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ORIGINAL ARTICLE

SURGICAL TREATMENT OF RETROPERITONEAL NEUROBLASTOMA IN CHILDREN. CLINICAL EXPERIENCE

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ABSTRACT

Purpose of the study. Was to analyze our experience of surgical treatment of retroperitoneal neuroblastoma in children and the influence of radical surgical treatment on the disease outcomes.
Materials and methods. The study included 35 patients (14 girls and 21 boys, mean age 3.3 years) receiving treatment for retroperitoneal neuroblastoma at the Department of Pediatric Oncology, National Medical Research Centre for Oncology, in 2016–2018. 32 patients underwent surgical treatment. The disease progression during neoadjuvant polychemotherapy was registered in 3 patients. Initially, surgery was performed in 5 patients; the rest of the patients underwent percutaneous trepan biopsy with immunohistochemical testing and subsequent neoadjuvant polychemotherapy. No patients developed complications in the early postoperative period.
In the article, we present our experience in the surgical treatment of pediatric patients with retroperitoneal neuroblastomas.
Results. Patients have been observed during 12 to 24 months. 23 of 28 radically operated patients are alive and have no signs of the disease recurrence or progression. 2 patients developed tumor recurrence and received anti-recurrence PCT and DGT. Currently the patients are in remission. 3 patients showed systemic progression due to primarily advanced disease.
Conclusion. Administration of modern surgical techniques and instrumentation allows radical surgical treatment for a large percentage of patients with locally advanced neuroblastoma.

Keywords:
pediatric patients, retroperitoneal neuroblastomas, surgical treatment, neoadjuvant polychemotherapy, radical tumor removal, progression

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ОРИГИНАЛЬНАЯ СТАТЬЯ

ХИРУРГИЧЕСКОЕ ЛЕЧЕНИЕ НЕЙРОБЛАСТОМ ЗАБРЮШИННОЙ ЛОКАЛИЗАЦИИ У ДЕТЕЙ. ОПЫТ КЛИНИКИ

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РЕЗЮМЕ

Цель исследования. Проанализировать собственный опыт хирургического лечения нейробластом забрюшинного пространства у детей и влияние радикальности хирургического лечения на исход заболевания.
Материалы и методы. В исследование включены 35 пациентов, проходивших лечение в отделении детской онкологии ФГБУ «НМИЦ онкологии» Минздрава России с 2016 по 2018 гг. с нейробластомами забрюшинного пространства. Средний возраст пациентов составил 3,3 года. Из них было 14 девочек и 21 мальчик. Хирургическое лечение проведено 32 пациентам. У 3 больных отмечена прогрессия заболевания на фоне проводимой неоадъювантной ПХТ. Изначально оперативное вмешательство было выполнено 5 больным, остальным пациентам проводилась чрескожная трепанбиопсия с иммуногистохимическим исследованием и последующей неоадъювантной полихимиотерапией. В раннем послеоперационном периоде осложнений не отмечено ни у одного пациента.
В статье нами представлен собственный опыт хирургического лечения пациентов детского возраста с нейробластомами забрюшинного пространства.
Результаты. Пациенты наблюдаются в сроках от 12 до 24 мес. Из 28 пациентов, прооперированных радикально, живы без признаков рецидива и прогрессии заболевания 23. У 2 больных возник рецидив опухоли, им проведена противорецидивная ПХТ и ДГТ. В настоящее время пациенты находятся в ремиссии. У 3 пациентов отмечалась системная прогрессия заболевания, связанная с первично-генерализованным процессом
Заключение. Применение современных хирургических техник и инструментария позволяет в большом проценте случаев добиться радикального хирургического лечения при местно-распространенных формах нейробластомы.

