

Laparoscopic Adrenalectomy for Solitary Adrenal Metastasis From Lung Cancer

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ABSTRACT

Background and Objectives: Several studies have been reported on the problem of determining when laparoscopic adrenalectomy is indicated for solitary adrenal metastasis of malignant tumors. Our efforts at answering this question constitute the basis of this report.

Methods: From June 2010 to June 2011, laparoscopic adrenalectomy was performed in 10 lung cancer patients with solitary adrenal metastases (5 adenocarcinomas, 1 squamous cell carcinoma, 1 large cell carcinoma, 1 small cell carcinoma, and 2 pleomorphic carcinomas). The surgical results of all 10 patients were examined.

Results: Adrenal swelling was detected by computed tomography in all patients except 1 case of pleomorphic carcinoma. The findings of positron emission tomography-computed tomography were positive in 8 patients, including the 2 cases with pleomorphic carcinomas. Laparoscopic surgery was successfully performed in 9 cases. In the eighth patient (a case of pleomorphic carcinoma with adrenal swelling), laparoscopic adrenalectomy was attempted but conversion to open surgery was required because of clear evidence of pancreatic invasion.

Conclusion: The results obtained in this study, along with other published reports, support 4 criteria as operative indications for laparoscopic adrenalectomy in solitary adrenal metastasis from the lung: (1) the primary lung cancer is resected or can be cured by radical chemotherapy, (2) metastasis is limited to the adrenal gland only, (3) adrenal metastasis does not invade the surrounding organs, and (4) the size of the adrenal tumor does not exceed 10 cm. In cases of pleomorphic carcinoma, lapa-

roscopic adrenalectomy should be performed when positron emission tomography-computed tomography results are positive.

Key Words: Laparoscopic adrenalectomy, Adrenal metastasis, Lung cancer, Pleomorphic carcinoma.

INTRODUCTION

Metastatic tumors account for only 3% of incidental adrenal tumors.¹ However, metastatic adrenal tumors occur in 53% of patients with primary lung cancer.² Although the frequency of adrenal metastasis in resectable non-small cell lung cancer (NSCLC) is 1.6%,³ the frequency of adrenal metastasis in primary lung cancer is initially 5%–10%,⁴ and it increases up to 40% as the disease progresses.^{4,5}

Chemotherapy is performed for NSCLC with distant metastasis, but long-term survival is usually limited.⁶ Resection of the adrenal gland improves the prognosis of lung cancer patients with solitary adrenal metastases.⁶ Commonly, the respiratory physician and surgeon in charge of lung cancer treatment consult with a urologist regarding the resection of solitary adrenal metastases in these patients. The surgical procedure is minimally invasive, and it is standard practice for the adrenalectomy to be performed laparoscopically. However, laparoscopic adrenalectomy is not consistently used for the treatment of metastatic adrenal tumors because of risks such as tumor breakup or dissemination.

The use of laparoscopic adrenalectomy is described for the treatment of solitary adrenal metastasis from lung cancer, and criteria are discussed supporting the operative indications for adrenal metastasis as discussed in earlier reports.^{7–10}

PATIENTS AND METHODS

Laparoscopic adrenalectomy was performed at Nagoya City University Hospital and an associated institution in 10 lung cancer patients with solitary adrenal metastases from June 2010 to June 2011. After discussions with physicians who treat lung cancer, it was decided that laparoscopic

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surgery should be performed at our hospital if the following criteria were met: (1) the primary lung cancer had been resected or could be cured by radical chemotherapy, (2) metastasis was restricted to the adrenal gland, (3) adrenal metastasis did not invade the surrounding organs, and (4) the adrenal tumor size did not exceed 10 cm.

We ascertained that if the primary cancer was not or could not be resected completely, this would eventually lead to regrowth at the original tumor site, even if the adrenal metastasis had been resected successfully. Thus, in these cases in which control of the primary cancer was not achieved, laparoscopic adrenalectomy was not indicated. We performed open surgery in patients who did not meet the second criterion. All of the adrenal masses were discovered by computed tomography (CT) and positron emission tomography (PET) imaging during diagnosis of the primary disease and the follow-up period.

