Is Nephron-Sparing Surgery in the Treatment of Unilateral Wilms’ Tumor Justified?

Abstract

Objectives. Estimation of the efficiency and radicalism of nephron-sparing surgery in 10 children with unilateral Wilms’ tumor stage I disease after preoperative chemotherapy or with metachronous bilateral Wilms’ tumor (BWT) who previously underwent nephrectomy because of tumor.

Material and Methods. In 6 children with unilateral WT, in 1 with the tumor of a solitary kidney, and in 3 with metachronous BWT, resection of the tumor (in 9) and enucleation (in 1) with renal preservation were performed. The resected tumors were mostly localized peripherally on the lower or upper pole of the kidney. Criteria for resec−

Conclusions. Partial nephrectomy in unilateral Wilms’ tumor is recommended only in very selected patients with well-responding stage I tumor when the resected margin of the tumor in the kidney is clear. In the case of developed tumor in a solitary kidney, nephron-sparing surgery is the method of choice (Adv Clin Exp Med 2008, 17, 1, 77–82).

Key words: Wilms’ tumor, nephron-sparing surgery, children.
The oncological effectiveness of nephron-sparing surgery and its role in the management of unilateral Wilms’ tumor in children has been widely disputed [4, 6, 9, 15, 16]. The risk of local recurrence in patients with a low stage I disease and low-risk histology after radical nephrectomy is minimal and the five-year survival rate is 90% of cases. Similarly, the risk of postoperative complications following radical surgery is lower than in nephron-sparing operations: partial nephrectomy or an enucleation of the tumor. However, these results were obtained in retrospective research [2–4].

In the 1980s, data collecting procedures were started in order to gather information about the long-term side effects of anticancer treatment in children cured of malignancies. Wilms’ tumors were also taken into account. The research indicated that unilateral nephrectomy in a child might damage the contralateral kidney because of hyperperfusion and substitute-force hyperfiltration, which may be responsible for the production of focal segmental glomerulosclerosis. This was first noted by Hosetter et al. in an experiment carried out on animals [3, 5]. Clinical research corroborated the observation that hyperfiltration might be responsible for premature renal damage of a healthy kidney in children who have undergone unilateral nephrectomy for Wilms’ tumor [6–8, 13, 14, 16]. In all such cases, focal segmental fibrosis of the parenchyma of the healthy kidney may proceed [13].

The question is whether it is advisable to remove the whole kidney even if the tumor is small, does not exceed the fibrous bag of the kidney, or its localization is polar and the remaining part of the kidney is not affected. The present authors’ previous report presented the first five-year clinical observation of a three-year boy with unilateral stage I Wilms’ tumor who had successfully undergone surgery removing the pole of the kidney, but sparing the remaining two thirds of its parenchyma [10–12]. In two reports [10, 11] the present authors also discussed both the indications and contraindications for nephron-sparing operations in children with Wilms’ tumor. The aim of the following study is to evaluate the effectiveness of treatment involving nephron-sparing surgery in 10 children registered by the First Polish Wilms’ Tumor Study Group in the period from 1995 to 2003.

**Material and Methods**

Between January 1995 and February 1, 2003, 500 patients aged from 0 to 16 years, 22 with bilateral tumor and 478 with unilateral Wilms’ tumor, were treated according to the protocol in 10 Polish Pediatric Oncology Units. The treatment protocol, which was similar to that proposed by the SIOP (Societe Internationale d’Oncologie Pediatrique), included total delayed nephrectomy after preoperative chemotherapy in all patients older than six months. The therapy consisted of vincristine (VCR) 1.5 mg/m² on days 1, 8, 15, and 22 and actinomycin D (AMD) 0.015 mg/kg on days 1–3 and 15–17. At the time of surgery, 7 of the 10 patients had stage I and 3 had stage II disease. Initial investigations included abdominal ultrasoundography before and after the chemotherapy, computed tomography and chest radiography, as well as the measurement of laboratory parameters and urinary catecholamine estimation. Tumor volumes were calculated before and after the end of preoperative chemotherapy according to the SIOP recommendation.

After the completion of preoperative chemotherapy, resection of the tumor was performed. The final decision for renal preservation was made at the time of operation by the surgeon and oncologist to ensure free margins and good postoperative renal function. All the operations, with one exception, were performed on a kidney with good blood circulation. In one patient with metachronic BWT, when the tumor was localized centrally the blood circulation was stopped for 15 minutes by clamps which fixed the artery and renal vein. The kidney was cooled with physiological solution to a temperature...
of 15°C. Single sutures were used on the renal parenchyma after mechanical homeostasis, performed with the use of a harmonic knife, and the renal collecting system, which had to be repaired.

