ORIGINAL ARTICLE

Bilateral Wilms’ tumor with areas of focal anaplasia: a case report

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Abstract  Wilms’ tumor constitutes the large majority of renal tumors in children and bilaterality is observed in 4% to 8% of the cases. The multimodality of treatments for this type of tumor has been the subject of study over the past decades, resulting in a survival rate that is close to that of unilateral Wilms’ tumor. The ultimate goal in treating these patients is the complete removal of all the tumor components and maintenance of good long-term kidney function. The current concept is nephron-sparing surgery with preoperative and postoperative chemotherapy and/or radiotherapy in selected cases. The main benefit of nephron-sparing surgery is the preservation of the renal parenchyma and the reduction of the long-term complications of kidney failure. Presented herein is the case of a 4-year-old girl with bilateral Wilms’ tumor with areas of focal anaplasia that was treated with preoperative chemotherapy, bilateral nephron-sparing surgery, and postoperative radiotherapy in the follow-up.

Tumor de Wilms bilateral con áreas focales de anaplasia: reporte de un caso

Resumen  El tumor de Wilms comprende la gran mayoría de los tumores renales en niños; la bilateralidad es observada en el 4% a 8% de los casos. La multimodalidad de tratamientos para este tipo de tumores ha sido objeto de estudio en décadas pasadas, resultando en una tasa de supervivencia que se aproxima a la de tumores unilaterales. El objetivo final del tratamiento en estos pacientes es la eliminación completa de todos los componentes tumorales y mantenimiento de una buena función renal a largo plazo. El concepto actual es la cirugía conservadora de nefronas con quimioterapia preoperatoria y postoperatoria y/o radioterapia en casos seleccionados. El principal beneficio de la cirugía conservadora de nefronas es la...
Case presentation

A 4-year-old girl from Veracruz was brought by her mother to the emergency department. She had a 3-month progression of asthenia, adynamia, anorexia, weight loss of 3 Kg, fever peaks that did not respond to antipyretic or antimicrobial agents, an increased abdominal perimeter, and epistaxis. She had no past history of urinary symptoms and her blood pressure was normal.

During her initial pediatric evaluation, laboratory tests and radiology studies were ordered. The full blood count showed mild normocytic anemia, the urinalysis reported microscopic hematuria and creatinine of 0.5mg/dL, and electrolytes and liver function tests were normal. The ultrasound study revealed a tumor that was dependent on the middle and upper third of the right kidney. It was rounded and smooth, well defined, moderately echogenic, and heterogeneous due to the presence of irregular lineal hypoechoic and rounded anechoic areas that showed important internal vascularity. The tumor measured 87 x 58 x 57 mm and the portion of the kidney from the hilum towards the lower pole was uninvolved. There was an increase in the size of the left kidney secondary to a tumor with the same characteristics as that of the right kidney, only larger. It measured 126 x 78 x 96 mm, and a scant portion of the inferior parenchyma was uninvolved.

A computerized tomography (CT) scan was ordered that showed bilateral tumors dependent on the two kidneys. The tumor on the left kidney had irregular edges and measured approximately 7 x 5 x 6 cm at its largest diameters and the tumor on the right kidney was rounded with necrotic areas in its interior. Images were taken at the coronal and axial planes (figs. 1 and 2).

The patient was taken to the Pediatric Oncology Department with the abovementioned findings, and biopsy was requested. An incisional biopsy with no complications was performed and revealed a highly vascularized bilateral renal tumor, with great probability of being a nephroblastoma. Chemotherapy was begun based on the fifth National Wilms’ Tumor Study (NWTS-5) protocol. The patient remained clinically stable and chemotherapy was started in the hospital and the cycle was completed with the girl as an outpatient. She presented with alopecia due to the chemotherapy, but otherwise was practically asymptomatic. The pathology study reported a triphasic nephroblastoma (Wilms’ tumor) with focal anaplasia.

Once the patient completed the 6 weeks of chemotherapy, she was readmitted for pediatric urologic evaluation. A CT scan revealed a low-density right kidney interpolar anterior lesion measuring 33 x 30 x 29 mm with a mean density of 40 HU that did not affect the pyelocaliceal system. The lesion on the left kidney measured 45 x 34 x 39 mm and the density in the upper pole ranged from 35 to 40 HU, affecting the upper pyelocaliceal system (figs. 3 and 4). Both kidneys showed contrast medium excretion through the ureters that collected in the bladder. Small nodulations arising from the lymph nodes were located in the para-aortic region at the level of the renal hilum. A kidney scintigram was done to evaluate kidney function using the radiopharmaceutical, Tc99m DTPA (TechneScanMAG3™). Perfusion was synchronous, but not as asymmetric for the left kidney. The right kidney was normal in shape, size, and location with adequate concentration of the radiotracer, the capillary and venous phases and transit were satisfactory, with a slow and prolonged elimination curve. The left kidney was situated normally, diminished in size, the usual morphology was modified, and the concentration of the radiotracer was slightly reduced, the capillary and venous phases and renal transit were adequate with a deficient elimination curve. The left kidney was 35.72mL/min (45% contribution), and the GFR of the right kidney was 42.34mL/min (54% contribution).

A nephron-sparing bilateral nephrectomy was performed (bilateral heminephrectomy) and it revealed a solid right kidney tumor of approximately 60 x 40 mm that encompassed part of the inferior vena cava and a left kidney tumor of approximately 80 x 60 cm with multiple adherences. The patient was stable after surgery and placed in the pediatric intensive care unit (PICU). Her immediate and mediate postoperative progression was favorable (figs. 5 and 6). Uresis of 1 to 1.5 mL/Kg/h was reported with no...
complications and the patient was released into the pediatric urology ward. Her progression continued with no complications and she was released from the hospital and sent home. The histopathologic report on the surgical specimens from the partial heminephrectomy stated Wilms’ tumor with areas of focal anaplasia and no neoplastic lesion in the surgical margins.