Ключевые слова:
пациенты детского возраста, нейробластомы забрюшинного пространства, хирургическое лечение, неоадъювантная полихимиотерапия, радикальное удаление опухоли, прогрессия

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INTRODUCTION

Neuroblastoma is the most common tumor of the peripheral nervous system, occurring in childhood. The incidence of neuroblastoma is 7–8 % of all malignant tumors of childhood [1; 2]. Neuroblastoma is localized mainly in the retroperitoneal space, less often in the mediastinum and on the neck. The source of tumor development in the retroperitoneal space is the adrenal gland in 32 % of cases, sympathetic ganglia located paravertebral in 28 % of cases [3–6]. The biological diversity of neuroblastomas associated with genetic mutations or their absence significantly affects the clinical course of the disease. There are cases of spontaneous tumor regression. This is especially true for children under the age of 1 year. Thus, according to various authors, spontaneous tumor regression in children under 1 year occurs in 50–70 % of cases [7; 8]. At the same time, the presence of N-myc gene amplification, deletions at the 1p36 locus, as well as the age of a child older than 1 year are unfavorable factors, and event-free survival in this group of patients, according to numerous studies, does not exceed 40 % [1; 9].

The diverse course of neuroblastomas in childhood, from spontaneous regression to active progression, dictates the need for different approaches to the treatment of this pathology. Intensification of therapy in high-risk patients makes it possible to achieve more significant results in treatment. Thus, various authors propose the use of systemic radiotherapy using 131I–MIBG, high-dose chemotherapy with autotransplantation of polypotent stem cells [10–13].

Surgical treatment of retroperitoneal neuroblastoma, in particular, locally widespread forms, caused by the involvement of major vessels and adjacent organs in the process, causes particular difficulties [1; 14]. The question of the expediency of radical removal of the tumor with a high risk of surgical

Table 1. Characteristics of patients by the prevalence of the tumor process

Criteria for the characteristics of the tumor process	Patients' quantity			
Primary tumor localisation	Adrenal gland		Paravertebrally	
	12 (34.3 %)		23 (65.7 %)	
Tumour process development	Focal form		Generalised form	
	25 (71.4 %)		10 (28.6 %)	
Risk groups	Middle		High	
	16 (45.8 %)		19 (54.2 %)	
INSS staging	St I	St II	St III	St IV
	2 (5.7 %)	9 (25.7 %)	14 (40 %)	10 (28.6 %)

Table 2. Radiological (CT or MRI) risk factors (IDRFs) for patients with abdominal/retroperitoneal neuroblastoma according to INRG

Group 1	A tumor infiltrating the portal vein and/or hepatoduodenal ligament, including branches of the superior mesenteric artery of the mesentery root, including the ventral trunk and/or trunk of the superior mesenteric artery, infiltrating one or both renal pedicles, including the aorta and/or IVC, including the iliac vessels, pelvic tumor in the area of the sciatic tenderloin
Group 2	A tumor with a spread into the spinal canal (regardless of the level) spread to more than 1/3 of the spinal canal in axial projection and/or the leptomeningeal space is not traced and/or the signal from the spinal cord is pathologically altered
Group 3	Infiltrates the surrounding organs and structures of the pericardium, diaphragm, kidney, liver, pancreatoduodenal zone, mesentery

complications in patients with generalized forms of neuroblastomas that do not allow time to start systemic therapy remains debatable. According to a number of authors, radical removal of the tumor (more than 95 % of the volume) improves the results of treatment of high-risk patients [15–19], other authors say that total removal of neuroblastoma with a high risk of intra- and postoperative complications is inappropriate, since high-risk neuroblastoma is a systemic process with possible metastatic damage to the liver, bone marrow and bones [20–22].

The purpose of the study: to analyze our own experience of surgical treatment of retroperitoneal neuroblastoma in children and the effect of radical surgical treatment on the outcome of the disease.

MATERIALS AND METHODS

The study included 35 patients who were treated at the Department of Pediatric Oncology of the National Medical Research Centre for Oncology from 2016 to 2018. The average age of patients was 3.3 years. Of these, there were 14 girls and 21 boys. The staging of the tumor process was carried out according to the INSS criteria. All patients were treated in accordance with the NB 2004 protocol. According to the localization of the tumor in 12 patients (34.3 %), the primary tumor was localized in the projection of one of the adrenal glands, in 23 (65.7 %) there was a paravertebral spread of the tumor along the main vessels. 10 patients (28.6 %) had primary generalization of the tumor process with metastases to the liver, bones and bone marrow, and 25 patients (71.4 %) had localized stages of the disease. The largest number of patients were with stage 3 of the disease – 14 patients (40 %), with stage 4–10 patients (28.6 %), with stage 2–9 patients (25.7 %), and with stage 1–2 patients (5.7 %). The high risk group was determined in 54.2 % of patients, the average risk group in 44.8 % of patients. The characteristics of patients by the prevalence of the process are presented in Table 1.