Patient demographic characteristics and disease history are summarized in **Table 1**. There were 8 male and 2 female patients in the study, with a median age of 61

years (range, 55–75 years). Adrenal tumors were located on the left side in 7 patients and on the right side in 3 patients. Both synchronous metastasis of primary lung cancer and solitary adrenal metastasis were seen in 6 patients. *Synchronous metastasis* means the metastasis was discovered within 6 months after treatment of primary tumor, whereas *metachronous* refers to those discovered after 6 months of treatment. The median adrenal tumor diameter, which was measured using the long and short axes from the coronal section on a CT image, was 3.7 cm (range, 2.8–8.0 cm). Histopathologic examination showed 5 adenocarcinomas, 1 squamous cell carcinoma, 1 large cell carcinoma, 1 small cell carcinoma, and 2 pleomorphic carcinomas. In 9 of 10 cases, adrenal swelling was detected using CT; the CT scan of 1 patient with pleomorphic carcinoma did not show a change in the adrenal gland (patient 9). PET/CT was performed in 8 patients, including patient 9, who had a pleomorphic carcinoma and exhibited no adrenal gland changes on the basis of CT results, and all cases were positive. The operative outcomes of all 10 patients were examined along with their postoperative courses.

Table 1.
Characteristics and Clinical Course of Each Patient With Solitary Adrenal Metastasis From Lung Cancer

Patient No.	Gender	Age (y)	Location of Adrenal Tumor	Adrenal Tumor Size (cm)	Pathology of Lung Cancer	Syn ^a or Met ^a	Treatment of Lung Cancer	CT ^a Findings of Adrenal Gland	PET ^a -CT Findings of Adrenal Gland
1	Male	55	Left side	30 × 28	Adenocarcinoma	Syn	Adjuvant chemotherapy + right superior lobe resection	Swelling	Positive
2	Male	63	Left side	21 × 20	Adenocarcinoma	Syn	Left superior lobe resection	Swelling	Positive
3	Female	72	Left side	35 × 30	Adenocarcinoma	Met	Left superior lobe resection + gamma knife	Swelling	Not obtained
4	Male	69	Right side	40 × 40	Adenocarcinoma	Met	Right superior lobe resection	Swelling	Positive
5	Male	75	Right side	40 × 30	Large cell	Syn	Chemoradiation	Swelling	Positive
6	Male	63	Left side	80 × 50	Squamous cell	Met	Chemoradiation	Swelling	Positive
7	Female	77	Left side	49 × 40	Small cell	Syn	Chemoradiation	Swelling	Not obtained
8	Male	75	Left side	45 × 30	Pleomorphic	Syn	Left pneumonectomy	Swelling	Positive
9	Male	63	Left side	No swelling	Pleomorphic	Syn	Right superior lobe resection	Normal	Positive
10	Male	69	Right side	43 × 39	Adenocarcinoma	Met	Right superior lobe resection/mediastinal lymph node gamma knife	Swelling	Positive

^aCT = computed tomography; Met = metachronous; PET = positron emission tomography; Syn = synchronous.

RESULTS

Operative outcomes are shown in **Table 2**. In 8 cases a transabdominal approach was selected; in the other 2 cases (patients 3 and 9), a retroperitoneal approach was used because of the appearance of strong adhesions in the abdominal cavity after previous surgery (**Figure 1**). During the operation, an ultrasonic-driven scalpel was not used because of the risk of spreading tumor cells to the surrounding tissues. A proper transabdominal approach was usually made by a wide cut in the peritoneum on the inferior surface of the liver, thereby opening up the retroperitoneal space. With this approach, the front part of the inferior vena cava and the right kidney vein were exposed, and the risk of vascular injury was avoided.

