Case Report

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Multimodal Tumor Therapy in a 31-Year-Old Pregnant Woman with Wilms Tumor

T. Maurer[a] C. Zorn[a] E. Klein[b] G. Weirich[c] A.J. Beer[d] J.E. Gschwend[a] N. Zantl[a]

Departments of [a]Urology, [b]Gynecology, [c]Pathology and [d]Radiology, Technische Universität München, Klinikum rechts der Isar, Munich, Germany

Key Words
Chemotherapy · Nephroblastoma · Pregnancy · Surgery · Wilms tumor

Abstract
Wilms tumor, or nephroblastoma, is the most common malignant tumor of the urinary tract in children, but is rarely found in adults. Here, we report the first case of a female patient with a Wilms tumor, diagnosed during pregnancy, who underwent radical nephrectomy and adjuvant chemotherapy before and after delivering a healthy child. Generally, treatment should follow the guidelines established for the pediatric setting. Copyright © 2009 S. Karger AG, Basel

Introduction

Wilms tumor, or nephroblastoma, is the most common malignant tumor of the urinary tract in children but is rarely found in adults with an incidence rate of <0.2 per million per year and only about 300 cases described in the literature. Presently, a high cure rate can be achieved in children with multimodal therapy regimes, even in patients with advanced stages of the disease. Wilms tumor in adolescents or adults was long thought to have a worse prognosis at all stages of the disease. However, a recent retrospective pooled analysis of the National Wilms Tumor Study (NWTS) demonstrated comparable survival rates in adult Wilms tumor patients if treatment followed the guidelines established for children [1], a finding confirmed by the Society of Pediatric Oncology (SIOP) [2].

However, treatment of Wilms tumor patients during pregnancy remains a great challenge to the clinician with only a few cases described in the literature [3–6]. Here, we report for the first time on a female patient with a Wilms tumor, diagnosed during pregnancy, who underwent multimodal therapy before and after delivering a healthy child.

Case Report

A 31-year-old native African woman from Ghana was admitted during her third pregnancy at 18 weeks gestation complaining of persistent hyperemesis gravidarum. Her general and obstetrical history was uneventful; she had already delivered 2 healthy children. Laboratory findings including urine analysis, as well as the ultrasound scan of the fetus were normal. The patient displayed no hematuria or flank pain or any other urological symptom. A routine abdominal sonography revealed an 8 × 6 × 4 cm mass in the lower pole of the right kidney (fig. 1).

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Tobias Maurer, MD
Department of Urology, Technische Universität München
Klinikum rechts der Isar, Ismaninger Strasse 22
DE–81671 Munich (Germany)
Tel. +49 89 4140 2522, Fax +49 89 4140 4818, E-Mail t.maurer@lrz.tum.de

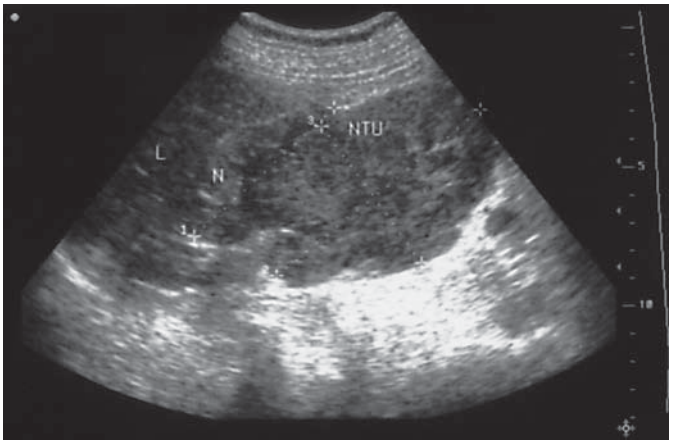

Fig. 1. Ultrasound showing the right kidney with a large mass evolving from the lower pole. L = Liver; N = kidney; NTU = tumor of the kidney.

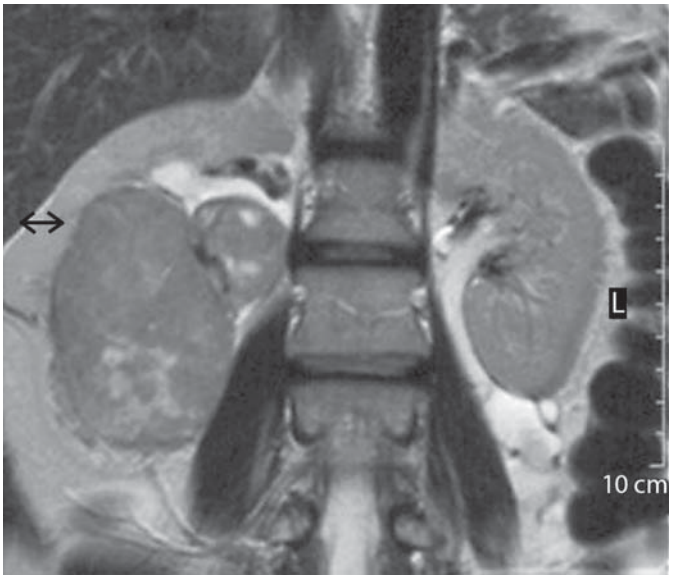

Fig. 2. T2-weighted pulse sequence (coronal plane) shows the large lobulized tumor mass of the right kidney with areas of hemorrhage and necrosis.

