the classical WT.

**Gene expression profile**

ERWT has not been extensively studied due to its rarity. However, in a famous study by Roberts et al., of the expression of the Wilms’ tumor suppressor gene, WT1, all sporadic WT cases were found to express the gene whereas only two of eight ERWT cases expressed WT1. Both WT1-positive ERWT cases were endometrial primaries. The WT1-negative ERWT cases included retroperitoneal (3), pararenal or paravesical (2) and paraspinal (1) primaries. These findings suggest that some cases of ERWT are related to classical renal WT by more than mere morphologic resemblance, as indicated by the detection of WT1 expression in at least a subset of these rare tumors. Furthermore, the results suggest different pathogenesis of subsets of ERWT.

**Management**

As there are no specific guidelines for this entity, most treating oncologists prefer adapting the NWTS protocol.

**REFERENCES**


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