

## Wilms' s Tumor: An Example Of Risk-Adapted and Well Tolerated Therapy

Khyati D Shah<sup>1\*</sup> and Peter M Anderson<sup>2</sup>

<sup>1</sup>Tri-county Pediatrics, 165 Amendment Ave, Rock Hill, USA

<sup>2</sup>Cleveland Clinic, Pediatric Hematology/ Oncology and Bone marrow transplant, USA

\*Corresponding author: Khyati D Shah, Tri-county Pediatrics, 165 amendment Ave, Rock Hill, SC 29745, USA, Tel: +1-803-329-2700; Fax: +1- 803-329-2722; E-mail: drkhyati22@gmail.com

Received date: January 12, 2018; Accepted date: March 19, 2018; Published date: March 23, 2018

Copyright: © 2018 Shah KD, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

### Abstract

Wilms tumor (WT) is the most common malignant renal tumor in children. It can present with an abdominal mass and macroscopic hematuria. A 2 year old boy presented with acute onset of bilious vomiting and macroscopic hematuria. He was diagnosed with Stage 4 WT with lung metastasis and treated with risk-adapted therapy. Initial surgery was followed by risk based chemotherapy; lung radiation was needed and he currently remains in remission. Due to the recent advances in treatment based on risk stratification of WT, the overall survival for children diagnosed with WT has increased, but treatment of lung metastases can be challenging.

**Keywords:** Wilms tumor; Nephroblastoma; Hematuria; Abdominal mass; Kidney cancer

### Abbreviations

WT: Wilms Tumor; CT: Computed Tomography; NTWS: National Wilms Tumor Study Group; SIOP: International Society of Pediatric Oncology

### Introduction

WT is the most common renal malignancy in childhood and the second most frequent intra-abdominal pediatric cancer after Neuroblastoma [1,2]. Due to the recent advances in clinical care and management, the overall survival (OS) has increased to 90%. Naturally, for children with distant metastasis the OS is lower but has also improved with risk adapted therapy to >60% [1]. Onset of symptoms can be gradual before asymptomatic abdominal mass is discovered. Other common systemic signs and symptoms can include hematuria, increased abdominal girth, poor appetite, malaise, and microcytic anemia with or without iron deficiency and thrombocytosis. Hypertension, presumably because of increased renin activity, is present in approximately 25% of children with WT [3].

We share our experience with an unusual presentation of Wilms tumor in a 2 year old child with acute onset of bilious emesis and macroscopic hematuria. This child's treatment illustrates many current principles of risk-adapted treatment.

### Case Presentation

2 year old otherwise healthy African American child presented with vomiting for 2 days with green emesis within 30 minutes of eating. He was afebrile and had no diarrhea. His mother reported decrease in oral intake, decrease in wet diapers and 1 episode of "pink stain" on the diaper on the day of presentation. He had a negative history of abdominal pain, recurrent fever, weight loss, fatigue, night sweats or change in behavior. He had a history of constipation and his mother

had previously felt an abdominal mass that seem to decrease in size after having a bowel movement.

On examination, child appeared to be lethargic with tachycardia (134) and had elevated blood pressure (113/86). Abdominal examination revealed a grapefruit sized firm, mobile and non-tender mass in the right upper quadrant. Bowel sounds were normal. Complete blood count showed hemoglobin borderline for his age (11.0 with microcytosis). Comprehensive metabolic panel, serum lipase and ammonia levels were within normal limits. Urine analysis revealed macroscopic hematuria with "red color urine" and more than 100 RBC in urine microscopy results. Abdominal X-ray showed a mass like soft tissue attenuation on right upper abdomen.

CT abdomen and pelvis with contrast was done, which showed a large heterogeneous mass arising from the right kidney, measuring 11 cm × 9 cm, concerning for WT, several bibasilar pulmonary nodules concerning for metastatic disease. CT chest showed 4 pulmonary nodules (3 on the right and 1 on the left, all less than 1 cm in diameter) consistent with lung metastases. He underwent total right nephrectomy. Pathology showed favorable histology in the primary tumor and no evidence of tumor in abdominal lymph nodes sampled. Stage 4 Wilms due to metastatic pulmonary disease with favorable histology was the diagnosis.