MRI confirmed the diagnosis of a large tumor of the right kidney suspicious for a renal cell carcinoma or nephroblastoma (fig. 2). Subsequently, radical nephrectomy without adrenalectomy was performed at 19 weeks of gestation. Pathologic analysis showed a Wilms tumor of the right kidney invading the renal pelvis, classified stage II according to the NWTS-5 (fig. 3). Estrogen and progesterone receptors were not expressed in the tumor.

The patient received chemotherapy with vincristine 1.5 mg/m^2 weekly (maximum 2 mg) and 45 μg/kg dactinomycin (maximum 2 mg) every 3 weeks from 22 weeks gestation (fig. 4). Prior to every chemotherapy application, fetal sonography and cardiotocography and routine laboratory values were performed. The fetus developed adequately. Despite alopecia, nausea with vomiting and recurrent abdominal pain, no side effects were observed. Supportive treatment with antiemetics (metoclopramide, granisetron), laxatives (bisacodyl) and mild analgesics (paracetamol) was administered as needed.

At 32 weeks gestation the abdominal pain aggravated, predominately during fetal movements. Cesarean section was performed at 33 weeks of gestation after sufficient lung maturation of the fetus. The child was a healthy boy of 2,400 g, adequately developed for gestational age, APGAR 8 and 9 after 5 and 10 min. Except for mild anemia he did not show any signs of bone marrow suppression.

After delivery chemotherapy was continued with vincristine 1.5 mg/m^2 (maximum 2 mg), dactinomycin 45 μg/kg (maximum 2 mg) every 3 weeks and doxorubicin 50 mg/m^2 (maximum cumulative dosis 300 mg) every 6 weeks for 6 additional cycles. No severe adverse effects were observed. At the 4-year follow-up the mother showed no evidence of disease and the child had developed normally.

Discussion

Preoperative diagnosis of an adult Wilms tumor is difficult as no typical radiographic signs, tumor markers or clinical presentation exist that can distinguish it from a more common renal cell carcinoma. Furthermore, because of the rarity of the disease, adults with Wilms tumors are at risk of either under-treatment or incorrect treatment. The poor compliance to the existing therapeutic guidelines established for children may, at least partly, explain the worse prognosis of this patient group [7]. It has been repeatedly reported that significant survival improvement can be achieved in adult patients if the multimodal treatment protocols used in pediatric settings are employed in adult patients [2]. The most recent update on treatment outcomes in adults with favorable histological type Wilms tumor from the NWTS group showed a 5-year relapse-free survival of 77.3% and a disease-specific survival of 95.7% [3]. Treatment toxicity is higher than in children, but acceptable in terms of high remission rates [2]. As this tumor entity is rarely observed in adults, it is recommended that all patients be entered into the study protocols of the NWTS or SIOP.

Wilms tumor diagnosed during or after pregnancy is extremely rare, with only a few cases reported in the literature [3–6]. One 19-year-old female patient with a favorable histology Wilms tumor underwent perioperative chemotherapy with vincristine, dactinomycin and doxorubicin postpartum. 16 years later she again presented

