Journal of Pediatric Surgery (2006) **41**, 168–172

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Journal of Pediatric Surgery

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Primary hepatic metastases in nephroblastoma—a report of the SIOP/GPOH Study

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Index words:
Nephroblastoma;
Liver;
Metastases;
Surgery;
Children

Abstract

Purpose: Remarkable progress could be achieved in the treatment of nephroblastoma within the last decades. In all children with Wilms' tumor, 5-year overall survival rate reaches more than 90% in the SIOP/GPOH Study Group. Despite this fact, there is a small group of patients who have tumor lesions in the liver primarily representing a challenge in treatment. Data of this group are analyzed.

Methods: To define survival and success of treatment in this group of patients, we reviewed the records of 29 of 1365 patients enrolled in the SIOP 93-01/GPOH Study and the SIOP 2001/GPOH Study between April 1, 1994, and September 30, 2004.

Results: Median age at diagnosis was 10.61 years (range, 0.19-34.16 years). All patients but two underwent nephrectomy. Liver metastases were operated in 11 children at time of nephrectomy, in 4 patients secondarily, whereas in 11 patients, liver lesions were treated alone with chemotherapy and radiotherapy, respectively. In 3 children, no treatment could be initiated. Sixteen patients received radiotherapy additionally. Median follow-up was 64 months (range, 3-157 months). Eleven patients died in the course at a median of 13.07 months (range, 0.25-42 months) after initial diagnosis. These included 7 patients who never had surgery for their liver lesions and 4 patients who had incomplete and/or atypical resections of their metastatic liver lesions. All patients who underwent complete resection of hepatic metastases (n = 9) survived. Eight children survived with a nonsurgical treatment. Overall survival was below 60% in the whole group up to now.

Conclusions: Liver metastases are much less frequent than metastases to other sites. Our report suggests that Wilms' tumor complicated by metastases of the liver primarily has a less favorable outcome. Chemotherapy and radiotherapy play an important role in treatment. Radical surgery for nephrectomy as well as surgery of liver lesions cannot be overemphasized to prevent local and distant recurrence.

Wilms' tumor represents the most common malignant renal tumor in childhood. Within the last decades, striking improvement in terms of survival could be achieved in the treatment with a multidisciplinary management. Whereas survival was 30% in the 1930s, now in all children with Wilms' tumor, 5-year overall survival rate

Presented at the 36th Annual Meeting of the American Pediatric Surgical Association, Phoenix, AZ, May 29-June 1, 2005.

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doi:10.1016/j.jpedsurg.2005.10.021

reaches more than 90% in the SIOP/GPOH Study Group. Despite this fact, several issues remain of concern and ongoing discussion. These are relapsing nephroblastoma and metastatic disease. Investigators focus with this study on a small group of patients who have tumor lesions in the liver at the time of diagnosis of nephroblastoma. The purpose of this study is to evaluate the data of the SIOP/GPOH Study Group to identify factors in treatment that affect prognosis of these patients with primary hepatic metastases of nephroblastoma.

1. Methods

To define survival and success of treatment of this group of patients, we reviewed the records of 1365 patients enrolled in the SIOP 93-01 and the SIOP 2001/Wilms' tumor study of the German Society of Pediatric Oncology and Hematology between April 1, 1994, and September 30, 2004. These studies conform to the Declaration of Helsinki and were approved by the ethic commissions of all participating centers.

2. Patient data and results

Of these 1365 patients, 29 (2.12%) had metastases to the liver at time of diagnosis of the nephroblastoma. The median age at diagnosis for these 29 patients was 10.61 years (range, 1.37-10.61 years) with 9 males and 20 females in the group.

2.1. Diagnostic evaluation

Liver lesions were diagnosed with computed tomography, magnetic resonance imaging, and ultrasound. All patients received more than one of the above-mentioned studies.

Fifteen patients had left-sided tumors, 12 patients had right-sided tumors, and 2 patients had a bilateral Wilms' tumor. In addition to hepatic metastases, 22 patients had metastatic lesions in the lungs. Other sites of metastases included bones (n = 3), thrombosis of the inferior cava vein (n = 3), mediastinal (n = 2), and the diaphragm (n = 1).

Table 1 Surgery on hepatic lesions in patients with primary hepatic metastases of nephroblastoma (n = 29)

Surgery	Patients	%	Patients survived
Primary	11	37.9	7
Complete	6	20.7	6
Incomplete	5	17.2	1
Secondary	4	13.8	3
Complete	3	10.3	3
Incomplete	1	3.4	0
None	14	48.3	7
None, but Ctx	4	13.8	3
None, but Ctx and RT	7	24.1	4
None/unknown	3	10.3	1 (?)
Total	29	100	18

Ctx indicates chemotherapy; RT, radiotherapy.

Table 2 Histological subtype and survival in patients with primary hepatic metastases of nephroblastoma (n = 29)

Histological subtype	Patients	%	Patients survived
Low risk	4	13.8	2/4
Intermediate risk	18	62.1	14/18
High risk	4[a]	13.8	1/4
Unclassified	3	10.34	1/3

Ten (34.5%) patients had additional nephroblastomatosis.
[a] Including 2 patients with diffuse anaplasia.

2.2. Surgery

All patients but two underwent tumor nephrectomy. Liver metastases were operated in 11 children at time of nephrectomy. Primary complete resection could be achieved in 6 patients, whereas in 5 children, surgery of liver lesions was incomplete. Of these 5 children, 4 died in the further course. Complete resection of hepatic lesions could be achieved in 3 patients in a second attempt, which survived with additional chemotherapy and radiotherapy. One patient, where secondary resection still was incomplete, died because of local relapse. Fourteen patients never underwent surgery for their liver lesions (see Table 1).

2.3. Histological classification

Histology was classified as low risk in 4, intermediate risk in 18, and high risk in 4, with two children having diffuse anaplastic tumors. In 3 children, the tumor could not be classified histologically owing to refuse of any therapy or to death before initiation of therapy. In 10 cases, nephroblastomatosis was found additionally (see Table 2).

2.4. Chemotherapy and radiation

Nineteen patients received preoperative chemotherapy, 14 according to stage IV disease of the protocols of the SIOP 93-01/GPOH and the SIOP 2001/GPOH Wilms' tumor study, consisting of actinomycin D, vincristin, and doxorubicin. In 5 children, doxorubicin was omitted.

Seven patients did not receive chemotherapy preoperatively. This group comprised the 6 patients who underwent primary nephrectomy and 1 patient with a Smith-Lemli-Opitz syndrome, in whom no therapy was initiated. In 3 children, only insufficient data are available. Of these 10 children without preoperative chemotherapy, 5 patients died.

Of 14 patients who never had surgery for their liver metastases, 4 were treated with chemotherapy alone, with 3 survivors in this group. Another 7 children received chemotherapy and radiotherapy additionally, and among