Surgical treatment was performed in 32 patients. In 3 patients, the progression of the disease was noted against the background of neoadjuvant PCT.

Initial surgical intervention was performed in 5 patients, the remaining patients underwent percutaneous trepan biopsy with immunohistochemical examination and subsequent neoadjuvant polychemotherapy.

When planning a surgical intervention, we used data from spiral computed tomography with angiography, magnetic resonance imaging data and ultrasound examination of the abdominal cavity and retroperitoneal space. The risk factors for surgical intervention in imaging (IDRF) described in the International Neuroblastoma Risk Group (INRG) guidelines for imaging and staging neuroblastoma [23] and characterizing the involvement of major vessels and other adjacent organs in the tumor process were taken into account. Figure 1 schematically shows the relationship between the tumor and the main vessels in the absence of risk factors during imaging (IDRF) and in their presence.

Table 2 presents detailed radiological criteria for inclusion of patients in the group with risk factors for imaging according to INRG.

Among the operated patients, 12 had no risk factors during imaging and 19 had. Figure 2 shows the frequency of involvement of the main vessels

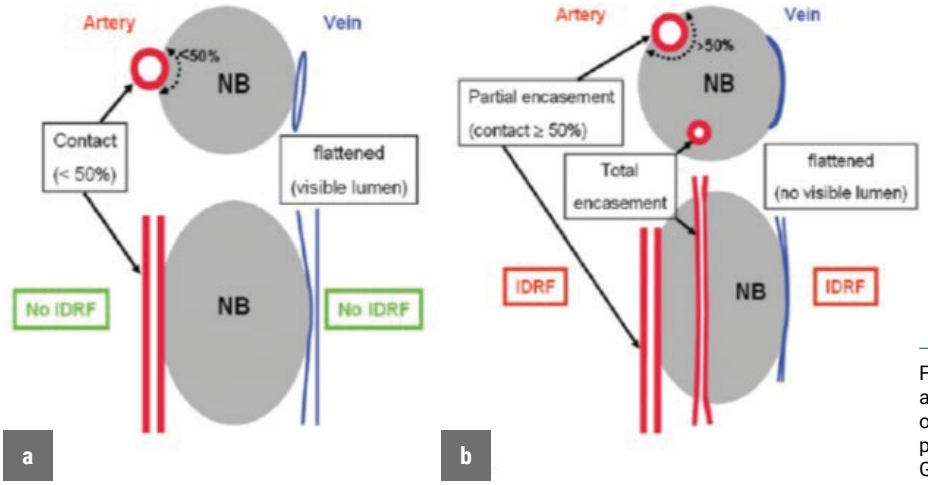

Fig. 1. Diagram of the ratio of tumor and major vessels in the absence of risk factors (DFR) (a) and their presence (b) (Monclair T, Brodeur G.M., 2009).

and adjacent organs in the tumor process. More often, the vessels of the renal pedicle, the aorta, and the superior mesenteric artery were involved in the process.

As illustrative examples of risk factors assessment during visualization, we give 2 clinical examples.

Clinical example 1. Patient K. 5 years old with the diagnosis: undifferentiated retroperitoneal neuroblastoma with bone metastases. StIV. A high-risk group. The presented CT scans (Fig. 3, 4) show a reduction in tumor mass in the retroperitoneal space after neoadjuvant polychemotherapy. The residual tumor involves the aorta and the renal arteries on both sides in a process with a muff-like covering. The tumor also covered the lower mesenteric artery, flattened the left renal vein on itself.

Figure 5 shows an intraoperative image after removal of a tumor with skeletonized main vessels of the retroperitoneal space. The tumor was removed completely in this case.

