Case Report *Iran J Ped Hematol Oncol. In Press*

Rare Presentations of Wilms Tumor in Children: Case Report

Athena Modanlou MD[1], Ahmad Tamaddoni MD[2,*], Hassan Mahmoodi Nesheli MD[1], Sahar Sadr Moharerpour MD[1]

1. Clinical Research Development Unit of Amirkola Children's Hospital, Babol University of Medical Sciences, Babol, IR Iran.
2. Non-Communicable Pediatric Diseases Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, IR Iran.
*Corresponding author: Dr Ahmad Tamaddoni, Non-Communicable Pediatric Diseases Research Center, No 19, Amirkola Children's Hospital, Amirkola, Babol, Mazandaran Province, 47317-41151, IR Iran. E-mail: drtamaddoni@yahoo.com.
ORCID: 0000-0002-3684-8754.

Abstract
Wilms tumor (WT) is the most common malignant tumor (neoplasm) of the urinary tract in early childhood. The median age at WT diagnosis is 3-4 years and 90% of cases are diagnosed before the age of 7 years. In this report, three patients with WT, aged 12, 17, and 16 were presented (adolescent age). Left kidney involvement was observed in these three cases. The clinical presentation in case one was the complaint of abdominal pain with a palpable abdominal mass. The second case was presented with hematuria and abdominal mass. The clinical symptoms in case three included left flank pain and weight loss. Although WT is usually presented in children younger than 7 years of age, its diagnosis should also be considered in older children with abdominal pain, palpable mass and gross hematuria.
Key Words: Child, Neoplasms, Wilms tumor

Introduction

Wilms tumor (WT) is one of the most common renal tumors in childhood, and its incidence in children younger than 15 years is about 10 cases per million (1). The majority of cases are diagnosed in children less than five years of age (2). In most countries, the median age for unilateral WT at diagnosis is 32-44 months. Mitry et al., reported that 90% of patients were diagnosed by the age of 7 years (3). Ninety percent of the total incidence of WTs occurs in children younger than 7 years old and 98% in those younger than 15 years. In contrast, its prevalence is rather stable after 15 years old (1). The clinical presentation of WT in young children is not different from that adolescents (4). Although the presence of an abdominal mass detected by abdominal palpation can be considered as the typical clinical presentation in some children, the renal tumors can be presented with hypertension, hematuria or in rare cases as a consequence of central nervous system metastasis with an obstructive hydrocephalus. The diagnosis of WT has also been reported by the use of prenatal ultrasonography (5-7). Totally, 4-7% of all WTs are synchronous bilateral WTs (BWTs) presented at a younger age (mean age, 2.6 vs. ~3.3 years) compared to unilateral WTs. Prognosis is excellent after the treatment of unilateral WT (8).

It is now apparent that there are at least two WT-associated gene loci located on the short arm of chromosome 11: WT1 at 11pl3 associated with the WAGR syndrome, congenital heart disease and ear anomaly. Beckwith–Wiedemann (BWS) syndrome including rabdomyosarcoma, hypoglycemia, macroglossia, hepatoblastoma, omphalocele, macrosomia, distinct facies,

hemihypertrophy, and embryonal tumours is another presentation of WT (9).

Treatment of WT is currently based upon tumor staging, the presence of favorable or unfavorable histology, and age. The Children's Oncology Group (COG) developed a specific treatment protocol (10). The overall survival rate of WT has increased to more than 90% (11). Recent report indicated that the high birth weight may be related to the subgroup of WT, which is characterized by the presence of perilobar nephrogenic rests (12). Laparoscopic surgery has been greatly expanded in children (13). Preoperative chemotherapy is generally proceed nephrectomy (14).

Regarding high incidence of WT in early childhood, we presented three patients with WT who aged 12, 17, and 16 years old.

Case report

In this report, we presented three adolescent girls with the dignosis of WT (12, 17, and 16 years old) with left kidney involvement, but with different clinical manifestations.