The Gerota fascia was cut from the renal vein; the peria-adrenal tissue surrounding the kidney was then resected including the fatty tissue around the renal capsule and the renal vein at the border of the inferior vena cava. By use of a left-sided transabdominal approach, the muscular fascia of the descending colon from the lungs to the level of the common iliac artery was cut, exposing and spreading the retroperitoneal space. With 1 exception (ie, patient 8 with a pleomorphic carcinoma), no patient exhibited adhesions to the surrounding organs, and laparoscopic adrenalectomy was successfully carried out in these 9 cases. In 1 of the 2 patients with a pleomorphic carcinoma (patient 8), a CT scan showed adrenal swelling, and pancreatic invasion was suspected. Because there are no effective therapies for pleomorphic carcinoma except surgery, it was decided to perform a resection in this patient. To this end, laparoscopic adrenalectomy was attempted by a transabdominal approach, but conversion to open surgery was required because pancreatic invasion was evident.

Regarding the other case of pleomorphic carcinoma (patient 9), CT showed no changes in the adrenal gland; however, adrenal metastases were diagnosed on the basis of positive PET-CT findings (**Figure 2**). Laparoscopic adrenalectomy was accomplished without any problems in this patient. Mass formation was not macroscopically evident in the resected sample. In the adrenal gland, invading tumor cells formed a duct-like structure. Positive staining for thyroid transcription factor 1 (TTF-1), which is expressed in lung adenocarcinomas,^{11,12} was evident. However, TTF-1-positive cells that grew by forming a duct structure were observable in the primary lung lesion of this patient; thus the adrenal lesion was diagnosed as an adrenal metastasis of lung origin (**Figure 3**).

Table 2. Outcome of Patients After Laparoscopic Adrenalectomy for Solitary Adrenal Metastasis

Patient No.	Approach	Operative Time (min)	Blood Loss (mL)	Complications of Surgery	Pathology	Microscopic Margins	Follow-Up Period (mo)	Local Recurrence	Metastasis Site	Disease-Free Survival (mo)	Overall Survival (mo)	Alive
1	Trans ^a	186	4	LESS ^a to conventional	Metastasis of LC ^a	-	11	-	-	11	11	Yes
2	Trans	229	73	None	Metastasis of LC	-	9	-	Lung	4	9	Yes
3	Retro ^a	71	5	None	Metastasis of LC	-	12	-	Lung	5	12	Yes
4	Trans	120	50	None	Metastasis of LC	-	4	-	-	4	4	Yes
5	Trans	180	10	None	Metastasis of LC	-	19	-	Liver	15	19	Yes
6	Trans	150	50	None	Metastasis of LC	-	6	+	Local	4	6	Yes
7	Trans	172	77	None	Metastasis of LC	-	12	-	-	12	12	Yes
8	Trans	568	2730	Open surgery/pancreas tail and spleen resection	Metastasis of LC	-	2	+	Lymph node	2	3	No
9	Retro	160	50	None	Metastasis of LC	-	23	-	-	23	23	Yes
10	Trans	200	110	Adhesion to base of liver	Metastasis of LC	+	4	-	-	4	4	Yes

^aLC = lung cancer; LESS = laparoendoscopic single site surgery; Retro = retroperitoneal; Trans = transperitoneal.

Operation field of laparoscopic adrenalectomy

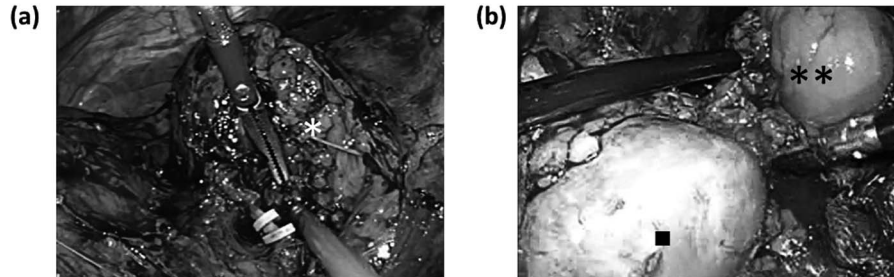


Figure 1. (a) Case 1. Left adrenalectomy (asterisk) by transperitoneal approach. (b) Case 9. Left adrenalectomy (asterisks) by lateral retroperitoneal approach. The Gerota fascia was removed from the upper pole of the left kidney (square).

