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Surgical treatment for abdominal neuroblastoma in the laparoscopic era

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Abstract
Background: The role of laparoscopy in children with cancer has not been fully defined. The aims of this study were to develop an optimal surgical procedure for the treatment of abdominal neuroblastoma in the laparoscopic era and to evaluate the advantages and disadvantages of laparoscopy in the pediatric population.
Methods: Since July 1997, 37 children were diagnosed with abdominal neuroblastoma at our center, and 44 surgical procedures were performed on them. Patients with advanced neuroblastoma underwent laparoscopic biopsy, open biopsy, and delayed primary or second-look excision, whereas early neuroblastoma cases had either laparoscopic or open excision. We compared the length of the operation, intraoperative blood loss, length of hospital stay, complications, and time to start postoperative feeding and chemotherapy for the laparoscopic and open surgery groups.
Results: Length of stay and time to postoperative feeding and chemotherapy were significantly lower in the laparoscopic group than the open surgery group. However, there were no significant differences between the two groups in length of operation and intraoperative blood loss.
Conclusion: Laparoscopic biopsy and excision of abdominal neuroblastoma are effective and efficient surgical procedures in children.

Key words: Neuroblastoma — Laparoscopy — Biopsy — Excision

Neuroblastoma is one of the most common solid tumors in children and often requires surgical intervention as part of a planned multimodal treatment. Holcomb et al. have reported two pediatric cases of thoracoscopic surgery for the diagnosis of mediastinal neuroblastoma [3], and Saenz et al. have described the use of minimally invasive biopsies in two abdominal and three mediastinal neuroblastomas [10]. Several groups have performed laparoscopic surgery in adult gastric, ovarian, pancreatic, colon, and gallbladder cancers, but the functionality of laparoscopic surgery in the diagnosis and treatment of childhood solid tumors has not yet been evaluated. Therefore, we set out to compare, two groups that underwent laparoscopic and open procedures for the diagnosis and treatment of abdominal neuroblastoma in children in terms of their clinical parameters and postoperative morbidity.

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Materials and methods

Since July 1997, 55 children have been diagnosed with abdominal neuroblastoma at the Saitama Children's Medical Center. Of these, 18 infants exhibited spontaneous regression of their localized neuroblastoma and required neither surgery nor chemotherapy [12]. A total of 44 surgical procedures were conducted on the remaining 37 cases of abdominal neuroblastoma. The patients' records were reviewed, and data on length of operation, intraoperative blood loss, time to postoperative feeding, length of hospital stay, time to start postoperative chemotherapy, and complications were collected retrospectively. The data were analyzed using an unpaired *t*-test, and $p < 0.05$ was considered to be significant.

Laparoscopic procedures

Laparoscopic tumor excision

Right adrenalectomy, left adrenalectomy, and excision of retroperitoneal tumor were performed. The patient was placed in a lateral decubitus position, and a 12-mm trocar was inserted through a small incision of the umbilicus using an open technique. The abdominal cavity was insufflated with carbon dioxide to a pressure of 8–10 mmHg, and two or three additional 5-mm ports were inserted. A 5-mm Harmonic Scalpel and electrocautery were used to dissect the retroperitoneum, mobilize the colon, and approach the neuroblastoma. Large blood vessels and the adrenal vein were mobilized by blunt dissection. The neuroblastoma was removed in an endoscopic bag through a 12-mm umbilical port. The retroperitoneal space was examined for any evidence of bleeding and lymph node swelling. Additional lymph nodes were sampled whenever necessary. In cases of

Table 1. Surgical procedures in the cases with abdominal neuroblastoma

Stage and procedures	Number
Early neuroblastoma (INSS stages 1 and 2)	18
Laparoscopic excision	4
Open excision	14
Advanced neuroblastoma (INSS stages 3 and 4)	26
Laparoscopic biopsy	6
Open biopsy	9
Delayed primary laparoscopic excision	1
Delayed primary or second-look open excision	10

INSS, international neuroblastoma staging system

delayed primary laparoscopic excision of advanced tumor, paraaortic and pararenal lymphadenectomy were also performed simultaneously.