Clinical report 2. Patient B. 4 years old with a diagnosis of retroperitoneal ganglioneuroblastoma. An accidental finding during ultrasound examination of the abdominal cavity. According to the MRI study,

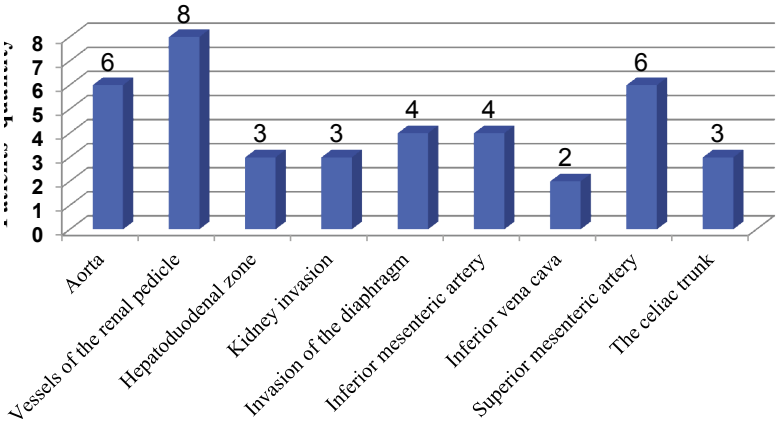

Fig. 2. The frequency of involvement of the main vessels and adjacent organs in the tumor process.

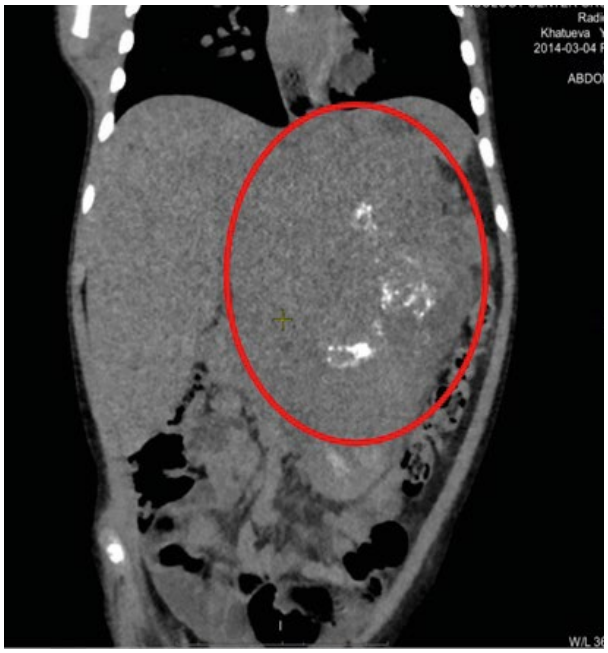

Fig. 3. CT scans before 6 courses of polychemotherapy of patient K. The primary prevalence of the tumor before induction polychemotherapy.

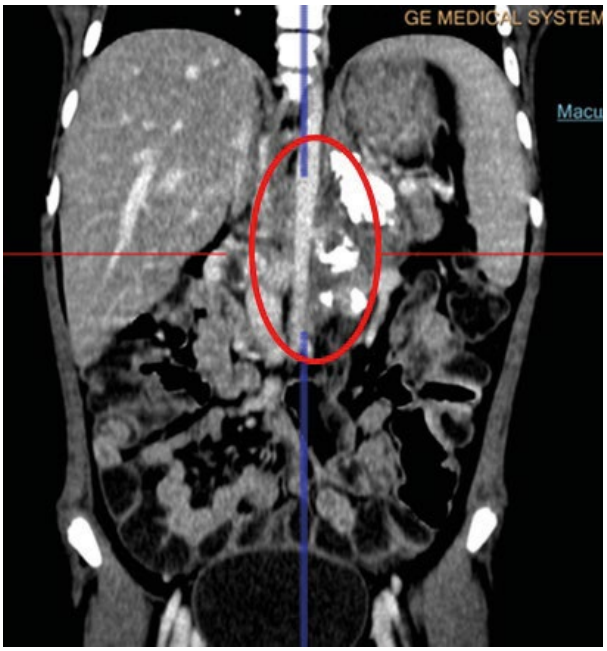

Fig. 4. CT scans (tumor prevalence) after 6 courses of polychemotherapy of patient K.

we did not find classical risk factors in imaging. The computed tomography images shown in Figure 6 show that all the main vessels only adhere to the tumor, without their muff-like covering, however, the area of location between the vessels is the inferior vena cava, renal vessels, elements of the hepatoduodenal ligament, aorta, superior mesenteric artery causes no less difficulties than during operations in patients with risk factors during visualization. In order to get to this tumor, it was necessary to isolate all the elements of the hepatoduodenal ligament, separate from the inferior vena cava, and isolate the superior mesenteric artery (Fig. 7). Therefore, risk factors in imaging are very conditional, but they help the surgeon to adequately assess the possibilities of radical surgical treatment.