CT and PET-CT findings in the adrenal gland

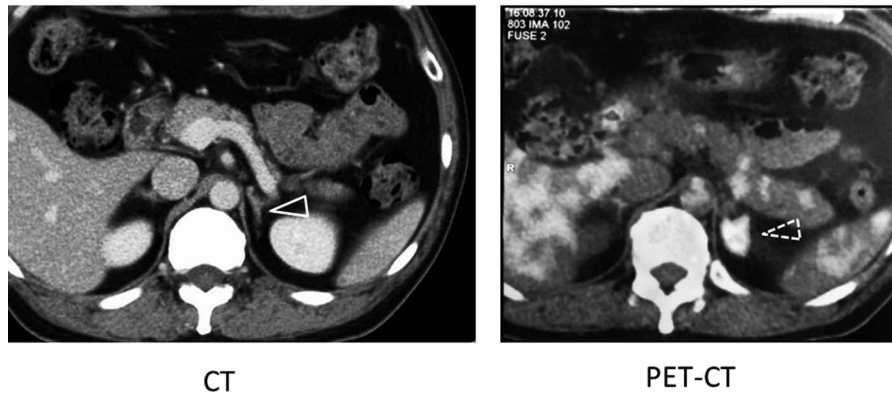


Figure 2. CT and PET-CT findings obtained from a patient with pleomorphic carcinoma in whom complete laparoscopic adrenalectomy was performed. CT showed an adrenal gland (solid triangle) that was normal in size (no swelling). PET-CT of the adrenal gland indicated a positive result (dashed triangle).

In contrast, 1 case was found in which the surgical margin was positive (patient 10). In this case, mediastinal lymph node metastasis was detected after lung cancer surgery. The primary lung cancer was an adenocarcinoma (Table 1). A laparoscopic right adrenalectomy was performed by a transperitoneal approach, but the adrenal gland was found strongly adhered to the base of the liver and could not be detached. Therefore part of the adrenal tumor capsule was left on the base of the liver, and a laparoscopic right adrenalectomy was performed.

In the 9 cases in which laparoscopic adrenalectomies were accomplished, the mean operation time was 172 ± 50 minutes and the bleeding volume was 50 ± 31 mL. In the 1 case of pleomorphic carcinoma in which laparoscopic adrenalectomy was accomplished (patient 9), the operation time was 160 minutes and the bleeding volume was 50 mL. This finding shows that laparoscopic adrenalectomy is possible even if a metastatic adrenal tumor is present in a patient with

pleomorphic lung carcinoma (Table 2). Serious perioperative complications were absent, and the resection stump was negative in 9 of 10 cases. The mean observation period after the adrenalectomy was 10.8 months (range, 2–23 months). Nine of 10 patients survived this period. The patient with pleomorphic carcinoma in whom the operation was converted to open surgery (patient 8) died of metastatic liver disease 2 months after adrenalectomy. In 5 of 10 patients (50%), new metastases developed or a recurrence occurred after adrenalectomy: 1 local recurrence, 1 local recurrence involving the lymph node, 2 lung metastases, and 1 liver metastasis. The mean time to disease progression (from laparoscopic adrenalectomy to pathologic progression) was 8.8 months (range, 2–23 months).

DISCUSSION

Adrenal metastases are infrequent in resectable NSCLC.³ Certain patients with isolated adrenal metastases, in