Discussion

Wilms’ tumor makes up the large majority of kidney tumors in children and bilateralism is observed in only 4% to 8% of the cases. Treatment multimodality for this type of tumor has been studied over the past decades and as a result, the survival rate approaches that of unilateral Wilms’ tumor.1,2 The treatment goals for a child with bilateral Wilms’ tumor are to completely eradicate the tumor and spare as much normal kidney tissue as possible, in the hope of reducing the risk for chronic kidney failure.3 In the NWTS-4 study, patients with bilateral Wilms’ tumor had a lower disease-free survival (DFS) rate and overall survival (OS) when compared with the patients with localized Wilms’ tumor (including those of anaplastic histology), with the exception of the patients with stage IV disease. In those patients OS was higher than that of the patients with bilateral Wilms’ tumor. The NWTS-4 study reported that complication-free survival (CFS) at 8 years in patients presenting with bilateral Wilms’ tumor that had favorable histology was 74% and the OS was 89%; in relation to anaplastic histology, the CFS was 40% and the OS was 45%.4 In the NWTS-5 (COG-Q9401) study, the CFS at 4 years in patients with bilateral Wilms’ tumor was 61% and the OS was 81%; in the cases of anaplastic histology, CFS was 44% and the OS was 55%.5,6 Similar results were reported in a study conducted at a single institute in Holland on patients with bilateral Wilms’ tumor with an OS at 10 years of 78% (n = 41), and there was significant morbidity in terms of kidney failure (32%) and secondary tumors (20%).7 The incidence of end-stage kidney failure could be reflected in the fact that the Dutch study had a longer follow-up period.

Treatment has changed from an initial surgical approach to preoperative chemotherapy, in an attempt to reduce tumor size and spare the renal parenchyma. The first COG trial that formally studied bilateral Wilms’ tumors reflects the current recommendation of not performing an initial biopsy or laparotomy. Primary excision of the tumor should not be attempted; instead patients should be given preoperative chemotherapy containing vincristine, dactinomycin, and doxorubicin. In a case series of 49 patients with Wilms’ tumor that received preoperative therapy according to the SIOP-93-01 guidelines, it was established that surgery should be performed when there were no more signs of tumor regression through imaging studies. The treatment duration median was 80 days prior to nephron-sparing surgery. The CFS rate at 5 years was 83.4% and the OS was 89.5%. All patients except one underwent nephron-sparing surgery in at least one of the kidneys. Despite the good survival rate, 14% of the patients presented with end-stage kidney disease.8 Just as was described in a retrospective review conducted at the St. Jude Children’s Research Hospital, in another case series 9 out of every 10 patients with bilateral Wilms’ tumor with favorable histology successfully underwent bilateral nephron-sparing procedures after receiving preoperative chemotherapy.9 One patient of the case series presented with kidney failure after the bilateral nephron-sparing surgery. Two patients that had anaplastic histologies died, although the death of one of them was due to treatment complications. The OS for this group of patients was 83%. Those authors recommend that bilateral nephron-sparing surgery should be considered in all patients presenting with bilateral Wilms’ tumor that have favorable histology, even when preoperative imaging studies indicate that the lesions are inoperable.9

For the patients receiving preoperative chemotherapy, it is essential to evaluate the pathologic anatomy of the tumor after 4 to 8 weeks. The ideal time for performing biopsy or

![Figure 2](image-url) Axial view in computed tomography scan showing both kidneys with large tumor volume.

![Figure 3](image-url) Coronal view in excretory tomography scan showing left kidney lesion in the upper pole, measuring 45 x 34 x 39 mm.
Resection in patients whose treatment has not followed a protocol is not clear, because the minimal reduction of the tumor can reflect the differentiation or anaplastic histology induced by chemotherapy.

Nevertheless, continual therapy with no evaluation of the tumor pathology in a patient with bilateral Wilms’ tumor can increase the secondary effects with no additional benefit for tumor control. Anaplastic histology presents in 10% of the patients with bilateral Wilms’ tumor and responds precariously to chemotherapy. Once the diagnosis is made, complete resection should be carried out. The diagnosis is not made directly; in an NWTS-4 case series of 27 patients, there was discordant pathology in 20 of them. This underlines the necessity for obtaining tissue from both kidneys. Seven children that over time were found to present with diffuse anaplastic tumors underwent central biopsies in order to establish the diagnosis, but the anaplasia was not found in the central biopsies. Anaplasia was identified in only 3 out of 9 patients when an open wedge biopsy was performed, and in 7 out of 9 patients that underwent partial or total nephrectomy.

Conclusions

The treatment goal in bilateral Wilms’ tumor is the removal of tumor tissue and the preservation of kidney function. This is being achieved today through initial chemotherapy followed by nephron-sparing surgery. Modern chemotherapeutic regimens produce survival rates of 90% and this success has brought about a change of emphasis in regard to reducing toxicity. Although there are different philosophies regarding preoperative chemotherapy in the United States and Europe, the main message is that the majority of patients with bilateral Wilms’ tumor can have long-term survival, regardless of the sequence of the therapeutic interventions. Despite this success, there are still patients in whom the current treatment is suboptimal and includes those patients presenting with bilateral anaplastic or recurring disease.

Conflict of interest

The authors state that there is no conflict of interest.
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References