Laparoscopic tumor biopsy

The patient was placed in a supine position, and a 12-mm trocar was inserted through a small incision of the umbilicus using an open technique. The abdominal cavity was insufflated to a pressure of 8–10 mmHg, and two more 5-mm ports were inserted. The retroperitoneum was dissected using electrocautery and a Harmonic Scalpel. The large vessels surrounding the tumor, such as the inferior vena cava and renal vein, were mobilized by blunt dissection. The biopsy was incisional, using a scissors or knife. To prevent thermal damage of the resected specimen and decrease exfoliation of the tumor cells, energy sources such as electrocautery and the Harmonic Scalpel were not used for the actual biopsy. The insufflation pressure was increased to 12 mmHg to prevent blood loss from the surface of the incised tumor, and the specimen was removed in a small plastic bag. To achieve complete hemostasis, fibrin glue was applied to the surface of neuroblastoma. To avoid port site recurrence, high-dose adjuvant chemotherapy was given as early as possible.

Results

Our patient population was comprised of 24 boys and 13 girls ranging in age from 4 months to 13 years (median, 28 months). There were 18 patients in the early neuroblastoma group and 19 in the advanced neuroblastoma group. All surgical procedures conducted for the diagnosis and treatment of these abdominal neuroblastomas are listed in Table 1.

In the advanced neuroblastoma group, 11 delayed primary or second-look surgeries were performed, but only one laparoscopic tumor excision was done. Therefore, in the advanced neuroblastoma group, the data for laparoscopic incisional biopsy were compared with those for open incisional biopsy. In the early neuroblastoma group, data from 14 open tumor excisions were compared with those from four laparoscopic tumor excisions.

We found that in the early neuroblastoma group, time to start postoperative feeding and length of hospital stay was significantly less in the laparoscopically excised patients than in those with open tumor excisions. There was no difference between the two groups in length of operation and intraoperative blood loss (Table 2). Similarly, in the advanced neuroblastoma group, time to start postoperative feeding and time to chemotherapy were significantly shorter in the laparoscopic biopsy cases than in the open biopsy cases. However, there was no difference between them in terms of length of operation and intraoperative blood loss (Table 3).

Table 2. Clinical data for laparoscopic and open excision in early neuroblastoma

	Laparoscopic	Open
Length of operation (min)	100 ± 10	112 ± 40
Blood loss (ml)	12 ± 10	43 ± 31
Start postop feeding (h)	31 ± 15	76 ± 23[a]
Length of stay (day)	5.3 ± 0.6	10.5 ± 4.1[a]

Data expressed as mean ± SD
[a] p value <0.05 between both groups

Table 3. Clinical data for laparoscopic and open biopsy in advanced neuroblastoma

	Laparoscopic	Open
Length of operation (min)	120 ± 23	101 ± 36
Blood loss (ml)	28 ± 27	43 ± 50
Start postop feeding (h)	33 ± 11	129 ± 72[a]
Start postop chemotherapy (day)	3.7 ± 1.5	11.2 ± 7.2[a]

Data expressed as mean ± SD
[a] p value <0.05 between both groups

Although there were no intraoperative or postoperative complications in any case, one laparoscopic tumor excision for stage I neuroblastoma was converted to an open excision after a large tumor was found behind the inferior vena cava.

One laparoscopic tumor excision, combined with paraaortic and pararenal lymphadenectomy after high-dose chemotherapy of a stage IV neuroblastoma that originated from the left adrenal gland, took 2 h and 44 min. The patient lost 15 ml of blood during the procedure, which was done using five ports. However, we were unable to obtain a good view of the contralateral right paraaortic lymph nodes in the small abdominal cavity. Moreover, fibrotic changes caused by the course of chemotherapy made blunt dissection around the large vessels very difficult.

Discussion

Neuroblastoma is the second most common solid malignant tumor in children. Investigations of its pathology and biology have suggested that there are both favorable and unfavorable subgroups in localized and disseminated neuroblastomas [7, 8]. Although surgery alone can take care of localized neuroblastoma in the favorable subgroup [6], disseminated neuroblastoma generally fails in the unfavorable subgroup, necessitating multimodal treatment [10].

Recent advances in minimally invasive surgery and endosurgery have allowed these techniques to be used in infants and children, resulting in a decrease in surgical stress and an improvement in postoperative morbidity [1, 9]. There have been very few reports of minimally invasive surgery for pediatric malignancies [2, 3, 10], so the pros and cons of these procedures in this patient population still need to be defined. In this study, we sought to evaluate the advantages and disadvantages of laparoscopic surgery in pediatric abdominal neuroblastoma by measuring certain clinical parameters and postoperative morbidity.