Case 1:

A 12-year-old girl was admitted to Amirkola Children's Hospital due to the abdominal pain and palpable large abdominal mass, noted 5 days before hospital admission (weight: 52 kg and height: 159 cm (10-25% percentile)). The whole left abdomen was filled with a palpable mass. The genitourinary examination was normal. Laboratory evaluation was significant for lactate dehydrogenase (LDH) that was 1070 U/L (give normal range), Bun:15.1 mg/dL, and Cr= 0.8 mg/dL. Serum α- fetoprotein (FP), 24 hours urine vanile mandelic acid (VMA), urine analysis (U/A), and her blood pressure were normal. Her chest-X ray was normal. Abdominal ultrasound was performed and the presence of a heterogeneous big mass in lower pole of left kidney with 155×98 mm size with internal vascularity and limited distorting renal capsule were confirmed. Spiral contrast computed tomography (CT) scan of lungs, mediastinum, abdomen, and pelvis were performed revealing a 100×104 mm hypodense left renal mass extended into the right hemithorax with at least two pulmonary nodules (8×7.5 mm), segment V of the liver (size of mass 12×16 mm), lymphadenopathy and tumor expanded to the renal vein, and aortocaval lymph nodes (9×5 mm). Since the size and the extension of the tumor mass made its surgical removal very difficult, only biopsy was done and wilms tumor was confirmed by a pathologist (stage IV). She underwent chemotherapy and irradiation as well. Her chemotherapy protocol included vincristine, actinomycine, adriamycine, and cyclophosphamide . There was no congenital anomaly and no family history of similar malignancy. Her initial response to treatment was well.

Case 2:

A 17-year-old girl was referred to our children's hospital with a history of gross hematuria of two weeks duration. An abdominal mass in left lower quadrant was detected by abdominal palpation. Her renal function revealed Bun=13 mg/dL and Cr= 0.7 mg/dL. An abdominal ultrasound indicated the presence of a heterogeneous big mass in left kidney with size of 160×155 mm, but the right kidney was normal in size. An abdominal CT scan was performed and demonstrated a large abdominal mass with size of 150×100 mm in the left kidney distorting the whole structure of the kidney. Biopsy of the mass suggested a circumscribed WT of mixed tubule papillary and blastemal pattern, limited to the kidney with no vascular and lymphatic invasion and favorable histology (stage I). She underwent exploratory laparotomy with left radical nephrectomy and lymphadenectomy. Her blood pressure (BP) was normal and laboratory tests including Bun, creatinine 24 hours VMA and U/A, and serum α-FP were normal. The post-surgery patient was treated using vincristine and actinomycine

protocol. At the time of this report, patient was in general good health.

Case 3:

A 16-year-old girl was presented with generalized weakness, left flank pain, and weight loss (13 Kg in 3 months). Physical examination revealed a mass in left lower quadrant of the abdomen. Laboratory tests including Bun=12 mg/dL and Cr= 0.85 mg/dL and U/A, 24 hours VMA, and serum α-FP were normal. An abdominal ultrasound displayed the presence of a heterogeneous mass in left kidney with size of 150×155 mm . Abdominal CT scan confirmed a mass in left side of kidney distorting whole structure of the left kidney. The tumor was not metastasized to other organs (lungs, bone and chest). She underwent exploratory laparotomy with left radical nephrectomy and lymphadenectomy.

Pathology of the tumor mass revealed a circumscribed WT of mixed tubule papillary and blastemal pattern with lymphatic invasion (stage 3). Her BP was normal.

During surgery, tumor capsule had ruptured into the peritoneum and spread the tumor cells in abdomen. This case was treated using a more intensified chemotherapy protocol and irradiation. The chemotherapy protocol was vincristine, actinomycine, and adriamycin. Her response to treatment was excellent.

Discussion

As occurrence of WT is rare in children more than 10 years old, we reported three cases of WTs in adolescent girls presented with abdominal mass.

Some studies suggested that the preoperative diagnosis of WT was extremely difficult because there were no specific radiographic findings that could distinguish it from the more common renal neoplasms (15, 16), which was similar to our study.

Khanna et al., showed the limited sensitivity of CT in the diagnosis of peritoneal spread of malignancy (11), but in one of our cases CT scan was performed and revealed a 100×104 mm hypodense left renal mass extended into the right hemithorax with at least two pulmonary nodules (8×7.5 mm), segment V of the liver (with mass' size of 12×16 mm), lymphadenopathy, and tumor expanded to the renal vein and aortocaval lymph nodes (9×5 mm).