He was initially started on the standard of care 3 drug chemotherapy regimen (vincristine, dactinomycin, and doxorubicin) as per Children's Oncology group AREN 0533. When repeat CT Chest done in 6 weeks showed persistence of lung metastases, additional drugs were added (cyclophosphamide and etoposide) as well. He also had whole lung radiation therapy (10.8 Gy). He responded very well to this treatment and currently in remission >2 years.

### Discussion

WT, also known as nephroblastoma, is the predominant renal tumor in children older than 3 months and younger than 6 years. WT has a peak incidence between 2 and 5 years, with 98% diagnosed before age 10 years [4]. There are two distinct histopathologic types of WT -

favorable and unfavorable. The unfavorable type consists of WT with anaplasia and is associated with worse prognosis [3].

WT can also be a component of rare genetic syndromes like WAGR syndrome (WT, aniridia, genitourinary abnormalities, gonadoblastoma, and mental retardation), Denys-Drash syndrome and Beckwith-Wiedemann Syndrome. The WT gene is on the short arm of chromosome 11. Other genes that seem to have an association with WT prognosis are loss of heterozygosity at 16q and p53.

Common clinical presentation includes abdominal distention or pain, a palpable abdominal mass, hematuria, hypertension, anorexia, vomiting and/or malaise [4]. About 5% of children may present with bilateral WT. Approximately 12% of WT patients will have evidence of hematogenous metastases at diagnosis, with 80% having pulmonary metastases [3]. Bone metastases are very rare.

A CT scan of the abdomen and pelvis is generally the imaging study of choice for those patients suspected of having a renal tumor. This will confirm the presence of a solid renal mass and will afford the opportunity to visualize the contralateral kidney to confirm its presence (and function) and to exclude synchronous bilateral disease with a high degree of sensitivity [3]. Accurate staging of patients with WT is imperative and the staging system developed by the National Wilms Tumor Study Group (NWTSG) and currently in use in the COG (Children's Oncology Group) is a surgicopathologic staging system [3]. Historically, the most important prognostic variables for patients with WT have been the histopathologic tumor classification and surgical stage [5].

Improvements in survival with few long term effects have occurred as the result of risk adapted surgery, radiation, and chemotherapy. Current standard of care is based on cooperative group trial results conducted by the International Society of Pediatric Oncology (SIOP) in Europe and NWTSG/COG in North America. Main objectives of these trials and studies are to treat patients according to well-defined risk groups in order to achieve not only high cure rates, but also to decrease the frequency and intensity of acute and late toxicity [6]. The current approach for treatment of WT in North America is to perform surgery followed by risk-based chemotherapy. The treatment strategy in Europe consists of initial neoadjuvant chemotherapy, then nephrectomy and postoperative chemotherapy, and sometimes radiotherapy [7]. Radiation is very effective, but now used only in higher risk situations. Patients with pulmonary metastases that completely respond to initial chemotherapy may be spared whole lung radiation. On the other hand, an incomplete response of lung metastases to initial chemotherapy may require more intense chemotherapy and whole lung radiation. Whole lung radiation can be very effective since WT responds to doses of radiation <12 Gy. Isolated lung relapses can also be treated with stereotactic body radiotherapy (SBRT) in which 1-5 larger fractions are given very precisely to the lung nodule(s).

Successful management of WT necessitates attention to correct staging of the tumor and a collaborative effort between pediatric oncologists, surgeons, radiologists, pathologists, and radiation oncologists [8]. 5HT inhibitors (e.g. ondansetron) and neurokinin inhibitors (e.g. fosaprepitant) have greatly improved immediate and delayed nausea associated with chemotherapy. Chemotherapy drugs commonly used in the treatment of WT include dactinomycin, vincristine and doxorubicin and in higher risk patients also cyclophosphamide and etoposide. Doxorubicin cardiac toxicity can be ameliorated using dexrazoxane. Long term adverse effects of

chemotherapy and radiation are uncommon and can include asymptomatic decrease in lung or kidney function, infertility associated with cyclophosphamide, and secondary malignancies [9]. Because of renal-sparing surgery in bilateral WT, the overall incidence of renal failure in children treated for WT is less than 1% [10]. Approximately 15% of favorable histology and 50% of anaplastic histology WT will recur [11-15] with most relapses occurring quickly – usually within 2 years of diagnosis.