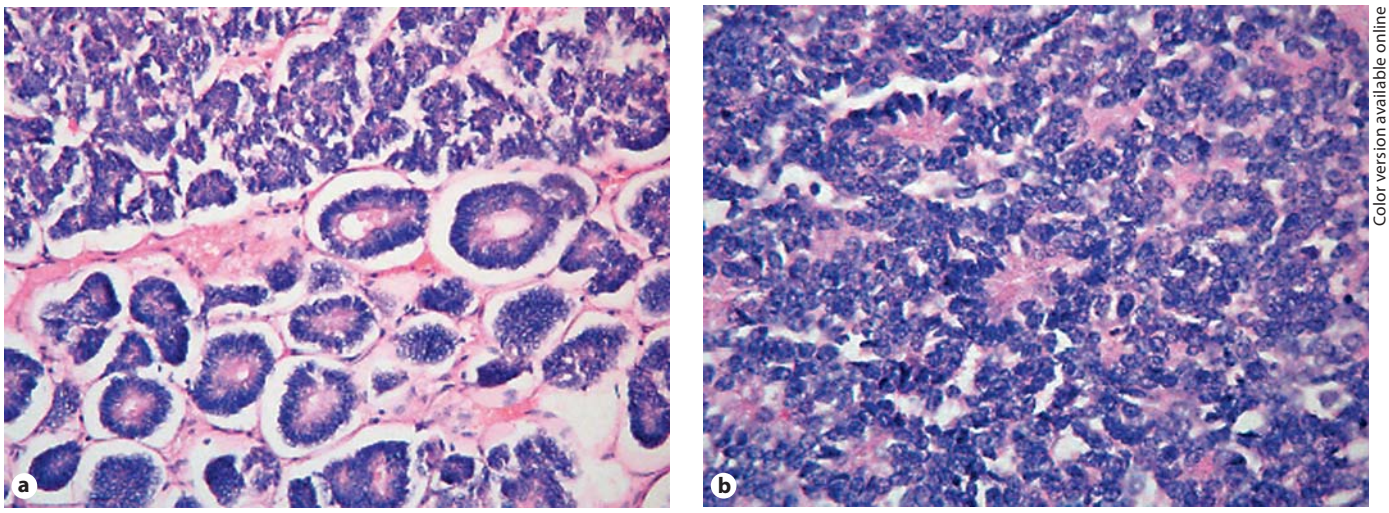

Fig. 3. a Solid (upper half) and glandular (lower half) growth pattern of tumor cells. HE. ×200. **b** Homer-Wright rosettes characteristic for neuroblastic differentiation as found in nephroblastoma. HE. ×400.

with a Wilms tumor in the contralateral kidney after pregnancy. Following neoadjuvant chemotherapy with the same regimen, a left nephrectomy and intraoperative irradiation therapy were undertaken. After the operation the patient required hemodialysis and expired 6 months later with no adjuvant chemotherapy initiated [5]. Another 19-year-old patient with a stage IIa Wilms tumor received no adjuvant chemotherapy after left nephroureterectomy and presented with local and distant recurrences (lung, vertebrae, paraspinal mass) causing motor deficit, pain, weakness and paresthesia of the right lower extremity 8 months later at 25 weeks gestation. A chemotherapy regime of vincristine and dactomycin was initiated. After delivery and irradiation of the tumor bed, chemotherapy was extended with ifosfamide, carboplatin, etoposide and cyclophosphamide. The authors reported complete remission without any signs of fetal toxicity [4].There is only anecdotal experience on chemotherapy of adult Wilms tumor patients during pregnancy [4]. Thus cytotoxic therapy remains a challenge. Chemotherapy during pregnancy is possible as is known from treatment of tumors found more frequently during women's reproductive age, such as breast cancer or hematologic diseases. For the perfect selection of cytotoxic drugs, detailed knowledge of the toxicity and risk of teratogenity for the fetus is crucial. Determining the adequate dosage poses major difficulties due to pharmacokinetic changes during pregnancy, but nevertheless should be selected to reach therapeutic doses in order to avoid recurrences [8].

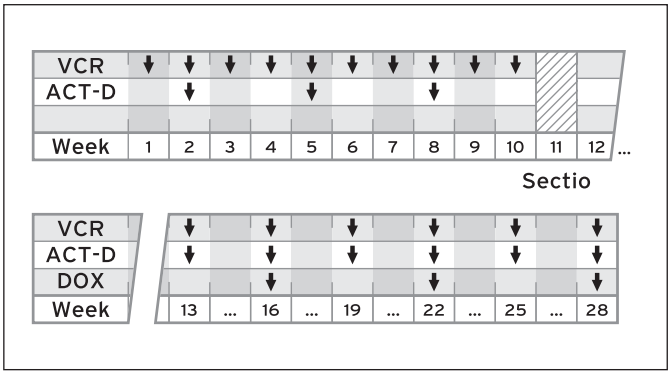

Fig. 4. Overview of chemotherapy treatment. VCR = Vincristine; ACT-D = actinomycin-D; DOX = doxorubicin.

In children born to mothers who received chemotherapy during pregnancy due to hematological malignancy, birth weight, learning and educational performance were normal, and no congenital, neurological, or psychological abnormalities were noted. With a median follow-up of 18.7 (range 6–29) years no cancer or acute leukemia was observed. The authors of this study conclude that chemotherapy at full dosage can be safely administered during pregnancy, even during the first trimester [9]. However, as only a few cases have been published, there are only limited data concerning long-term effects of intrauterine cytotoxic therapy on the offspring.

There are no controlled trials on surgical management of cancer in pregnancy. Surgical interventions pose some risk to the fetus, especially laparotomy for abdominal tumors and procedures undertaken during the first trimester. If indicated, surgery should be performed in the second trimester since the risk of involuntary induction of labor and subsequent abortion is minimized. Intraoperative monitoring of the fetus as well as the use of tocolytics should be considered on a individual basis [10].

As the preoperative diagnosis of an adult Wilms tumor is difficult, we primarily recommend radical surgical resection for histological diagnosis. Radical surgery can be safely performed during pregnancy. Postoperative adjuvant chemotherapy with vincristine and dactinomycin can also be administered during pregnancy. Induction of labor and premature termination of gravidity without harming the fetus, though, may seem reasonable.

In conclusion, to provide maximum patient benefit, treatment of nephroblastoma in adults should always follow the guidelines established for the pediatric setting.

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