Histological examinations of all the tumors included estimation of the percent degree of tumor cell necrosis, definition of the histological type of the tumor according to the SIOP classification, and microscopic investigation of the tumor margin. All the patients received postoperative chemotherapy as recommended by the protocol for stage II, which consisted of two drugs (VCR, AMD), which lasted 22 weeks. One patient who relapsed after eight months received three-drug therapy (VCR, AMD, DOX) and radiotherapy of 15 Gy. Follow-up investigations included urine analysis, renal function tests, blood pressure monitoring, and abdominal ultrasonography.

Retrospective evaluation of the therapeutic results was carried out for the 10 patients aged from 2 months to 8 years who underwent partial resection for polar tumors. There were 5 males and 5 females among the patients. In 6 of them a unilateral tumor of the kidney was diagnosed, in 3 it was a tumor of the remaining contralateral kidney (metachronous BWT). In one patient the tumor developed in one healthy kidney. The other was dysplastic, small, and inefficient. The diagnosis in all the patients was based on ultrasonography and CT. In six patients the tumor were resected entirely by lower pole nephrectomy with a wide resection margin macroscopically free of tumor. In three patients it was the upper pole that was cut out. One patient of these three also had a double upper caliceal-pelvic system removed. In one patient with a metachronous tumor of the right kidney, enucleation of the tumor and its pseudo-capsule was removed with the use of a harmonic knife. In all patients the frozen-section biopsy with pathological examination confirmed that there were no tumor cells in the margin of remaining parenchyma of the resected kidney. The lymph nodes as well as the perirenal fat were free of tumor.

Results

No postoperative complications were observed after nephron-sparing surgery. Bleeding from the place where the tumor was located was moderate. A Redon’s drain introduced in the area of the operated kidney was removed 48 hours after the operation in all the patients. The healing process proceeded normally. No secretory dysfunction of the kidney was observed in the close postoperative period nor was it noticed in the remote postoperative period. The observation time for eight patients varied from 4 to 8 years. In one patient there appeared a local recurrence of the tumor. Nephrectomy was applied in this case. The results with respect to the diagnostic procedures, tumor localization, surgical treatment, and the histopathological examinations are presented in Tables 1 and 2.

Discussion

Radical tumor nephrectomy has become a “gold standard” in the treatment of patients with Wilms’ tumor, whereas partial nephrectomy is still controversial. In recent years, however, many authors have pointed out that the preoperative administration of chemotherapy in unilateral Wilms’ tumor patients as proposed by the SIOP has reduced tumor volume, size, and stage, prevented intraoperative tumor rupture, and facilitated the performance of nephron-sparing surgery in selected patients with stage-one disease [4, 6, 9, 11, 12, 16].

There has been much research on the application of a nephron-sparing surgical procedure in the treatment of bilateral Wilms’ tumors [11], where tumors develop simultaneously in both kidneys. The choice of an operative technique depends on the anatomical situation caused by tumor localization in two kidneys. The aim is to spare the largest possible part of the healthy parenchyma. It has to be remembered that in these children the surgical treatment is always carried out after long preoperative chemotherapy.

Nephron-sparing surgery in the treatment of unilateral Wilms’ tumor in children has not been studied as thoroughly so far. However, the problem seems equally important. Italian and German pediatric oncologists are the most experienced with respect to the problem [4, 15, 16]. Since 2003, Cozzi et al. [4] have published reports on 32 patients who underwent polar resections, enucleation of tumor from the renal parenchyma, or segmental or wedge-like resection of tumors. Long-term remission was achieved in many cases and a number of patients were cured. Recently, the same authors presented further observations on the development of the saved part of the kidney in children who had had a nephron-sparing operation because of Wilms’ tumor. The results were compared with those obtained for children with double renal calliceo-pelvic system removal. In both groups, part of the kidney together with the deficient secretory system was removed, but a substantial, functionally efficient part of the kidney was spared. In contrast to radical operations such as extended nephrectomy, which is a routine procedure in cases of renal cancer, no excessive com-
Pensatory growth of the other, healthy kidney on the opposite side was observed after nephron-sparing surgery. In the two groups mentioned above, the measurements of the renal volume in relation to the patient’s height and body weight were taken. The results were compared with parameters characterizing healthy children with two efficient kidneys. The research indicated that the degree of compensatory growth in the healthy kidney depends on the extent of the operation, i.e. on the amount of the removed parenchyma of the inflicted kidney, no matter whether it is removed because of the tumor or because of congenital malformations and developmental defect. It seems then that the nephron-sparing procedure is highly recommendable if there exist anatomical as well as oncological indications for such an operation [15].