In one study, the serum alpha-fetoprotein level was elevated in an infant with familial synchronous bilateral teratoid mass (17) while in our cases, the serum alpha-fetoprotein level was not increased.

Another study suggested that the relative excess risk of death for male was twice as high as female. The one-year and five-year survivals were higher for those diagnosed in the 1990s than 1980s; whereas, the trend in relative excess risk of death within 5 years across four triennia of diagnosis (1983–1994) was not statistically significant after adjustment for age, sex, and geographic region. Regional differences in survival were not significant (3), and survival was good in case 2 of the current study with favorable history and WT (stage I , III).

Giannoulia et al., reported that WT had a tendency to invade vascular structures (18). They found that intravascular extension into the renal vein occurred in 10% of the patients, predominantly on the right side. Moreover, cases 1 and 2 of the present study had a heterogeneous big mass in lower pole of left kidney with internal vascularity, expanded into the renal vein, and case 3 had abdominal mass in the left side of kidney with metastasis to lymph nodes.

One study demonstrated that the interaction between age and respiratory infection did not follow this pattern as the relationship between infection and WT was stronger among older children (12), which was not present in our cases.

In large national cohort study by Crump et al., it was demonstrated that the higher fetal growth was related to the enhanced risk of WT with onset before age 5 years

among females, but not later-onset WT among males (19); however, all of our cases were females with normal birth weight.

Survival rates for children with WT, especially with the development of additional chemotherapeutic regimens and the use of radiation therapy, have dramatically improved approaching 90% for even the most advanced stages of disease (14). Similarly, the survival in our cases was improved following chemotherapy and radiotherapy.

Rodrigues et al., recommended the adjuvant chemotherapy along with vincristine and dactinomycin for WT stages I and II as well as flank irradiation and doxorubicin for stage III-IV. In that study, overall survival rate was 100%, 92%, 70%, and 73% for patients with favorable histologic features and stage I, II, III, and IV, respectively. They found that the stage-based treatment according to the established protocols was essential for an improved prognosis (20). Similarly, in the present study, the first case was treated using vincristine and actinomycin, case 2 was treated with intensified protocol and irradiation, and case 3 was treated with vincristine, actinomycine, adriamycin, cyclophosphamide, as well as irradiation.

In adults with WT, flank pain is the most common complaint while it is presented as a palpable mass in children (21). In our study, case 3 was presented with flank pain and palpable mass similar to adult cases.

Mitchell et al., reported that a 6-week preoperative course of 2-drug chemotherapy led to improved stage distribution during six weeks, indicating an enhancement of 10% in stage I but a decrease of 20% in stage III tumors (22).

Conclusion

Although WT is usually presented in children younger than 7 years of age, its diagnosis should also be considered in older children with abdominal pain, palpable mass, and gross hematuria

Acknowledgment

We are grateful to the Clinical Research Development Committee of Amirkola Children's Hospital in Babol University of Medical Sciences and Mrs. Faeze Aghajanpour for their contribution to this study.

Conflicts of interest

The authors declare no conflicts of interest for this manuscript.

References

1. Okasho K, Nishiyama H, Watanabe J, Soda T, Mikami Y, Koyama T, et al. Adult wilms tumor in the renal pelvis: Case report with review of the literature. Urology. 2008;72(5):1185. e5-. e7.
2. Bailey L, Durkee C, Werner A, Finley Jr R. Wilms' tumors in adults. The American surgeon. 1987;53(3):149-55.
3. Mitry E, Ciccolallo L, Coleman MP, Gatta G, Pritchard-Jones K, Group EW. Incidence of and survival from Wilms' tumour in adults in Europe: data from the EUROCARE study. European journal of cancer. 2006;42(14):2363-8.
4. Lowe LH, Isuani BH, Heller RM, Stein SM, Johnson JE, Navarro OM, et al. Pediatric renal masses: Wilms tumor and beyond. Radiographics. 2000;20(6):1585-603.
5. Sayed HAR, Ali AM, Hamza HM, Abdalla MA. Long-term Follow-up of Infantile Wilms Tumor Treated According to International Society of Pediatric Oncology Protocol: Seven Years' Follow-up. Urology. 2011;77(2):446-51.
6. Watanabe R, Takahashi A, Suzuki M, Toki F, Kanazawa T, Hirato J, et al. Adolescent Wilms Tumor With Intraspinal and Bone Metastases: A Case Report and the Review of Literature. Journal of pediatric hematology/oncology. 2009;31(1):45-8.
7. Corapcioglu F, Dillioğlugil Ö, Sarper N, Akansel G, Çalışkan M, Arısoy AE. Spinal cord compression and lung metastasis of Wilms' tumor in a pregnant adolescent. Urology. 2004;64(4):807-10.