## Conclusion

Significant improvement has been made in the treatment of children with WT using risk-adapted strategies to maintain a high rate of cure while minimizing short, intermediate, and long-term toxicity [3]. Challenges remain in identifying novel molecular, histological and clinical risk factors for additional stratification of treatment intensity [8].

## Conflict of Interest

The authors declare that there is no conflict of interest.

## References

1. Hamilton TE, Shamberger RC (2012) Wilms tumor: Recent advances in clinical care and biology. *Semin Pediatr Surg* 21: 15-20.
2. Khyati DS, Anderson P, Nathalie C (2017) Pediatric Neuroblastoma and Anemia (Jehovah's Witness Case Report). *J Tumor Med Prev* 1: 555569.
3. Davidoff AM (2012) Wilms tumor. *Adv Pediatr* 59: 247-267.
4. Hartman DJ, MacLennan GT (2005) Wilms tumor. *J Urology* 173: 2147.
5. Breslow N, Sharples K, Beckwith JB, Takashima J, Kelalis PP, et al. (1991) Prognostic factors in nonmetastatic, favorable histology Wilms' tumor: Results of the Third National Wilms' Tumor Study. *Cancer* 68: 2345-2353.
6. Reinhard H, Aliani S, Ruebe C, Stöckle M, Leuschner I, et al. (2004) Wilms' tumor in adults: results of the Society of Pediatric Oncology (SIOP) 93-01/Society for Pediatric Oncology and Hematology (GPOH) Study. *J Clin Oncol* 22: 4500-4506.
7. Verschuur A, Van Tinteren H, Graf N, Bergeron C, Sandstedt B, et al. (2012) Treatment of pulmonary metastases in children with stage IV nephroblastoma with risk-based use of pulmonary radiotherapy. *J Clin Oncol* 30: 3533-3539.
8. Szychot E, Apps J, Pritchard-Jones K (2014) Wilms' tumor: biology, diagnosis and treatment. *Transl Pediatr* 3: 12-24.
9. Termuhlen AM, Tersak JM, Liu Q, Yasui Y, Stovall M, et al. (2011) Twenty-five follow-up of childhood Wilms tumor: A report from the childhood cancer survivor study. *Pediatr Blood Cancer* 57: 1210-1216.
10. Lange J, Peterson SM, Takashima JR, Grigoriev Y, Ritchey ML, et al. (2011) Risk factors for end stage renal disease in non-WT1-syndromic Wilms tumor. *J Urol* 186: 378-386.
11. Spreafico F, Pritchard JK, Malogolowkin MH, Bergeron C, Hale J, et al. (2009) Treatment of relapsed Wilms tumors: Lessons learned. *Expert Rev Anticancer Ther* 9: 1807-1815.
12. Berger M, Fernandez-Pineda I, Cabello R, Ramirez-Villar GL, Márquez-Vega C, et al. (2013) The Relationship between the site of metastases and outcome in children with stage IV Wilms tumor: Data From 3 European pediatric cancer institutions. *J Pediatr Hematol Oncol* 35: 518-524
13. Dome JS, Perlman EJ, Graf N (2014) Risk stratification for Wilms tumor: Current approach and future directions. *Am Soc Clin Oncol Educ Book* 2014: 215-223.
14. Green DM (2013) The evolution of treatment for Wilms tumor. *J Pediatr Surg* 48: 14-19.
15. Gracias EJ, Dome JS, Jennings LJ, Chi YY, Tian J, et al. (2016) Association of Chromosome 1q gain with inferior survival in favorable-histology Wilms tumor: A report from the children's oncology group. *J Clin Oncol* 34: 3189-3194.