The use of high-tech surgical equipment during surgical interventions (ultrasonic scalpel, modern bipolar electrocoagulating instruments) allowed to minimize the amount of blood loss and traumatization of healthy tissues.

RESEARCH RESULTS

According to the results of the operations performed, in 25 cases (78.3 %) we performed total removal of the tumor, in 3 cases (9.3 %) removal of more than 95 % of the tumor and in 4 cases (12.4 %) subtotal removal of the tumor from 50 to 95 % of the tumor mass was performed. Less than 50 % of the tumor was not removed in any case.

Complications include the development of intraoperative bleeding in 7 patients who developed from non-arterial vessels and were stopped by ligation or electrocoagulation. The volume of blood loss in these cases did not exceed 20 % of the CBV.

Also, according to many authors, complications of the operation include nephrectomy. Of the 32 operated patients, nephrectomy was performed in two due to the muff-like covering of the kidney by the tumor. In preparation for the operation, these patients were planned to perform a nephrectomy in advance.

In the early postoperative period, no complications were noted in any patient. In the late postoperative period, 2 months after the operation, one patient was found to have impaired blood supply to the contralateral kidney. The cause of this complication is not related to the technical stage of the surgical intervention, since during the operation they worked on the kidney vessels on the affected side, and the contralateral kidney and its vessels remained intact.

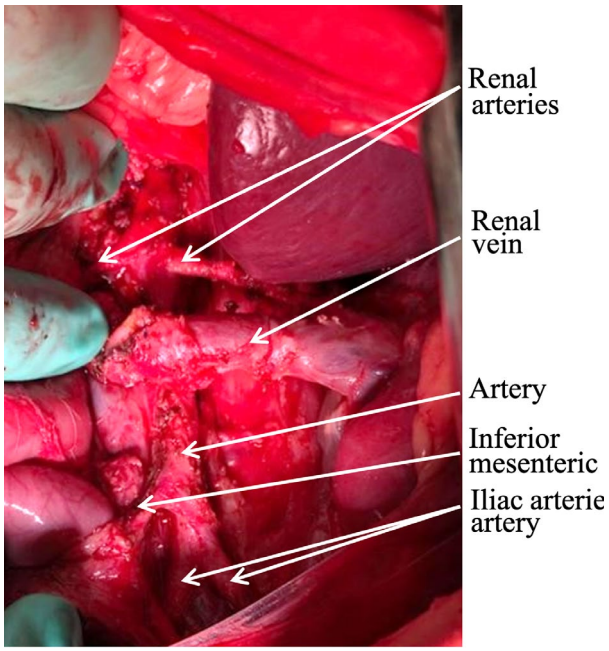

Fig. 5. Intraoperative image after removal of the tumor.

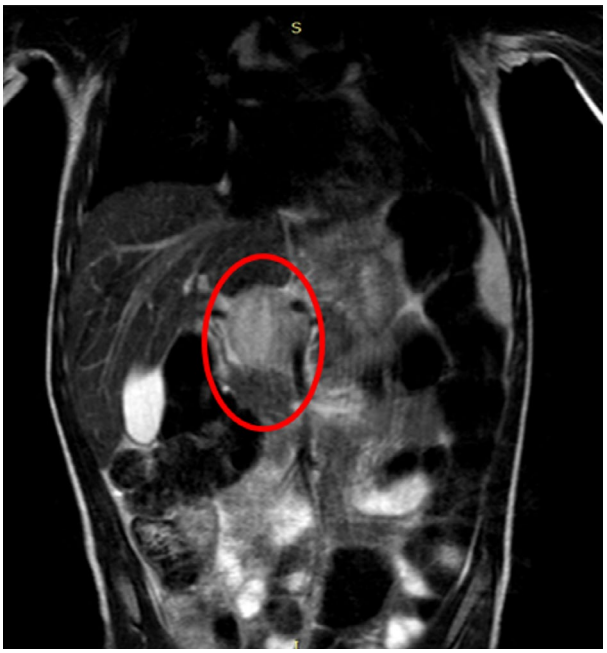

Fig. 6. Magnetic resonance imaging image of patient B. before surgical treatment.