Equally favorable results were achieved in five patients in Austrian medical centers of pediatric oncology. Urban et al. [9] reported five patients with stage I Wilms’ tumor who had undergone nephron-sparing surgery and were finally cured. The authors mentioned above emphasize the role of preoperative chemotherapy, which considerably diminished the volume of the tumor and facilitated the surgery. The conclusion is that children with stage I Wilms’ tumor which was significantly reduced (13–23%) after preoperative chemotherapy should be selected for a nephron-sparing operation. In the case of these five children aged 1 to 5 years, nephron-sparing surgery was found technically feasible in the course of the operation. The diameter of the tumor was below 4 cm, the tumor was restricted to one renal pole, and the spared part of the kidney constituted more than 50% of the parenchyma. All the children survived for five years without any symptoms of disease. They can thus be regarded as cured, and radical nephrectomy was not necessary.

Similarly, Moorman-Voestermans et al. [6] point to the beneficial influence of pre-operative chemotherapy, which makes it possible to qualify

Table 1. Patients characteristic and outcome

<table>
<thead>
<tr>
<th>Age, sex (Wiek, płeć)</th>
<th>Side, stage (Strona, stadium)</th>
<th>Ultrasound (USG)</th>
<th>Surgery (Leczenie chirurgiczne)</th>
<th>Outcome (Wynik leczenia)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 mo, f left lower pole stage I</td>
<td>3.3 × 2.8 × 2.9 V = 14.01 cm³ 2.8 × 2.5 × 2.5 V = 9.1 cm³</td>
<td>resection of lower pole</td>
<td>ANED 9 y</td>
<td></td>
</tr>
<tr>
<td>7 mo, m left upper pole stage I</td>
<td>6 × 5.5 × 3.4 V = 65.83 cm³ 5 × 5 × 3 V = 39 cm³</td>
<td>resection of upper pole</td>
<td>ANED 8 y</td>
<td></td>
</tr>
<tr>
<td>8 y, m right lower pole stage II</td>
<td>7.7 × 6.4 × 6 V = 154.6 cm³ 7 × 6 × 5 V = 109 cm³</td>
<td>resection of lower pole</td>
<td>marginal recurrence after 2 years chemotherapy + nephrectomy ANED 6 y</td>
<td></td>
</tr>
<tr>
<td>21 mo, m right lower pole stage I</td>
<td>4 × 2.9 × 3.6 V = 61.42 cm³ 2.8 × 2.5 × 3 V = 10.98 cm³</td>
<td>resection of lower pole</td>
<td>ANED 5 y</td>
<td></td>
</tr>
<tr>
<td>5 mo, f right lower pole stage I</td>
<td>4 × 4.5 × 3 V = 54.94 cm³ 3.5 × 3.8 × 2.3 V = 15.99 cm³</td>
<td>resection of lower pole</td>
<td>ANED 7.5 y</td>
<td></td>
</tr>
<tr>
<td>20 mo, f left upper pole stage I</td>
<td>3.9 × 3.8 × 3.3 V = 25.57 cm³ 3.2 × 3 × 2.6 V = 13.95 cm³</td>
<td>resection of upper pole</td>
<td>ANED 8 y</td>
<td></td>
</tr>
<tr>
<td>2 y, m left lower pole stage I</td>
<td>1.9 × 2.6 × 2.6 V = 6.17 cm³ 1 × 2.3 × 2 V = 2.4 cm³</td>
<td>resection of lower pole</td>
<td>ANED 7 y</td>
<td></td>
</tr>
</tbody>
</table>

ANED – Alive, No Evidence of Disease.
ANED – obecnie bez objawów choroby.
an increasing number of children with unilateral Wilms’ tumor for a nephron-sparing procedure. Yet this number is still not very high. Out of 79 children with Wilms’ tumor treated in a Dutch oncological center in Amsterdam, only 8 (8.8%) were administered a nephron-sparing procedure which was radical in microscopic terms. In a corpus of 533 patients aged 0 to 16 years registered at Polish oncological centers because of renal cancer, only 8 children with stage I Wilms’ tumor and 2 children with metachronous tumor were applied the nephron-sparing operation.

The analysis of Table 1 illustrating the material of the present study revealed that polar localization of the tumor and good response to preoperative chemotherapy were the principal indications for nephron-sparing surgery. There were two groups of children in whom such surgical strategy was considered. First, patients with small stage I unilateral tumor affecting only the pole of the kidney and, second, children with stage I Wilms’ tumor and 2 children with metachronous tumor were applied the nephron-sparing operation.