Histological findings in the lung and adrenal gland

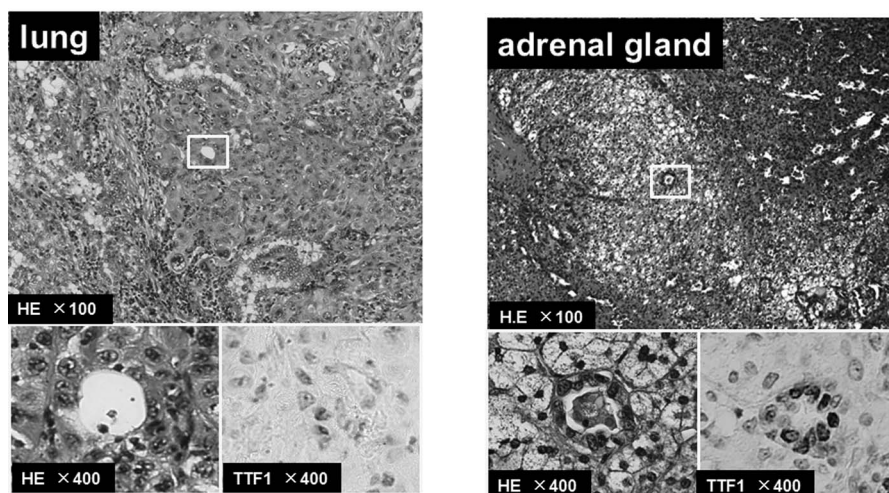


Figure 3. Histologic analysis of the lung and adrenal gland of the patient with pleomorphic carcinoma in whom complete laparoscopic adrenalectomy was performed. The left panel shows the histology of the lung. The upper panel shows hematoxylin-eosin (HE) staining of the primary lung cancer. A ductal structure can be seen in the center (square). The lower left panel is a 400 \times magnification of the square in the upper panel (HE staining). The lower right panel shows thyroid transcription factor 1 (TTF-1) staining of the ductal structure. TTF-1–positive cells are evident around the duct. The right panel shows the histology of the adrenal gland extracted by laparoscopic surgery. A ductal structure is evident in the center of the adrenal gland, as well as in the primary lung lesion (square) (upper panel, HE staining, original magnification $\times 100$). The lower left panel is a 400 \times magnification of the square in the upper panel (HE staining). The lower right panel shows thyroid transcription factor 1 (TTF-1) staining of the ductal structure. TTF-1–positive cells are evident around the duct.

whom the primary organ is resectable, have a long survival period after surgical resection of the adrenal metastases.¹⁴ Luketich and Burt⁶ indicated that excision significantly extended the survival period (31 months) compared with no excision (8.5 months) in metastatic cases of primary NSCLC. Nevertheless, there are pros and cons associated with the use of laparoscopic adrenalectomy in such cases. However, in recent years, operative efficacy and safety have been reported in cases of adrenal metastasis because of the development of new medical devices and technical improvements.^{7,13} Laparoscopic adrenalectomy was not inferior to open adrenalectomy with respect to safety and the anticancer effect,¹⁰ and it has proven itself as a minimally invasive treatment. Marangos et al¹⁴ performed a clinical analysis of laparoscopy in cases of adrenal metastasis and found that resection of solitary metastasis improved the prognosis, regardless of the primary disease.

To determine the types of cases that can be treated with laparoscopic adrenalectomy, the following criteria were proposed for the indication of laparoscopic adrenalectomy for the treatment of lung cancer patients with adrenal metastases: (1) the primary lung cancer could be

resected or cured by radical chemotherapy, (2) metastasis was restricted to the adrenal gland, (3) adrenal metastases had not invaded the surrounding organs based on imaging studies, and (4) the size of the adrenal tumor did not exceed 10 cm. By use of data obtained from our 10 patients and a literature search, the appropriateness of these criteria were examined. Porte et al¹⁵ proposed that in cases in which a primary tumor can be completely resected, patients with truly solitary adrenal metastasis can undergo resection with a good prognosis for long-term survival. In 9 of our 10 cases, laparoscopic adrenalectomy was successfully accomplished. However, in 1 case, adrenal adhesion to the liver was strong (patient 10), and a small amount of adrenal tumor capsule remained after resection. Laparoscopic adrenalectomy is usually performed by a transperitoneal approach, but the optimal approach in a situation such as this has not been reported in the literature. Martin Walz and his group in Essen, Germany, reported that there are various surgical approaches, which include the transperitoneal, lateral retroperitoneal, posterior retroperitoneal, and transthoracic approaches. Many surgeons prefer the transperitoneal approach because of the familiar operative field

and wider working space, but the posterior retroperitoneal approach has been shown to have several advantages over the other methods in terms of providing direct, rapid access to the adrenal gland without intruding into the intra-abdominal viscera.¹⁶

On the basis of our experience with 2 cases in which laparoscopic adrenalectomy was accomplished using a lateral retroperitoneal approach without any problems, we might consider using a lateral and posterior retroperitoneal approach because a transperitoneal approach could be difficult in patients with a history of carcinoma-tous abdominal surgery.