8. Millar AJW, Cox S, Davidson A. Management of Bilateral Wilms Tumours. In: van den Heuvel-Eibrink MM, editor. Wilms Tumor [Internet]. Brisbane (AU): Codon Publications; 2016 Mar. Chapter 5. Available from: https://www.ncbi.nlm.nih.gov/books/NBK373352/ doi: 10.15586/codon.wt.2016.ch5.
9. Grundy P, Wilson B, Telzerow P, Zhou W, Paterson MC. Uniparental disomy occurs infrequently in Wilms tumor patients. American journal of human genetics. 1994;54(2):282-9.
10. Liou P, Bader L, Wang A, Yamashiro D, Kandel JJ. Correlation of tumor-associated macrophages and clinicopathological factors in Wilms tumor. Vascular cell. 2013;5(1):5.
11. Khanna G, Naranjo A, Hoffer F, Mullen E, Geller J, Gratias EJ, et al. Detection of preoperative wilms tumor rupture with CT: a report from the Children's Oncology Group. Radiology. 2013;266(2):610-7.
12. Daniels JL, Pan IJ, Olshan AF, Breslow NE, Bunin GR, Ross JA. Obstetric history and birth characteristics and Wilms tumor: a report from the Children's Oncology Group. Cancer causes & control : CCC. 2008;19(10):1103-10.
13. Duarte RJ, Cristofani LM, Dénes FT, Odone Filho V, Tannuri U, Srougi M. Wilms tumor: a retrospective study of 32 patients using videolaparoscopic and open approaches. Urology. 2014;84(1):191-7.
14. Murthi G, Kocyildirim E, Sellathury S, Cuckow P, Wilcox D, Michalski A, et al. Wilms' tumour with persistent intravascular extension: A review of the surgical aspects of management. Journal of pediatric urology. 2006;2(5):439-45.
15. Kaur N, Gupta A, Attam A, Shrivastava U, Wadhwa N. Adult wilms' tumor: management considerations. International urology and nephrology. 2005;37(1):17-20.
16. Morabito V, Guglielmo N, Melandro F, Mazzesi G, Alesini F, Bosco S, et al. Adult Wilms tumor: Case report. International journal of surgery case reports. 2015;6c:273-6.
17. Okur A, Pinarli FG, Karadeniz C, Poyraz A, Fidan K, Basaklar C, et al. Familial synchronous bilateral teratoid Wilms tumor with elevated alpha-fetoprotein level. Tumori. 2012;98(6):179e-82e.
18. Giannoulia-Karadana A, Moschovi M, Koutsovitis P, Tolis G, Tzortzatou-Stathopoulou F. Inferior vena cava and right atrial thrombosis in children with nephroblastoma: diagnostic and therapeutic problems. Journal of pediatric surgery. 2000;35(10):1459-61.
19. Crump C, Sundquist J, Sieh W, Winkleby MA, Sundquist K. Perinatal risk factors for Wilms tumor in a Swedish national cohort. European journal of epidemiology. 2014;29(3):191-7.
20. Rodrigues FA, Ribeiro EC, Maroccolo Filho R, Silva EA, Diaz FAF. Adult Wilms Tumor During Gestational Period. Urology. 2009;73(4):929. e1-. e2.
21. Bozeman G, Bissada NK, Abboud MR, Laver J. Adult Wilms' tumor: prognostic and management considerations. Urology. 1995;45(6):1055-8.
22. Mitchell C, Pritchard-Jones K, Shannon R, Hutton C, Stevens S, Machin D, et al. Immediate nephrectomy versus preoperative chemotherapy in the management of non-metastatic Wilms' tumour: results of a randomised trial (UKW3) by the UK Children's Cancer Study Group. European journal of cancer. 2006;42(15):2554-62.