Early localized neuroblastomas, detected by mass

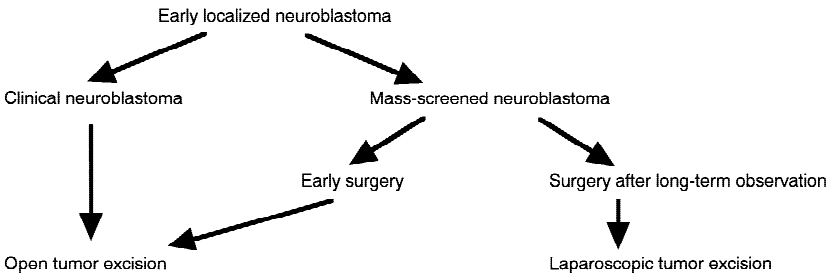

Fig. 1. Algorithm for the management of early neuroblastoma.

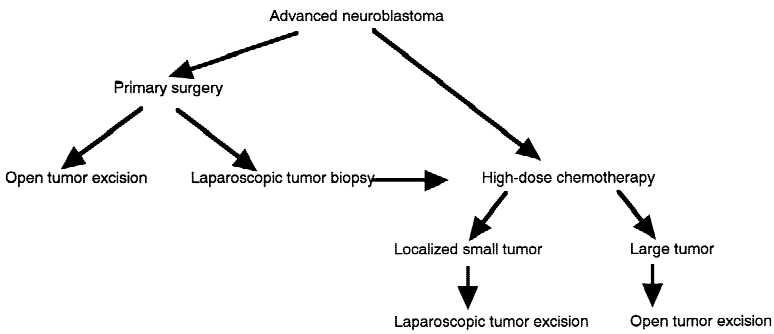

Fig. 2. Algorithm for the management of advanced neuroblastoma.

screening, belong to the favorable subgroup and can be easily resected laparoscopically [5, 11, 12]. Despite the favorable aspects of this subgroup, a complete histological and biological examination is required to fully understand their biological features. In our patient series, 11 of the 59 mass-screened neuroblastomas, which were diagnosed preoperatively as INSS stage I, had local lymph nodes metastases. On histological examination, nine of these 11 stage I neuroblastomas were changed to stage II. One case had local lymph node recurrence; the other had bone and bone marrow relapse. This finding suggests that mass-screened early neuroblastomas have a potential for tumor dissemination and port site recurrence. On the other hand, after 15 months of observation without any treatment, five mass-screened patients eventually had their tumors removed surgically. No swelling of local lymph nodes was observed preoperatively or intraoperatively in these patients, and pathological examination revealed ganglioneuroma in one case and well-differentiated ganglioneuroblastoma in the four others. If these tumors had any malignant potential, we should have seen distant metastases or metastasis in the local lymph nodes during the observation period.

In our set of early neuroblastoma cases, we found that laparoscopic tumor excision not only improved cosmetic appearance, but also reduced the time to start postoperative feeding; consequently, these patients had a shorter hospital stay than those who underwent open tumor excision. A study conducted by the Children's Cancer Group found that a small percentage of early neuroblastoma patients whose localized tumor was surgically removed subsequently relapsed and died of their disease [6]. Using a murine model, we have shown that the administration of high-dose chemotherapy shortly after laparoscopy can prevent port site recurrence [4]. However, the risks associated with chemotherapy are more severe than the surgical stress incurred with open procedures. Thus, even though laparoscopic tumor excision has certain advantages, we recommend that it be performed only in mass-screened cases whose neuroblastoma has been observed in the long term. In mass-screened patients requiring early surgical intervention, open excision should still be the preferred procedure (Fig. 1).

Our data show that laparoscopic tumor biopsy significantly reduces the time to start postoperative feeding as well as the time to postoperative chemotherapy in patients with advanced neuroblastoma. Besides its cosmetic advantage, laparoscopic tumor biopsy allows for the early delivery of adjuvant therapy, which in turn reduces the chances of port site recurrence [4]. We anticipate that safety, effectiveness, and all the other benefits of minimally invasive surgery will make laparoscopic tumor biopsy the preferred procedure whenever pathological and biological specimens are required before high-dose chemotherapy (Fig. 2).

This study shows that laparoscopic surgery has good results in terms of postoperative morbidity for both early and advanced-stage neuroblastomas. We conclude that precise indications for laparoscopic surgery in the diagnosis and treatment of abdominal neuroblastoma will lead to a better prognosis and an improved quality of life for children with neuroblastoma.

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