The initial decision selecting patients for nephron-sparing operation should be made collectively by all the physicians involved, both in the diagnostic procedures and in the treatment. The final decision belongs to the surgeon at the time of operation after local evaluation of the extent of the tumor.

Table 2. Patients characteristic and outcome

<table>
<thead>
<tr>
<th>Age, sex (Wiek, płeć)</th>
<th>Side, stage (Strona, stadium)</th>
<th>Ultrasound (USG)</th>
<th>Surgery (Leczenie chirurgiczne)</th>
<th>Outcome (Wynik leczenia)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 mo, f</td>
<td>left upper pole metachronous stage I post chem.</td>
<td>3 × 2 × 2.5 V₁ = 7.84 cm³ 2.8 × 2 × 1.2 V₂ = 3.51 cm³</td>
<td>resection of upper pole</td>
<td>ANED 3 y</td>
</tr>
<tr>
<td>2 y, f</td>
<td>left lower pole metachronous stage II post chem.</td>
<td>3.5 × 4 × 3.5 V₁ = 25.63 cm³ 3.4 × 3 × 2.6 V₂ = 13.87 cm³</td>
<td>resection of lower pole</td>
<td>ANED 6 y</td>
</tr>
<tr>
<td>5 y, f</td>
<td>right middle part metachronous stage II post chem.</td>
<td>7 × 6 × 5 V₁ = 109.83 cm³ 2 × 1.5 × 1 V₂ = 1.57 cm³</td>
<td>enucleation of tumor</td>
<td>ANED 5.5 y</td>
</tr>
</tbody>
</table>

ANED – Alive, No Evidence of Disease.
Metachronous – metachronous Wilms’ tumor.
ANED – obecnie bez objawów choroby.
Metachronous – metachroniczny.

we considered that this patient had been wrongly qualified for nephron-sparing surgery. First, the tumor presented a large volume on initial imaging studies. Its post-chemotherapy evaluation showed only moderate reduction of its initial volume of 30%. Secondly, according to the histopathology report of the respective specimen, regressive and/or necrotic changes induced by chemotherapy were present only in 20% of the tumor tissue.

It appears from the present authors’ experience that a nephron-sparing procedure should be recommended for small-sized unifocal tumors located in the area of one of the renal poles. For centrally located tumors, partial removal is dubious because the cutting line has to be very cautious so as not to damage the blood vessels inside the kidney and the storage system.

As mentioned above, a reduced volume of the tumor in the course of preoperative chemotherapy gives a greater chance for successful partial nephrectomy with no recurrence. In view of the risk of recurrence, the present authors believe that histopathological examination should be carried out inter-operatively in order to confirm the oncological clear margin in the area of the removal. The initial decision selecting patients for a nephron-sparing operation should be made collectively by all the physicians involved, both in the diagnostic procedures and in the treatment. The final decision belongs to the surgeon at the time of operation after local evaluation of the extent of the tumor.
tumor, the structure of the blood vessels, and the technical feasibility of heminephrectomy.

The SIOP recommends a nephron-sparing procedure only for selected cases of unilateral tumors when the peripheral character of the disease makes it fully controllable. Potential candidates for the operation are patients with coexisting defects of the other kidney, patients with genetically conditioned diseases who are prone to Wilms’ tumor, and patients with tumor on the only kidney. SIOP experts do not recommend a nephron-sparing procedure in any other patients with stage-one Wilms’ tumor [17]. The stance adopted by the SIOP assumes that in selected cases, partial nephrectomy makes it possible to control the disease.

In the National Wilms’ Tumor Study Group only four groups of patients with Wilms’ tumor are qualified for nephron-sparing surgery: those with aniridia, genitourinary malformations, and syndromes such as Beckwith Wiedemann and other overgrowth syndromes, in whom the risk of renal insufficiency or recurrence is high. Ritchey et al. concluded that partial nephrectomy is perhaps unjustified in stage one Wilms’ patients.

In conclusion the clinical experience of the present authors allows them to recommend a nephron-sparing surgery in the treatment of very selected children with very small stage-one unilateral Wilms’ tumor successfully reduced by preoperative chemotherapy and localized within a pole of the kidney. Partial nephrectomy in unilateral Wilms’ tumor in general cannot yet be recommended, but it promises to be a reasonable alternative surgical strategy to tumor nephrectomy in very selected patients. Children with a solitary kidney should be selected for this procedure. While enucleation cannot be recommended as a safe procedure in unilateral Wilms’ tumor, this procedure or kidney-sparing resection after preoperative chemotherapy remains the surgical procedure of choice in bilateral WT because it saves this patient from dialysis and renal transplantation.

References

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