The histopathology of the case that was treated with open surgery was a pleomorphic carcinoma. Pleomorphic lung carcinoma is a primary lung cancer that was defined in 1999 by the World Health Organization histologic classification system (third edition).¹⁷ The early rate of recurrence and prevalence rate of distant metastasis after treatment (including operative treatment) are higher than in other NSCLCs. The 5-year survival rate is approximately 10%, and the prognosis is very poor.¹⁸ Therefore careful judgment is necessary when selecting a treatment modality. However, considering that a standard chemotherapy regimen has not been established and medical treatment cannot cure pleomorphic carcinoma, surgery is thought to be beneficial for local control.^{19,20} With consideration of these characteristics, laparoscopic adrenalectomy was performed for solitary adrenal metastasis of pleomorphic lung cancer. The adrenal gland was enlarged in 1 case of pleomorphic carcinoma, and pancreatic invasion was suspected on the basis of CT findings (patient 8). Because the tumor had invaded the pancreas, the procedure was changed to open surgery. However, in the other case of pleomorphic carcinoma (patient 9), CT showed no changes in the adrenal gland, although PET-CT indicated positive signs of adrenal gland metastasis. Therefore laparoscopic adrenalectomy was performed in this patient with no complications.

The aforementioned findings suggest that the third criterion is appropriate. Regarding the fourth criterion, Eto et al²¹ reported that laparoscopic adrenalectomy can be performed safely in patients with adrenal tumors 10 cm or smaller (including adrenal carcinomas), thus supporting the fourth criterion. The procedures used for diagnosis of adrenal metastasis are CT, magnetic resonance imaging (MRI), biopsy, and PET-CT. The sensitivity of biopsy was reported as 81%,²² which is low, and it is difficult for a biopsy to determine adrenal metastasis in cases in which CT or MRI does not show

adrenal swelling, as in 1 of our cases of pleomorphic carcinoma (patient 9). The sensitivity of PET-CT was reported as 96%,²³ which is high, and the false-positive detection rate for smaller masses is only 4%.²⁴ Thus positive PET-CT results for adrenal glands should be considered indicative of malignant change, even if swelling is not evident on CT or MRI. Thus, for our primary lung cancer patient with pleomorphic carcinoma, laparoscopic adrenalectomy should have been performed after positive PET-CT results were obtained, even though no notable swelling was noted on CT or MRI. In cases 3 and 7, because adrenal swelling was clearly detected, the attending physician did not think PET-CT was necessary. However, the possibility of extra-adrenal metastasis dictates that PET-CT should be performed.

Tanvetyanon et al²⁵ reported that for an isolated adrenal metastasis from NSCLC, patients with a synchronous metastasis who underwent adrenalectomy had a shorter median overall survival than those with a metachronous metastasis. However, durable long-term survival was achieved in approximately 25% in both groups.¹³ Furthermore, the results of adrenalectomy for solid tumor metastasis in 317 patients recruited from 30 European centers were reported by Moreno et al.²⁶ There was a difference in survival between metachronous and synchronous adrenal metastasis when the primary disease was renal cancer. However, there was no difference when the primary disease was NSCLC. In our study, in a short follow-up period, no difference in survival was seen between synchronous and metachronous metastasis.

With respect to the relation between the disease-free interval and long-term survival, Kim et al² studied clinical parameters that might predict long-term survival after resection of isolated adrenal metastasis. A disease-free interval of >6 months and complete resection were the only predictors of improved survival. In our study, patients with metachronous adrenal metastasis were not dead at least within the follow-up period.

In conclusion, we submit that laparoscopic adrenalectomy can be used when guided by the 4 criteria discussed in this study. Moreover, in cases of pleomorphic carcinoma, a positive PET-CT result should necessitate surgery, regardless of CT and MRI findings. In addition, sufficient discussion among the urologist, physician, and surgeon treating the primary lung cancer is required.

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