Patients are observed for periods from 12 to 24 months. Of the 28 patients who underwent radical surgery, 23 are alive without signs of relapse and progression of the disease. 2 patients had a relapse of the tumor, they underwent anti-relapse PCT and DHT. Currently, the patients are in remission. Systemic disease progression was observed in 3 patients.

Of the 4 patients operated non-radially, only 2 are observed without signs of continued tumor growth and generalization.

All patients who had a recurrence or progression of the tumor process – 9 patients – belonged to the high-risk group.

DISCUSSION

A number of authors indicate that there was no significant difference in 5-year relapse-free survival among patients who underwent complete or incomplete resection [24–26]. At the same time, there are publications proving that surgical treatment should be in the form of complete resection of the tumor, and cases of partial resection are associated with a high risk of relapse of the disease, the need for careful monitoring and the possible use of radiation therapy [27]. According to our data, the development of relapse and progression of the disease occurred only in high-risk patients, which speaks in favor of the systemic nature of the disease and the influence on the progression of factors such as the prevalence of the primary process and the presence of genetic mutations, namely, amplification of MYC-N, deletion 1p36, allowing stratification of the patient into a high risk group. The development of relapses and progression of the disease in radically operated patients speaks in favor of the lack of significance of radicalism of surgical intervention. However, we can reliably say this by conducting a randomized study on a much larger amount of material. And yet, after a radical operation, there are fewer questions about the further tactics of treatment and management of patients with neuroblastoma, especially since the use of modern surgical techniques makes it possible to achieve radicalism of surgical treatment while minimizing the risks of complications.

CONCLUSION

Thus, the following conclusions can be made:

1. The use of modern surgical techniques and tools allows a large percentage of cases to achieve radical surgical treatment for locally common forms of neuroblastoma without the threat of serious complications.

2. Proper planning of surgical intervention taking into account risk factors during visualization allows minimizing intraoperative and postoperative complications.

3. Given the systemic nature of the lesion in neuroblastoma, it is impractical to conduct a radical operation with total removal of the tumor, accompanied by the development of complications that do not allow time to start systemic therapy.

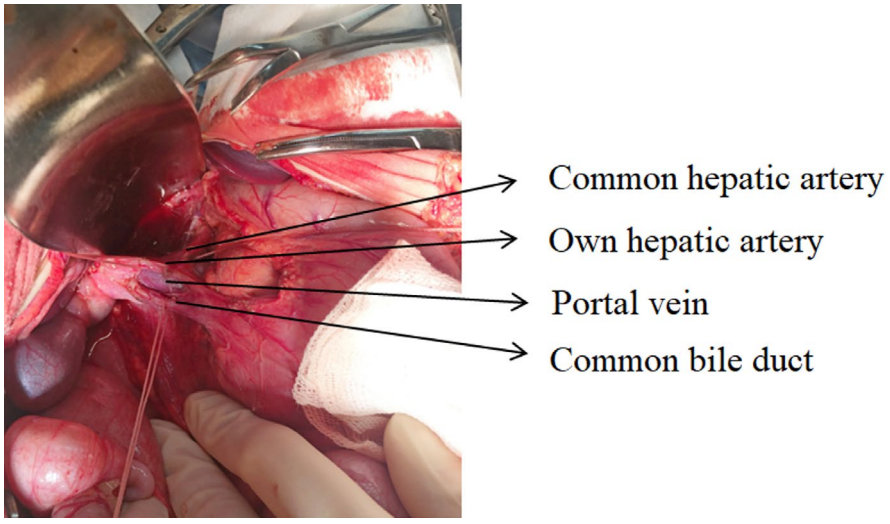

Fig. 7. Intraoperative image after removal of the tumor. Patient B.

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